

MATERNAL DEPRESSION AND ANXIETY AND IMPACT ON
PHYSICAL, COGNITIVE AND EMOTIONAL DEVELOPMENT OF
CHILDREN AT THREE YEARS OF AGE

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ABSTRACT

Perinatal depression and anxiety are defined as depression or anxiety during pregnancy up to one year after birth. Along with the immediate health impacts and losses in productivity for the mother, perinatal depression and anxiety can have long-term detrimental effects on both the mother and child. Studying changes in measures of depression and anxiety through pregnancy, the postpartum period, and beyond can aid in identifying the most suitable time periods for implementation of screening and preventive programs. The primary goal of this study was to examine the course of depression and anxiety in women from early pregnancy to three years postpartum and to identify predictors of depression and anxiety scores across this period. The secondary goal was to examine the role of maternal mental health and high-risk behaviours, as well as other important socio-demographic factors, in physical, cognitive, personal-social, and emotional-behavioural development of three-year-old children.

Overall maternal depression and anxiety scores declined across the study time points. Pre-pregnancy maternal mental health was a significant predictor of both longitudinal depression and anxiety scores. Early postpartum stress and affective lability three years after birth were associated with higher longitudinal depression and anxiety scores in the study. Emotional support in all stages of pregnancy and after birth significantly and consistently lowered the average depression scores. Having a not very satisfactory relationship with the father of the child as compared to no relationship significantly increased the depression scores over the study time points. Lagged variable analysis suggested that previous depression scores were more important predictors of subsequent depression scores than previous anxiety scores. Furthermore, early pregnancy depression scores were significant predictors of both depression and anxiety scores.

Prenatal maternal mental health (depression, anxiety, stress) was not significantly associated with early childhood development in this study. However, several maternal mental

health measures reported after pregnancy were associated with the physical, cognitive, personal-social, emotional, and behavioural development of children at three years of age. Maternal high-risk behaviours (smoking, alcohol consumption, and drug use), independently and in association with maternal family history of perinatal depression, were associated with early childhood development.

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The ‘Feelings in Pregnancy and Motherhood’ (FIP) study is a Canadian Institutes of Health Research (CIHR #145179) and Saskatchewan Health Research Foundation (SHRF) funded, longitudinal study of Canadian women residing in Saskatoon, Saskatchewan. Mothers were recruited in the second trimester of pregnancy and followed up to five years after the birth of the baby. Mothers were screened for depression, anxiety, and mood problems twice during pregnancy, in the early postpartum period, and at three and five years after the birth of the index child (five data points). Their children were observed for physical, cognitive, personal-social development, emotional, and behavioural development at birth, at three and five years of age. Data were also collected on a wide range of determinants of maternal mental health for both the mother and their children. Dr. Angela Bowen and Dr. Nazeem Muhajarine were the principal investigators for the study.

The original analysis of the resulting data as described in this thesis was conducted by Kamalpreet under the supervision of her co-supervisors Dr. Cheryl Waldner and Dr. Angela Bowen in consultation with her PhD committee members. The research from the thesis was also presented in various national conferences in the form of oral and poster presentations. Kamalpreet also contributed to the larger project in preparation and dissemination of the study data for future research. She completed the data cleaning, transformation and summarization of the study variables prior to proceeding with the thesis. The data summary was disseminated among the research team to plan for future research projects. She was also responsible for preparation of data dictionary at the end of data collection process and communicating it with the team members as well as the cataloguing team for the Research Advancement through Cohort Cataloguing and Harmonization (ReACH) Initiative. The initiative hopes to provide web-based

access to Canadian pregnancy and birth cohort data and biological samples to enhance capacity and quality of collaborative research related to Developmental Origins of Health and Disease (DOHaD).

To my Mom for her love, care, support, and belief in me.

To my beloved husband Chiranjeev and our two gems Sahaib and Ravjit.

TABLE OF CONTENTS

CHAPTER 1: PERINATAL DEPRESSION AND ANXIETY	1
1.1 Introduction.....	2
1.2 Perinatal depression	3
1.3 Perinatal anxiety.....	5
1.4 The association between maternal anxiety and depression.....	6
1.5 Economic costs of perinatal depression and anxiety	7
1.6 Time course and trajectory for depression and anxiety	9
1.7 Effects of depression and anxiety on the mother	9
1.8 Physiological consequences in children of in utero exposure to depression and anxiety	11
1.9 Effects on depression and anxiety on early childhood development	12
1.10 Risk factors for prenatal depression and anxiety	15
1.11 Study rationale and context.....	17
1.12 Data source and study settings	17
1.13 Goals and objectives of the study	18
1.14 References.....	22
1.15 Appendices.....	37
1.15.1 Appendix 1-A – Ethics Approval.....	37
CHAPTER 2: DESCRIPTIVE SUMMARY OF FEELINGS IN PREGNANCY & MOTHERHOOD STUDY DATA	42
2.1 Introduction.....	43
2.2 Methods.....	44
2.3 Results.....	46
2.3.1 Profile of the participants at enrollment.....	47
2.3.2 Comparison of mothers who were lost to follow-up as compared to those who participated in fourth round of data collection.....	49
2.3.3 Missing data patterns	51
2.3.4 Checking for Missing at Random (MAR).....	53
2.4 Discussion	56
2.4.1 Mechanisms of missing data	56
2.4.2 Methods to deal with missing outcome and covariate data.....	57
2.4.3 Implications for thesis research.....	58

2.5 Conclusions.....	59
2.6 References.....	61
CHAPTER 3: DIMENSIONS UNDERLYING THE CBCL AND PATTERN OF ITEM-FACTOR RELATIONSHIP OF CBCL/1.5 – 5 YEARS OBSERVED AMONG CANADIAN-THREE-YEAR OLDS.....	64
3.1 Introduction.....	66
3.2 Methods.....	68
3.2.1 Study sample	68
3.2.2 CBCL data collection tool.....	69
3.2.3 CBCL item structure	70
3.3 Missing data	71
3.4 Multivariate normality	71
3.5 Estimation methods.....	72
3.6 Empty cells.....	72
3.7 Model structure tested.....	73
3.8 Assessing model fit	74
3.9 Model output and reliability measures.....	76
3.10 Results.....	79
3.10.1 Step 1: Item factor analysis of individual behavioural syndromes	79
3.10.1.1 Emotionally reactive	80
3.10.1.2 Anxious/depressed behaviour	81
3.10.1.3 Somatic problems.....	82
3.10.1.4 Withdrawn behaviour.....	83
3.10.1.5 Sleep problems	84
3.10.1.6 Aggressive behaviour.....	85
3.10.1.7 Attention problems.....	86
3.10.2 Step 2: First-order correlated model	87
3.10.3 Step 3: Second-order correlated model.....	89
3.11 Discussion	91
3.12 References	94
3.13 Appendices.....	99

3.13.1 Appendix 3-A: Detailed description of the polychoric correlation method used with WLSMV estimator in Mplus.....	99
3.13.2 Appendix 3-B- Detailed description of item response theory-based model parameters and methods used to compute them	100
3.13.3 Appendix 3-C: Tables	103
3.13.3.1 Table 1: Model fit parameters for individual syndromes in the CBCL model as well as for the first-order and second-order model structure for the syndromes retained by IFA (N = 343).	103
3.13.3.2 Table 2: Standardized model estimates (factor loadings), their level of significance, coefficient of determination and the residual variance for the all the items retained in the final models for each of the individual syndromes of emotionally reactive, anxiety, somatic problems, withdrawn behaviour, sleep problems, aggressive behaviour and attention problems (N = 343).....	104
3.13.3.3 Table 3: Standardized model estimates (factor loadings) for the final correlated first-order model with anxious, sleep problems, withdrawn behaviour, aggressive behaviour, and attention problems (N=343).	106
3.13.3.4 Table 4: Standardized model estimates (factor loadings) for the final second-order model with anxious, sleep problems, and withdrawn behaviour loading on internal and aggressive behaviour and attention problems loading on externalizing behaviour (N=343)....	108
3.13.4 Appendix 3-D: Figures.....	110
3.13.4.1 Figure 1: First-order correlated model structure using five syndrome scales of withdrawn, sleep problems, anxious, attention problems and aggressive behaviours.	110
3.13.4.2 Figure 2: Second-order correlated model structure for Child Behavioural Check List 1/5-5 years.....	111
3.13.4.3 Figure 3: Plots showing the item difficulty parameters computed from the unstandardized thresholds from the model output as well as the probability of success ($\text{Pr}(Y=1)$ in giving a correct response when factor mean (theta) is zero.....	112
3.13.4.4 Figure 4: Test information curves for anxious, sleep problems, and withdrawn behaviour loading on the internalizing behaviour.....	113

CHAPTER 4: TIME COURSE AND FACTORS ASSOCIATED WITH MATERNAL DEPRESSION AND ANXIETY – FROM PREGNANCY TO THREE YEARS

POSTPARTUM.....	115
4.1 Introduction.....	117
4.2 Methods.....	118
4.2.1 Time course of data collection.....	118
4.2.2 Measures of depression and anxiety	119
4.2.3 Independent variables	120
4.2.4 Model building strategy	122
4.2.5 Selection of the methods of estimation	123
4.2.6 Unconditional analysis and model building.....	123
4.2.7 Lagged variable models	124
4.3 Results.....	125
4.3.1 Descriptive statistics for depression and anxiety	126
4.3.2 Factors associated with depression (EPDS) scores from early pregnancy (T1) to three years postpartum (T4).....	128
4.3.3 Prediction of current depression scores by previous depression scores.....	134
4.3.4 Prediction of current depression scores by previous anxiety scores	135
4.3.5 Prediction of current depression scores by simultaneous evaluation of both previous depression and anxiety scores	136
4.3.6 Factors associated with anxiety scores from early pregnancy to three years postpartum...	136
4.3.7 Prediction of current anxiety scores using previous anxiety scores.....	142
4.3.8 Prediction of current anxiety scores using previous depression scores	143
4.3.9 Prediction of current anxiety scores by simultaneous evaluation of both previous anxiety and depression scores	144
4.4 Discussion	144
4.5 References.....	151
4.6 Appendices.....	156
4.6.1 Appendix 4-A: Table of results from the unconditional or bivariate analysis of depression....	156
4.6.2 Appendix 4-B: Table of results from the unconditional or bivariate analysis of anxiety ...	158

CHAPTER 5: PREDICTORS OF BETTER PHYSICAL, COGNITIVE, PERSONAL - SOCIAL DEVELOPMENT OF CHILDREN AT THREE YEARS OF AGE – WHY SOME KIDS FAIR BETTER THAN OTHERS	160
5.1 Introduction.....	162
5.2 Methods.....	164
5.2.1 Child measures	165
5.2.1.1 Ages and Stages Questionnaire (ASQ3®)	165
5.2.1.2 Other child measures.....	167
5.2.1.3 Maternal measures	167
5.2.1.4 Model building strategy	169
5.3 Results.....	172
5.3.1 Communication skills	174
5.3.2 Gross motor skills	174
5.3.3 Fine motor skills.....	175
5.3.4 Problem-solving skills.....	176
5.3.5 Personal-social skills.....	178
5.3.6 Summary	181
5.4 Discussion	182
5.5 Limitations	187
5.6 Conclusions.....	187
5.7 References.....	189
5.8 Appendices.....	196
5.8.1 Appendix 5-A: Table 1 of unadjusted analysis for communication skills	196
5.8.2 Appendix 5-A: Table 2 of unadjusted analysis for gross motor skills	199
5.8.3 Appendix 5-A: Table 3 of unadjusted analysis for fine motor skills	202
5.8.4 Appendix 5-A: Table 4 of unadjusted analysis for problem-solving skills.....	205
5.8.5 Appendix 5-A: Table 5 of unadjusted analysis for personal-social skills.....	208
5.8.6 Appendix 5-B – Table 1: Descriptive summary of the influential data points that were removed from the multivariable analysis of problem-solving skills.....	211
5.8.7 Appendix 5-B - Table 2: Descriptive summary of the influential data points that were removed from the multivariable analysis of personal-social skills	212

CHAPTER 6: UNDERSTANDING THE EFFECTS OF MATERNAL HIGH-RISK BEHAVIOURS AND MATERNAL MENTAL HEALTH ON EARLY CHILDHOOD EMOTIONAL AND BEHAVIOURAL DEVELOPMENT – IS THERE A TIME SENSITIVE OR A MEDIATING EFFECT	213
6.1 Introduction.....	216
6.2 Methods.....	218
6.2.1 Dependent variables.....	219
6.2.2 Independent variables	220
6.2.3 Maternal mental health factors.....	220
6.2.4 Maternal high-risk behavioural factors	221
6.2.5 Maternal socio-demographic factors.....	221
6.2.6 Natal and child-related factors	222
6.2.7 Statistical model building strategy	223
6.3 Results.....	226
6.3.1 Aggressive behaviour at three years	228
6.3.2 Attention problems at three years	230
6.3.3 Anxiety/depression at three years	231
6.3.4 Sleep problems at three years.....	234
6.3.5 Withdrawn behaviour at three years	237
6.3.6 Summary	238
6.4 Discussion	239
6.5 Limitations	246
6.6 Conclusions	247
6.7 References.....	248
6.8 Appendices.....	257
6.8.1 Appendix 6-A – Table1: Unadjusted analysis of high scores for aggression behaviours ($\geq 93^{\text{rd}}$ percentile).	257
6.8.2 Appendix 6-A – Table 2: Unadjusted analysis of high scores for attention problems ($\geq 93^{\text{rd}}$ percentile).	260
6.8.3 Appendix 6-A – Table 3: Unadjusted analysis of high scores for anxious/depressed behaviour ($\geq 93^{\text{rd}}$ percentile).	263

6.8.4 Appendix 6-A – Table 4: Unadjusted analysis of high scores for sleep problems ($\geq 93^{\text{rd}}$ percentile).....	266
6.8.5 Appendix 6-A – Table 5: Odds ratios, p-values and 95% confidence limits for the predictors (with proportional odds assumption was not true) of children with high scores for sleep problems ($\geq 93^{\text{rd}}$ percentile) at three years of age.....	269
6.8.6 Appendix 6-A – Table 6: Unadjusted analysis of high scores for withdrawn behaviour ($\geq 93^{\text{rd}}$ percentile).....	270
CHAPTER 7: CONCLUSION AND POLICY IMPLICATIONS	273
7.1 Overview of thesis objectives	274
7.2 Maternal depression and anxiety.....	274
7.3 Early childhood development	277
7.3.1 Physical, cognitive, and personal-social development of the children	277
7.3.2 Emotional and behavioural development of children at three years of age	280
7.4 Summary of the long-term implications of maternal depression and anxiety	283
7.5 Contributions of this research and suggestions for future work	285
7.6 Limitations of the research.....	288
7.7 Policy implications for maternal and child health	292
7.8 References.....	296

LIST OF TABLES

Table 2-1: Description of the Feelings in Pregnancy study participants at the time of enrollment (N=648).....	47
Table 2-2: Comparison summary of the average depression and anxiety scores for the women who were lost to follow up before the fourth round of data collection as compared to those who completed the fourth round of data collection.	49
Table 2-3: Comparison of mothers who were lost to follow-up and those who participated in the fourth round of data collection.....	50
Table 2-4: Missing data patterns for depression and anxiety scores over the four years from T1 (early pregnancy) to T4 (three years after birth).....	52
Table 2-5: Summary of the association between risk factor information collected during the study and missing depression and anxiety outcomes variables (n=648).	53
Table 3-1: Mean (standard deviation), median (interquartile range) and range ^a of the observed first-order and second-order latent variables and maximum scores possible based on the original scale (Achenbach & Rescorla, 2000).....	80
Table 3-2: Estimated correlation matrix for the six first-order latent variables of aggressive behaviour, attention problems, emotionally reactive, anxious, sleep problems, and withdrawn behaviour from the first-order correlated model structure.....	88
Table 3-3: Estimated correlation matrix for the five remaining first-order latent variables of aggressive behaviour, attention problems, anxious, sleep problems, and withdrawn behaviour. 89	89
Table 3-4: Estimated correlation matrix for the first-order and second-order latent variables	90
Table 4-1: Summary of the covariates considered in model building, data type, and coding, and periods during which each variable was available for analysis.	121
Table 4-2: Summary of the lagged variables available for analysis for each time point assessed in the models using linear regression.	124
Table 4-3: Summary of the depression and anxiety scores for study participants (N=333).....	126
Table 4-4: Estimated difference in depression measured as EPDS scores from early pregnancy (T1) to three years after birth (T4) associated with factors retained in the final multivariable model that did not contribute to an interaction term.....	128
Table 4-5: Estimated pairwise differences in depression measured as EPDS scores from T1 to T4 time points associated with interaction effects between the history of depression and study time points in the final multivariable model.	131
Table 4-6: Estimated pairwise differences in depression measured as EPDS scores from early pregnancy to three years postpartum associated with interaction effects between the history of depression and stress at T1 in the final multivariable model.....	132
Table 4-7: The association between previous depression and anxiety scores (lagged variables) and subsequent measures of depression measured as predicted change in EPDS scores for every unit increase in lagged variable with 95%CI.	135

Table 4-8: Estimated difference in anxiety scores from early pregnancy to three years postpartum associated with factors retained in the final multivariable model that did not contribute to an interaction term.....	137
Table 4-9: Estimated pairwise differences in anxiety measured as EPDS-3A scores from early pregnancy to three years postpartum associated with interaction effects between history of depression and study time points in the final multivariable model.....	138
Table 4-10: Estimated pairwise differences in anxiety measured as EPDS-3A scores from early pregnancy to three years postpartum associated with interaction effects between history of depression and stress at T1 in the final multivariable model.....	141
Table 4-11: The association between previous depression and anxiety scores (lagged variables) and subsequent anxiety scores measured as predicted change in EPDS-3A scores for every unit increase in the lagged variable with 95%CI.....	143
Table 5-1: Summary of distribution of children in the study population based on the categorization of data above the cut-off point for communication, gross motor, fine motor, problem-solving and personal-social skills used for model building.....	166
Table 5-2: Estimated odds ratio, p-value, and 95% confidence intervals for significant predictors of high communication skills (top third of normal ASQ3® scores) in the final multivariable model based on ordinal regression (n=313).....	174
Table 5-3: Estimated odds ratio, p-value, and 95% CI of significant predictors of high gross motor skills (top third of normal ASQ3® scores) in the final multivariable model based on ordinal regression (n=333).....	175
Table 5-4: Estimated odds ratio, p-value, and 95% CI of significant predictors and confounders of high fine motor skills (top third of normal ASQ3® scores) in the final multivariable model based on ordinal regression (n=338).....	176
Table 5-5: Estimated odds ratio, p-value, and 95% CI of significant predictors of high problem-solving skills (top third of normal ASQ3® scores) in the final multivariable model based on ordinal regression (n=322).....	177
Table 5-6: Estimated odds ratio, p-value, and 95% CI of significant predictors of high personal-social skills (top third of normal ASQ3® scores) in the final multivariable model based on ordinal regression (n=322).....	179
Table 5-7: Estimated odds ratio, p-value, and 95% CI of two-way comparison of the interaction effects of early pregnancy (T1) smoking and sex of the child in the model for high personal-social skills (top third of normal ASQ3® scores).....	180
Table 5-8: Summary of the significant predictors, interactions, confounders, and mediators of high ASQ scores from the final multivariable models.....	182
Table 6-1: Mean (standard deviation), median (interquartile range), and range of the re-specified transformed CBCL (1.5 – 5 year) in the study population (N=343).....	227
Table 6-2: Distribution of re-specified transformed CBCL (1.5 – 5 year) in the study population for regression analysis (N=343).....	228

Table 6-3: Odds ratios, 95% confidence limits and p-values for the significant predictors of high aggressive behaviour scores (≥ 93 rd percentile or $\geq 13/21$) among children at three years of age (N=336).....	230
Table 6-4: Odds ratios, 95% confidence limits, and p-values for the significant predictors of high scores for attention problems (≥ 93 rd percentile or $\geq 5/8$) among children at three years of age (n=342).....	231
Table 6-5: Odds ratios, 95% confidence limits, and p-values for the significant predictors of high anxious/depressed scores (≥ 93 rd percentile or $\geq 4/7$) among children at three years of age (n=337).....	232
Table 6-6: Odds ratios, 95% confidence limits, and p-values for the pairwise comparisons of interaction effects of early postpartum (T3) alcohol consumption and family history of perinatal depression in predicting high anxious/depressed scores (≥ 93 rd percentile or $\geq 4/7$) among children at three years of age (n=337).	234
Table 6-7: Odds ratios, p-values and 95% confidence limits for the predictors (proportional odds assumption true) and confounders of high scores for sleep problems (≥ 93 rd percentile or $\geq 4/7$) among children at three years of age (n=333).	236
Table 6-8: Odds ratios, p-values and 95% confidence limits for the predictors (where the proportional odds assumption did not apply) of children above the 93rd percentile for sleep problem scores ($\geq 4/7$) as compared to children below the 93rd percentile (n=333).	236
Table 6-9: Odds ratios, 95% confidence limits, and p-values for the significant predictors and confounders of high scores for withdrawn behaviour (≥ 93 rd percentile or $\geq 3/4$) at three years of age (n=343).	237
Table 6-10: Significant predictors, confounders, and moderators of emotional and behavioural development of children at three years of age measured by high scores ($\geq 93^{\text{rd}}$ percentile) from a re-specified Child Behaviour Checklist 1.5–5 (CBCL).....	239

LIST OF FIGURES

Figure 3-1: Item distribution and structure of the seven first-order latent variables and two second-order latent variables of CBCL 1.5 – 5 years as described by the developers (Achenbach & Rescorla, 2000)	71
Figure 3-2: First-order individual syndrome scales after the removing highly kurtotic items that were used to test individual model fit.....	73
Figure 3-3: Sample Item Characteristic Curve (ICC) for item (Can't sit still) loading on the attention deficit subscale indicating good discrimination (shape and slope) properties and item with relatively high difficulty as the item span between -1 and +3 on the trait scale.....	78
Figure 3-4: Summary of item standardized factor loadings (standard error) and item correlations (standard error) for the emotionally reactive latent variable. ‘emot’ represents the latent variable emotionally reactive. Unidirectional arrows represent the factor loadings of items on the latent variable, and bi-directional arrows represent the correlations amongst the items.....	81
Figure 3-5: Summary of item standardized factor loadings (standard error) and item correlations (standard error) for the anxious/depressed latent variable. ‘anxi’ represents the latent variable anxious/depressed and unidirectional arrows represent the factor loadings of items on the latent variable.....	82
Figure 3-6: Summary of item standardized factor loadings (standard error) and item correlations (standard error) for the somatic problems latent variable. ‘somat’ represents the latent variable somatic problems and unidirectional arrows represent the factor loadings of items on the latent variable.....	83
Figure 3-7: Summary of item standardized factor loadings (standard error) and item correlations (standard error) for the withdrawn behaviour latent variable. ‘withdra’ represents latent variable withdrawn behaviour and unidirectional arrows represent the factor loadings of items on the latent variable.....	84
Figure 3-8: Summary of item standardized factor loadings (standard error) and item correlations (standard error) for the sleep problem latent variable. ‘sleep’ represents the latent variable sleep problems. Unidirectional arrows represent the factor loadings of the items on the latent variable, and bidirectional arrow represents correlations between the items.	85
Figure 3-9: Summary of item standardized factor loadings (standard error) and item correlations (standard error) for the aggressive behaviour latent variable. ‘aggre’ represents the latent variable aggression. Unidirectional arrows represent the factor loadings of the items on the latent variable, and bidirectional arrows represent the correlation between items.....	86
Figure 3-10: Summary of item standardized factor loadings (standard error) and item correlations (standard error) for the attention problem latent variable. ‘atten’ represents the latent variable attention problems, and unidirectional arrows represent the factor loadings of items on the latent variable.....	87
Figure 4-1: Flow chart summarizing the number of mothers screened positive for depression and their status during subsequent time points. Mothers who were screened positive for the first time at later time points were labelled as a new (N) case at that time point.....	126

Figure 4-2: Flow chart summarizing the number of mothers screened positive for anxiety and their status during the subsequent time points. Mothers who were screened positive for the first time at later time points were labelled as a new (N) case at that time point.....	127
Figure 4-3: Plot of interaction effects of reported history of depression and study time points on average predicted EPDS scores.	130
Figure 4-4: Plots of interaction effects of reported history of depression and stress at T1 on average predicted EPDS scores. The difference in EPDS scores based on a history of depression is reported for women with and without stress at early pregnancy (T1) (4a) and based on stress in early pregnancy (T1) for women with and without a history of depression (4b).	133
Figure 4-5: Plot of marginal mean predicted EPDS scores with 95% CI for each study time point from early pregnancy (T1) to three years after birth (T4).	134
Figure 4-6: Plot of interaction effects of reported history of depression and study time points on average predicted anxiety scores	139
Figure 4-7: Plot of interaction effects of reported history of depression and stress at T1 on average predicted anxiety scores. The difference in anxiety scores based on history of depression is reported for women with and without stress at T1 (7a) and based on stress at T1 for women with and without history of depression (7b).	140
Figure 4-8: Plot of marginal mean predicted anxiety scores with 95% CI for each study time point from early pregnancy (T1) to three years postpartum (T4).	142
Figure 5-1: Margins plot of predicted probability of high problem-solving skills (top third of normal ASQ3® scores) based on the period of birth order of the baby (n=322).	178
Figure 5-2: Predicted probability of high personal-social skills (top third of normal ASQ3® scores) based on the interaction effects of sex of the child and early pregnancy smoking based on the final multivariable ordinal regression (n=322).	181
Figure 6-1: Predicted probability of high anxiety/depression scores ($\geq 4/7$ or at or above the 93 rd percentile) based on the interaction effects of alcohol consumption in early postpartum (T3) period and family history of perinatal depression (n=337).....	233
Figure 7-1: Predictors of depression and anxiety from early pregnancy to three years after childbirth. Arrows represent time points that significantly predict subsequent depression or anxiety scores. T1 – Early pregnancy, T2 – Late pregnancy, T3 – Early postpartum, T4 – Three years after childbirth. ALS – Affective lability scores measuring mood disorders in the mothers.	275
Figure 7-2: Predictors of physical, cognitive, and personal – social skills of children at three years of age. Orange represents the mediation effects in the model, green represents interaction effects, blue represents the confounders, and black represents significant predictors.....	279
Figure 7-3: Predictors of emotional and behavioural development of children at three years of age. Green represents interaction effects, blue represents the confounders, and black represents significant predictors.....	282
Figure 7-4: Representation of the focus of screening and support programs recommended to prevent the development of chronic depression and anxiety and reduce developmental delays in the children at three years of age.	293

LIST OF ABBREVIATIONS

AGA	Appropriate for Gestational Age
ALS	Affective Liability Scores
APGAR	Appearance, Pulse, Grimace, Activity, Respiration
ASQ	Ages and Stages Questionnaire
CBCL	Child Behaviour Checklist
CFA	Confirmatory Factor Analysis
CFI	Comparative Fit Index
DALY	Disability Adjusted Life Years
EPDS	Edinburgh Postnatal Depression Scale
FIP	Feelings in Pregnancy & Motherhood
IC	Information Curve
ICC	Item Characteristic Curve
IFA	Item Factor Analysis
IQR	Inter Quartile Range
LGA	Large for Gestational Age
LR	Likelihood Ratio
MAR	Missing at Random
MCAR	Missing Completely at Random
MI	Multiple Imputation
ML	Maximum Likelihood
MNAR	Missing Not at Random
OECD	Organization for Economic Cooperation and Development
OR	Odds Ratio
PHAC	Public Health Agency of Canada
PND	Perinatal Depression
PPD	Postpartum Depression
R ²	Coefficient of Determination

RMSEA	Root Mean Square Error of Approximation
SD	Standard Deviation
SGA	Small for Gestational Age
T1	Early Pregnancy
T2	Late Pregnancy
T3	Early Postpartum
T4	Three Years After Birth
TLI	Tucker Lewis Index
VPC	Variance Partition Component
WHO	World Health Organization
WLSMV	Robust Weighted Least Square Estimator
WRMR	Weighted Root Mean Square Residuals
YLD	Years Lived with Disability
χ^2	Chi-square
95% CI	95% Confidence Limits

CHAPTER 1: PERINATAL DEPRESSION AND ANXIETY

1.1 Introduction

Mental health disorders, including depression and anxiety, are an important cause of disability and lost productivity both in Canada and across the globe. Globally, mental health and substance use disorders were responsible for 6.6% of all ‘disability adjusted life years’ (DALYs) ([WHO, 2017b](#)) in 2015, with depressive disorders contributing 2.2% and anxiety disorders contributing 1.0% of the global DALYs ([Kassebaum et al., 2016](#)). One DALY corresponds to ‘one lost year of healthy life’ ([WHO, 2017b](#)). Mental health, neurological, and substance use disorders alone were responsible for an estimated loss of US \$2.5 – \$8.5 trillion worldwide in 2010 ([Bloom et al., 2012](#)).

When compared to other physical disorders, mental health problems rank very high both in terms of time impacted by illness and the proportion of the population affected. Depression is the third leading contributor to the ‘years lived with disability (YLD)’ ([WHO, 2017b](#)) among all ages and sexes ([Vos et al., 2016](#)) and anxiety is the ninth leading contributor. In Canada in 2015, the prevalence of depressive disorders was estimated to be 4.7% which corresponds to 6.9% of the total YLD, and the prevalence of anxiety disorders was estimated to be 4.9% corresponding to 4.0% of the total YLD ([WHO, 2017a](#)). In Canada, approximately 3.5 million people were diagnosed with mood or anxiety disorders in 2009 – 2010 ([PHAC, 2016](#)).

Women appear to be disproportionately impacted by depression and anxiety. In 2015, the global prevalence of depression was estimated to be 4.4% with a higher prevalence in women (5.1%) as compared to men (3.6%) ([WHO, 2017a](#)). Similarly, the global prevalence of anxiety disorders was estimated to be 3.6% with a higher prevalence in women (4.6%) than in men (2.6%) ([WHO, 2017a](#)). Two critical areas of focus in mental health research for women are perinatal depression and anxiety, not only because of the effects on the wellbeing of the mother

at a very significant time in her life, but also due to the potential consequences in her developing child.

1.2 Perinatal depression

Perinatal depression is defined as depression during pregnancy and up to one year after birth ([BCRMHP, 2006](#); [Seth et al., 2016](#)). Mental health problems during the perinatal period, primarily depression and anxiety, are ubiquitous in both high- and low-income countries ([Prince et al., 2007](#); [Rahman et al., 2013](#)). A meta-analysis completed in 2005 reported the global prevalence of major/minor depression to range between 8.5% to 11.0% during pregnancy and 6.5% to 12.9% during the postpartum year ([Gaynes et al., 2005](#)). A cohort study from the United Kingdom of mothers who delivered between April 1991 and December 1992 reported that 13.5% of the women were screened positive for depression in late pregnancy (32 weeks) as compared to 9.1 % in the early postpartum period (8 weeks) ([Evans et al., 2001](#)). Similarly, a cohort study from Italy among mothers recruited between February 2004 and March 2007 reported a weighted period prevalence for depression of 12.4% (95% CI 10.2 – 14.6) during pregnancy and 9.6% (95% CI 7.0- 12.2) during the postpartum year ([Banti et al., 2011](#)).

The numbers from Canada are consistent with the global picture for maternal mental health. The Public Health Agency of Canada (PHAC) reported that at any point approximately 10% women in Canada would be screened positive for depression during pregnancy ([PHAC, 2012](#)). The Canadian Maternity Experience Survey (CMES) reported a prevalence of 7.5% for major depression during the postpartum period, with depression defined as Edinburgh Postnatal Depression Scale (EPDS) ([Cox et al., 1987](#)) scores ≥ 13 ([PHAC, 2009](#)). A more recent longitudinal cohort study from Canada reported comparable prevalences for depression of 14.1% in early pregnancy, 10.4% in late pregnancy and 8.1% at four weeks after birth ([Bowen et al.,](#)

[2012](#)). Thus, recent research suggests that prenatal depression appears to be more prevalent than postpartum depression, especially in high-income countries.

The symptoms of the first and last trimester of pregnancy and those of depression (for example feeling tired, mood swings, irritability, changes in appetite, sleeping problems) overlap to a large extent, thus making screening and diagnosis of depression confusing and difficult ([Kelly et al., 2001](#); [PHAC, 2012](#)). Similarly, the stereotypical image of pregnancy as ‘one of the happiest times of a woman’s life’ and the myth that pregnancy protects against the development of depression also discourage women from seeking help ([Blier, 2006](#); [PHAC, 2012](#)). Thematic analysis from qualitative studies of women suffering from depression report fear, shame, and feelings of being a bad mother ([Beck, 1993](#)), decreasing the likelihood that these mothers will seek treatment ([Dennis et al., 2004](#); [Dennis & Ross, 2006](#)). These feelings of shame and fear can seriously impact the mother-child relationship and parenting behaviours ([Pinto-Foltz & Logsdon, 2008](#)).

The WHO has suggested universal screening of mothers for mood disorders during the postpartum period, but there has been no specific directive for screening during pregnancy ([WHO, 2013](#)). Provincial guidelines from British Columbia recommend that mothers should be screened at least twice for depression; first time during the third trimester (between 28 – 32 weeks of pregnancy) and the second time immediately after childbirth ([BCRMHP, 2006](#)). The ‘MotherFirst’ strategy from Saskatchewan recommends perinatal screening for both depression and anxiety starting at 28 - 34 weeks of pregnancy, followed by in hospital screen during birth, then 2 - 3 weeks after birth and, subsequently when mothers come in contact with the health services during the immunization of their infants ([Bruce et al., 2012](#)). Mothers who screen positive for anxiety or depression should be offered appropriate treatment. However, the

guidelines and recommendations for follow-up screening with home visits or by telephone and suggestions on who should be engaged to provide these services are not consistent across Canada ([Dennis, 2010](#); [Glauser et al., 2016](#); [Letourneau et al., 2011](#)).

1.3 Perinatal anxiety

Perinatal anxiety is defined as anxiety during pregnancy and up to one year after birth ([Leach et al., 2015](#)). Similar to depression, anxiety disorders are also twice as likely to be diagnosed in women as compared to men ([Kessler et al., 1994](#); [Somers et al., 2006](#); [Wittchen, 2002](#)). Perinatal anxiety may include generalized anxiety disorder, panic disorder, phobias, obsessive compulsive disorder, and postpartum post-traumatic stress disorder; symptoms may include hyperventilation, excessive worry, restlessness, and sleeplessness ([Anniverno et al., 2013](#)).

The global prevalence of maternal perinatal anxiety between 2006 and 2014 was reported to range between 2.6% to 39% during pregnancy and 3.7% to 20% in the postpartum period in a systematic review of research indexed on PubMed, PsycInfo, and Web of Science ([Leach et al., 2015](#)). A study of a large community sample in England (N=8,323) reported a prevalence of 21% of clinically significant anxiety symptoms during early pregnancy among a cohort of mothers that were recruited between April 1991 and December 1992 ([Heron et al., 2004](#)). Only 64% of those screened positive during pregnancy, also screened positive at eight weeks postpartum ([Heron et al., 2004](#)). Although the information available regarding the prevalence of anxiety in pregnancy in Canada is limited, the percentage of the women affected by anxiety disorders in any given year in Canada has been estimated to be about 16% in 2002 ([Bowen et al., 2008](#); [PHAC, 2002](#)).

Thus, like depression, the prevalence of anxiety appears to be higher during pregnancy than in the postpartum period and might be higher than the prevalence of depression during pregnancy ([Goodman & Tyer-Viola, 2010](#); [Heron et al., 2004](#); [Lee et al., 2007](#)). In Canada, only two provinces of British Columbia and Saskatchewan have proposed guidelines to screen mothers for perinatal anxiety ([BCRMHP, 2006](#); [Bruce et al., 2012](#)). Despite the higher prevalence and similar impact of perinatal anxiety on pregnancy and fetal outcomes as compared to perinatal depression, there appears to be no national or universal consensus regarding screening, prevention, and treatment of perinatal anxiety disorders.

1.4 The association between maternal anxiety and depression

Several studies report medium to large correlations between anxiety and depressive symptoms during pregnancy ([Biaggi et al., 2016](#); [Lancaster et al., 2010](#); [Sutter-Dally et al., 2004](#)). The National Comorbidity Survey from the United States reported that depression and anxiety are highly comorbid, with almost 60% of individuals with major depression also meeting the criteria for an anxiety disorder ([Kessler et al., 2003](#)). Another more recent study from the United States including 4451 mothers in the Pregnancy Risk Assessment Monitoring System (PRAMS) reported comorbidity of 6.3% (95% C.I. 5.4 – 7.3) ([Farr et al., 2014](#)). Of the 18% screened positive for anxiety, 35% also screened positive for depression ([Farr et al., 2014](#)). One Canadian study from British Columbia reported comorbidity of 13.1% for postnatal depression and anxiety among a sample of 667 women. ([Falah-Hassani et al., 2016](#)).

Empirically it is difficult to discriminate between the constructs of anxiety and depression ([Watson et al., 1988](#)). Cognitive models state that perception of threat and harm is central for both anxiety and depression and that anxiety is in response to future threat; whereas, depression is the response to imminent or past event ([Beck, 1979](#); [Dobson, 1985](#)). Emotional models of

anxiety and depression also complement the cognitive models ([Dobson, 1985](#)). Shared genetic aetiologies have also been proposed as one of the reasons for comorbidity of anxiety and depression ([Hettema, 2008](#)).

Comorbidity has been found to be associated with higher rates of smoking, drinking, and being stressed both in the prenatal and postnatal period ([Farr et al., 2014](#)). However, it is not yet understood whether this comorbid state is associated with more severe symptoms as compared to the occurrence of either depression or anxiety. Prenatal anxiety is also considered a strong to moderate predictor of subsequent depression following childbirth ([Hayworth et al., 1980](#); [Johnstone et al., 2001](#); [Neter et al., 1995](#); [Watson et al., 1984](#)).

1.5 Economic costs of perinatal depression and anxiety

Perinatal depression and anxiety result in lost productivity in addition to direct costs to the health care system. A study from Minnesota reported that for both men and women, the severity of symptoms monotonically increased the loss of productivity by 1.6% for every one unit increase in the depression scores ([Beck et al., 2011](#)). Further, the loss of productivity was higher among full-time employees as compared to part-time employees ([Beck et al., 2011](#)).

Similar losses were seen when assessing the impact of perinatal mental health in Australia, the United Kingdom, and the United States. An Australian study found that approximately 100,000 new parents will be affected by perinatal depression at an economic cost of AUS \$433.52 million (CAN \$440.32 million) per year ([PANDA, 2012](#)). The greatest costs were attributed to losses in productivity in the workplace. Similarly, a study from the United Kingdom reported perinatal mental health problems cost £8.1 billion (CAN \$13.3 billion) annually ([Bauer et al., 2014](#)). Lifetime estimated costs of perinatal depression and perinatal anxiety per woman were £75,728 (CAN \$ 124,150) and £34,811 (CAN \$ 57,070) respectively

([Bauer et al., 2014](#)). Approximately three-quarters of the costs in this study were attributed to impacts on the affected children ([Bauer et al., 2014](#)).

Depression among working mothers in the United States is reported to cost US \$44 billion per year in lost productivity and US \$12.4 billion in health care expenditures ([Dagher et al., 2012](#)). The same study reported that mothers with postpartum depression have 90% higher health care costs, and were four times more likely to visit the emergency room as compared to non-depressed mothers ([Dagher et al., 2012](#)). Chisholm et al. ([2016](#)) reported the estimated direct cost for treatment of depression and anxiety over the next fifteen years (2016 – 2030) in the United States would be US \$147 billion.

While there appears to be no information regarding the specific economic costs of perinatal depression available for Canada, the Conference Board of Canada's (CBC) Alliance for Sustainable Health Care estimated that depression and anxiety cost about \$50 billion annually ([CBC, 2016](#)). A history of depression and anxiety are important risk factors for mood disorders during pregnancy with 68% of the women reported to relapse during pregnancy after discontinuing the treatment before pregnancy ([Cohen et al., 2006](#)). In Ontario, Canada the cost for 2,953 women who discontinued their antidepressant therapy before pregnancy was estimated to be CAN \$20,456,982 annually for ensuing medical care for the women and their infants ([O'Brien et al., 2009](#)). Another study from Ontario concluded that the average health and social services cost per woman who gave birth was twice as high for mothers diagnosed with clinical depression and that increasing depression scores were strongly associated with nursing care costs ([Roberts et al., 2001](#)).

1.6 Time course and trajectory for depression and anxiety

Studying the course of depression and anxiety through pregnancy and the postpartum period and beyond can aid in identifying the most suitable time period or periods for implementation of screening and preventive strategies to mitigate the potential effects on children. Across the globe, a few studies have examined the persistence of symptoms of postpartum depression beyond the first postpartum year ([Beeghly et al., 2002](#); [Evans et al., 2001](#); [Horwitz et al., 2007](#); [Matthey et al., 2013](#)), second postpartum year ([Campbell, 1995](#); [Horowitz & Goodman, 2004](#); [McLennan et al., 2001](#); [Murray & Cooper, 1997](#); [Small et al., 1994](#)), and up to four years postpartum ([Kumar & Robson, 1984](#)). Contrary to the general impression that the early postpartum period is the most sensitive period for developing depression, several studies suggest that depression and anxiety scores are highest during pregnancy and that the severity of depression often decreases from prenatal to postpartum period ([Bowen et al., 2012](#); [Eberhard-Gran et al., 2004](#); [Evans et al., 2001](#); [Heron et al., 2004](#); [Ritter, 2000](#)).

Reports regarding the course of anxiety in the perinatal period are less consistent. Some studies have concluded that there is a general decline in anxiety scores between pregnancy and eight months postpartum ([Evans et al., 2001](#)). Others have reported that anxiety scores increase up to the late pregnancy period ([Da Costa et al., 1999](#)) through to the early postpartum period ([Stuart et al., 1998](#)) followed by decline later in the postpartum period ([Dennis et al., 2013](#); [Figueiredo & Conde, 2011](#); [Paul et al., 2013](#)).

1.7 Effects of depression and anxiety on the mother

During pregnancy, depressed or anxious mothers tend to be emotionally withdrawn, have a higher degree of concern about their pregnancy, are less socially active, and have more physical symptoms than mothers who are not depressed or anxious ([Dunkel Schetter, 2011](#); [Kelly et al.,](#)

[2001](#); [Norbeck & Tilden, 1983](#)). This can further result in decreased social support, poor nutrition, and relationship difficulties with their partner ([Joiner et al., 1999](#); [Wisner et al., 2002](#); [Wisner et al., 2009](#)). Depression and anxiety in pregnancy are also associated with other high-risk behaviours ([Chan et al., 2014](#)). Depressed mothers are more likely to smoke, consume alcohol, use drugs, have a history of physical or sexual abuse in pregnancy ([Evans et al., 2001](#)), and are less likely to regularly attend prenatal clinics which in turn can result in poor maternal and fetal outcomes ([Barker et al., 2011](#); [Kahn et al., 2002](#); [Walker et al., 2011](#)). They are also more likely to experience high-risk deliveries including higher risks for induced labour, pre-term birth, and caesarean sections ([Wilkie & Deligiannidis, 2014](#)).

Perinatal depression also affects the mother's capacity to develop and maintain positive family relationships. If depression is not diagnosed and treated it can have long-term effects on maternal health and child development ([Field, 1998](#)). Depressed mothers are more likely to be irritable or hostile. They also exhibit less warmth and interactive play behaviour (reading, singing, story telling, and playing games) with their children ([Field et al., 2006](#); [Lovejoy et al., 2000](#); [Paulson et al., 2006](#)). Interactive play behaviours are important for later cognitive, social, emotional, and physical development ([Bus et al., 1995](#)) particularly among boys ([Weinberg et al., 2006](#)). Depressed mothers are more likely to use harsher punishments and physical force ([McLearn et al., 2006a](#)). These differences in parenting behaviours appear to be universal and have been reported across cultural, socio-economic, and geographic boundaries ([Eapen et al., 2005](#); [Murray et al., 1996](#); [Righetti-Veltema et al., 2002](#)).

Maternal depression and anxiety affect other important child-rearing practices ([Field, 2010](#)). Mothers with chronic or postpartum depression are less likely to practice exclusive breastfeeding and are more likely to discontinue breastfeeding ([Dennis & McQueen, 2007](#),

[McLearn et al., 2006a](#); [McLearn et al., 2006b](#); [Pope & Mazmanian, 2016](#)). Babies of mothers with depression are also more likely to be subjected to undesirable sleep practices, such as prone position or bed sharing with their parents, and the mothers are more likely to report sleep problems in their infants ([Hiscock & Wake, 2001](#); [McLearn et al., 2006a](#)). Women with depression are also less likely to access preventive health services for their children, such as well baby visits and vaccinations, and are also more likely to utilize acute care services in the baby's first year ([Minkovitz et al., 2005](#)).

1.8 Physiological consequences in children of in utero exposure to depression and anxiety

Children of mothers with antenatal depression are four times more likely to be depressed ([Hay et al., 2010](#)). This increased risk may have its origin in the physiological changes that produce a lasting effect on the fetal development and infants' response to stress ([Monk et al., 2012](#)). Physiological changes associated with maternal prenatal anxiety include increased resistance to uterine artery flow ([Teixeira et al., 1999](#)) and higher blood cortisol concentrations ([Sarkar et al., 2008](#)). There is also trans-placental transfer of cortisol and a programming effect on hypothalamic-pituitary-adrenal (HPA) axis of the baby's response to stress ([Henry et al., 1994](#); [O'Connor et al., 2005](#); [Sarkar et al., 2008](#)) through change in the norepinephrine and serotonin levels, the hormone responsible for mood regulation ([Field et al., 2004](#); [Lundy et al., 1999](#)). Maternal cortisol concentrations in pregnancy have also been shown to have effects on the cortisol levels in preadolescent children ([O'Connor et al., 2005](#)), providing evidence of long-term effects in children of maternal prenatal depression and anxiety.

Fetal behavioural response to stress is indicated by increased fetal heart rate, increased fetal eye movement, and gross body movements ([Alder et al., 2007](#); [Dieter et al., 2001](#); [Sjostrom et al., 2002](#)). Fetal responses to stress were higher among depressed or anxious mothers as

compared to mothers who were neither depressed nor anxious providing evidence of altered stress response mechanisms *in utero* ([Monk et al., 2011](#); [Monk et al., 2000](#)). Infants born to depressed mothers, along with higher cortisol levels and altered levels of neurotransmitters, like norepinephrine, dopamine serotonin, also have relatively higher right frontal electroencephalogram (EEG) activity as compared to children of non-depressed mothers ([Diego et al., 2004](#)).

The ‘fetal programming hypothesis’ of David Barker states that the *in utero* environment can alter the development of the fetus during ‘particular sensitive periods’, with a permanent effect on the phenotype commonly known as ‘developmental plasticity’ ([Barker, 2004](#)). Developmental plasticity gives the ability to adapt to *in utero* insults. This plasticity, for example in response to undernutrition during fetal life and infancy, may impact the risks for later development of chronic diseases such as coronary artery disease, type 2 diabetes, stroke, and hypertension ([Barker, 2004](#)). Fortunately, developmental plasticity does not stop in the prenatal period, but continues into early childhood ([Lester et al., 2013](#)). Thereby, providing the opportunity to override and re-program the effects of prenatal stresses in the postpartum period. This further supports the need to identify the most sensitive time of exposure to maternal depression and anxiety to prevent developmental damage.

1.9 Effects on depression and anxiety on early childhood development

Early life positive experiences provide the necessary foundation for reducing health and social inequities later in life ([Wadsworth, 1988](#)). Approximately 25% to 30% of Canadian children enter school with some form of physical, socio-emotional, or cognitive delay ([GOC, 2011](#)). Among children of ages 0 – 5 years, the prevalence of emotional and behavioural disturbances range between 9.5% - 14.2% ([Brauner & Stephens, 2006](#)). Studies have reported

that behavioural problems tend to be very stable even at very young ages, suggesting the need for early screening and diagnosis of maladaptive behaviours ([Rose et al., 1989](#)).

Postpartum depression is a widely recognized risk for physical, behavioural and emotional development in children ([Friedman & Resnick, 2009](#)). Babies exposed to prenatal depression and anxiety are, for example, at greater risk for premature births and being small for gestational age ([Accortt et al., 2015](#); [Dunkel Schetter, 2011](#); [Orr & Miller, 1995](#); [Singer et al., 1999](#)) as well as being at higher risk of neonatal intensive care admission ([Misri et al., 2004](#)). Maternal prenatal depression and anxiety has also been associated with delayed neonatal adaptation at birth (lower one-minute Apgar scores and higher five-minute Apgar scores) and delayed development of sleep/wake patterns ([Aaron Jones et al., 1998](#); [Andersson et al., 2004](#); [Berle et al., 2005](#); [Field, 1998](#)). Neonates born to mothers who are depressed or anxious are reported to be more irritable, to have a difficult temperament, to feed and sleep poorly, and be harder to console ([Muzik & Borovska, 2010](#); [Whiffen & Gotlib, 1989](#); [Zuckerman et al., 1989](#); [Zuckerman et al., 1990](#)). Although there are several examples of impacts on neonatal health, research on the longer-term effects of perinatal depression and anxiety on child development is still emerging.

Babies born to depressed mothers are also less attentive and less responsive to facial expressions ([Lundy et al., 1999](#)), performed lower on behavioural and reflex assessments, and had higher frontal EEG activity as compared to those born to mothers without depression ([Abrams et al., 1995](#); [Lundy et al., 1999](#)). This is not surprising as children can perceive and exhibit moods using various facial expressions such as happiness, sadness, anger, fear, and surprise as early as three months of age ([Bornstein et al., 2011](#); [de Haan et al., 2002](#); [Halit et al., 2003](#)). Children typically have the greatest exposure to their mothers' facial expressions during

the first year of life. Muted insensitive and unresponsive behaviour and frequent sad, angry, or neutral facial expressions from the mother create a negative emotional environment ([Bornstein et al., 2011](#); [Lovejoy et al., 2000](#)). Thus, infants of mothers who are depressed tend to exhibit fewer expressions of interest and produce more sad and angry faces as compared to infants of non-depressed mothers ([Pickens & Field, 1993](#)).

By the time they are one year of age, children of mothers who are depressed are more likely to show signs of neurological deficit, including lower motor skills, lower weight percentiles, and less exploratory behaviours ([Field, 1992](#); [Tronick & Reck, 2009](#)). One of the few longitudinal studies retrieved revealed that preschool children (three years of age) of mothers who were depressed also had both higher internalizing and externalizing behaviours ([Field et al., 1996](#); [Lang et al., 1996](#)). Internalizing problems include syndromes concerning symptoms of anxiety, depression, withdrawal, and somatic problems. Externalizing problems include symptoms of conflicts with others, attention problems, and aggression ([Achenbach & Rescorla, 2000](#); [Carneiro et al., 2016](#)). There is some information on gender differences between boys and girls. Among preschool girls the prevalence of internalizing behaviours is higher; whereas, among preschool boys prevalence of externalizing behaviours is higher ([Koot & Verhulst, 1991](#); [Mesman et al., 2001](#)). However, comprehensive analysis of the protective or risk factors for the individual syndromes that constitute internalizing and externalizing problems have not been widely reported.

Similarly, detailed information is lacking regarding protective and risk factors for the physical, cognitive, and personal-social development of children at three years of age. Physical development includes gross activities, such as running and jumping, and fine motor skills development, such as buttoning a shirt and drawing pictures ([Aboud & Yousafzai, 2016](#)).

Cognitive development includes language and communication skills as well as problem-solving skills. Whereas, personal-social skills include the ability to care for themselves (washing hands, using utensils) and interact with others (playing games and understanding feelings and moods) ([Aboud & Yousafzai, 2016](#); [Shonkoff & Phillips, 2000](#)).

1.10 Risk factors for prenatal depression and anxiety

Several meta-analyses ([Beck, 1996](#); [O'Hara & Swain, 1996](#); [Robertson et al., 2004](#)) have summarized the predictors of postpartum depression. At least one systematic review has consolidated information on the risk factors of prenatal depression ([Lancaster et al., 2010](#)). Studies have identified a spectrum of socio-demographic, obstetric, psychological, and behavioural factors that have significant effects on prenatal or postpartum depression ([Stewart, 2003](#)). However, limited information is available on the risk factors of longitudinal maternal depression and anxiety scores and whether the effects of these factors on depression and anxiety scores differ at various times during the perinatal period.

Socio-demographic factors, for example, lack of social support, being physically or emotionally abused, living in economic disadvantage have been shown to increase the risk of developing perinatal depression ([Norbeck & Anderson, 1989](#); [Norbeck & Tilden, 1983](#)). Similarly, teenaged mothers or those above the age of forty, mothers with limited education and lower socio-economic status, and single or divorced mothers have higher long-term risks for perinatal depression and anxiety ([Robertson et al., 2004](#)).

Obstetric factors of difficult pregnancies and deliveries, including a long labour, extreme nausea and vomiting, loss (miscarriage, stillbirth, or termination), and a previous history of mood disorders were also associated with higher risk of perinatal depression ([Ajinkya et al., 2013](#); [Benute et al., 2010](#); [Kramer et al., 2013](#); [Rich-Edwards et al., 2006](#)). Maternal high-risk

behaviours such as smoking, alcohol consumption, or drug use also increased the risk of developing perinatal depression ([Norbeck & Anderson, 1989](#); [Norbeck & Tilden, 1983](#)).

Mothers with a history of anxiety or depression, family history of perinatal depression, and mothers who faced major life stressors were known to have a higher risk of perinatal depression ([Stewart et al., 2003](#)). History of depression, prenatal depression, and anxiety have been reported to be the strongest predictors of postpartum depression ([Beck, 1996](#); [Leigh & Milgrom, 2008](#)). Neuroregulatory pathways *in-utero* and child rearing practices *ex-utero* have been described as the mediators of the transgenerational effects of maternal depression ([Diego et al., 2004](#); [Kluczniok et al., 2016](#); [Lohoff, 2010](#); [Sullivan et al., 1996](#)).

Child-related factors also increased the risk of perinatal depression. Research indicates an unfortunate cycle of maternal depression and anxiety and newborn irritability, with the mother and child reinforcing each others' bad moods ([Petzoldt et al., 2014](#); [Zuckerman et al., 1990](#)). For example, stressed and anxious mothers were more likely to report colic or infant crying or newborn irritability ([Rautava et al., 1993](#); [St James-Roberts et al., 1998](#)), which in-turn leads to a feeling of incompetency ([Stifter & Bono, 1998](#)), increased parenting stress and significantly lowered parenting self-efficacy among new mothers ([Bond et al., 2001](#); [Cutrona & Troutman, 1986](#); [Leerkes & Burney, 2007](#)). Research supports that greater maternal parenting self-efficacy is associated with lowered risk of postpartum depression and stress ([Cutrona & Troutman, 1986](#)) and more sensitive and positive interactions with their infants ([Bohlin & Hagekull, 1987](#); [Leerkes & Crockenberg, 2002](#)). Positive mother-child interactions have been reported to be the cornerstone for attaining age-appropriate emotional and cognitive development ([Coleman & Karraker, 2003](#); [Troutman et al., 2012](#)). However, research is lacking on the importance of child-related factors on both longitudinal depression and anxiety scores in mothers.

1.11 Study rationale and context

The potential for detrimental effects of postpartum depression on parenting behaviours and the emotional and behavioural development of the child have been well researched ([Murray, 1992](#); [Murray & Cooper, 1996](#); [Murray & Cooper, 1997](#); [Murray et al., 2010](#)); however, few longitudinal studies have reported the long-term effects of postpartum depression ([Campbell, 1995](#); [Horowitz & Goodman, 2004](#); [McLennan et al., 2001](#); [Murray & Cooper, 1997](#); [Small et al., 1994](#)) and perinatal depression ([Deave et al., 2008](#); [Kumar & Robson, 1984](#)). None of the retrieved studies has explored the long-term effects of both perinatal depression and perinatal anxiety on specific measures of physical, cognitive, personal-social, emotional and behavioural development in children at three years of age. Childhood vulnerability to mental health problems results in a long-term risk of mental health disorders in adulthood and appears to have transgenerational effects. To obtain maximum benefit from the limited resources, research is needed to guide and focus services towards maternal anxiety and depression at the times when they are most likely to be effective. To date, most research focus in Canada has been in the postpartum period, with preconception and pregnancy periods unreported.

1.12 Data source and study settings

The ‘Feelings in Pregnancy and Motherhood’ (FIP) study is a longitudinal study of Canadian women residing in Saskatoon, Saskatchewan ([Bowen et al., 2012](#)). The study was planned to address existing gaps in the literature by examining the time course of perinatal depression and anxiety from pregnancy up to five years postpartum longitudinally and prospectively as well as study the effects of previous depression and anxiety scores on subsequent depression and anxiety scores. Mothers were screened for depression, anxiety, and mood problems twice during pregnancy, in the early postpartum period, and at three and five

years after the birth of the index child (five data points). Their children were observed for physical, cognitive, personal-social development, emotional, and behavioural development at birth, at three years and five years of age. Data were also collected on a wide range of determinants of maternal mental health for both the mother and their children.

This thesis includes research on mothers that completed the fourth round of data collection when their children were three years of age. The study was funded by the Canadian Institutes of Health Research (CIHR #145179), the Children's and Maternal Hospital Foundation of Saskatchewan, Saskatchewan Health Research Foundation (SHRF), and the University of Saskatchewan. The study was approved by University of Saskatchewan Behavioural Research Ethics Board (Beh-REB # 13-284) (Appendix 1-A).

1.13 Goals and objectives of the study

The overall goal of this thesis was to assess the course of depression and anxiety in mothers during early and late pregnancy, early postpartum, and at three years after birth, as well as to identify the time points during this period with the greatest potential to influence early childhood development.

The specific questions addressed in this research include:

1. What are the number of underlying dimensions of the Child Behaviour Checklist (1.5 – 5 years) using a Canadian cohort of preschoolers?
 - What is the reliability of individual re-specified subscales?

This work was a necessary precursor to later analysis using data collected with the re-specified Child Behaviour Checklist.

2. What is the time course of depression and anxiety from pregnancy through three years after childbirth among a cohort of Canadian mothers?

- What is the association between previously recognized risk factors for postpartum depression and maternal depression and anxiety scores measured from the pregnancy through three years after childbirth?
 - How do previous maternal depression and anxiety scores influence subsequent maternal depression and anxiety scores?
3. What are the predictors of better physical, cognitive, personal – social development of a cohort of Canadian children at three years of age?
- What is the most sensitive time period during and after pregnancy for attaining high physical, cognitive, and personal – social development?
 - How do maternal mental health and high-risk behaviours influence child physical, cognitive, and personal – social development?
 - What are the potential mediating and moderating effects of identified risk factors?
4. What are the effects of maternal mental health and maternal high-risk behaviours on early childhood emotional and behavioural development – Is there a more sensitive time period for detrimental effects?
- What are the risk factors for behavioural syndromes of aggression, attention problems, anxiety, sleep problems, and withdrawn behaviour among a cohort of healthy three-year-old children?
 - How do children of mothers with a history of depression score compare to children of mothers with no history of depression?
 - What are the effects of maternal mental health and maternal high-risk behaviours on the emotional and behavioural development of these children?

To answer the above research questions, the thesis has been organized into series of seven chapters.

Chapter 2 provides a descriptive summary of the participants originally recruited in the FIP study and a summary of losses to follow-up in the cohort and those who continued to participate when their children were three years of age.

Chapter 3 is manuscript 1, which uses Item Factor Analysis (IFA) to summarize the psychometric properties of the Child Behavioural Checklist (CBCL) (1.5 – 5 years) in 343 three-year-old children. The findings from this tool assessment analysis were later applied in Chapter 6.

Chapter 4 is manuscript 2, which describes the course of depression and anxiety in 333 women with singleton pregnancies who participated in the FIP study. Factors affecting Edinburgh Postpartum Depression Scale (EPDS) scores were examined using linear mixed models with random intercepts to account for repeated measures within individual mothers and an exponential correlation structure to account for the non-equidistant time points between visits ([Preacher & Hayes, 2004](#)). The effects of previous EPDS scores on later scores for depression and anxiety were investigated separately using lagged variables.

Chapter 5 includes manuscript 3, which examines the effects of maternal high-risk behaviours and maternal mental health on childhood physical, cognitive, and personal-social development at three years of age using data from 339 children from the FIP study. The Ages and Stages Questionnaire (ASQ®) measured communication skills, gross motor skills, fine motor skills, problem-solving, and personal-social skills of the children ([Squires et al., 2009](#)). Ordinal regression was used to identify the potential determinants of high normal scores for the five subscales of communication skills, gross motor skills, fine motor skills, problem-solving skills,

and personal-social skills in children at three years of age. Mediation effects were examined for variables of interest using the Sobel-Goodman test ([Preacher & Hayes, 2004](#)).

Chapter 6 contains manuscript 4, which explored the effects of maternal high-risk behaviours and maternal mental health on early childhood emotional and behavioural development including data from the same 343 children born to 338 mothers from the FIP study (including five women with twin pregnancies). The re-specified Child Behavioural Checklist (1.5-5 years) (CBCL) from manuscript 1 reported in Chapter 3 was used to measure emotional and behavioural development of the children at three years of age. Ordinal regression was used to identify significant risk factors for high scores for behavioural syndromes of anxiety, sleep problems, withdrawn behaviour, aggression, and attention deficit among a sample of healthy three-year-old children. Mediation effects were again examined using the Sobel-Goodman test ([Preacher & Hayes, 2004](#)).

Chapter 7 is the final chapter and as such contains recommendations for public health policy, limitations, areas for future research, and conclusions.

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1.15 Appendices

1.15.1 Appendix 1-A – Ethics Approval



UNIVERSITY OF
SASKATCHEWAN

Behavioural Research Ethics Board (Beh-REB)

Certificate of Re-Approval

PRINCIPAL INVESTIGATOR
Angela Bowen

DEPARTMENT
Nursing

BEH#
13-284

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT
School of Public Health
Saskatoon SK

STUDENT RESEARCHER(S)
Kamalpreet Banga

FUNDER(S)
CANADIAN INSTITUTES OF HEALTH RESEARCH (CIHR)
SASKATCHEWAN HEALTH RESEARCH FOUNDATION (SHRF)

TITLE
Feelings in Pregnancy & Motherhood: Child and Maternal Outcomes

RE-APPROVED ON
15-Jun-2017

EXPIRY DATE
14-Jun-2018

Delegated Review: Full Board Meeting:

CERTIFICATION

The University of Saskatchewan Behavioural Research Ethics Board (Beh-REB) is constituted and operates in accordance with the current version of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2 2014). The University of Saskatchewan Behavioural Research Ethics Board has reviewed the above-named research project. The proposal was found to be acceptable on ethical grounds. The principal investigator has the responsibility for any other administrative or regulatory approvals that may pertain to this research project, and for ensuring that the authorized research is carried out according to the conditions outlined in the original protocol submitted for ethics review. This Certificate of Approval is valid for the above time period provided there is no change in experimental protocol or consent process or documents.

Any significant changes to your proposed method, or your consent and recruitment procedures should be reported to the Chair for Research Ethics Board consideration in advance of its implementation.



UNIVERSITY OF
SASKATCHEWAN

Behavioural Research Ethics Board (Beh-REB)

Certificate of Re-Approval

PRINCIPAL INVESTIGATOR	DEPARTMENT	Beh #
Angela Bowen	Nursing	13-284
INSTITUTION (S) WHERE RESEARCH WILL BE CARRIED OUT		
School of Public Health Saskatoon SK		
STUDENT RESEARCHER(S)		
Kamalpreet Banga		
FUNDER(S)		
CANADIAN INSTITUTES OF HEALTH RESEARCH (CIHR)		
SASKATCHEWAN HEALTH RESEARCH FOUNDATION (SHRF)		
TITLE:		
Feelings in Pregnancy & Motherhood: Child and Maternal Outcomes		
RE-APPROVED ON	EXPIRY DATE	
30-Jun-2016	29-Jun-2017	

Full Board Meeting

Delegated Review

CERTIFICATION

The University of Saskatchewan Behavioural Research Ethics Board has reviewed the above-named research project. The proposal was found to be acceptable on ethical grounds. The principal investigator has the responsibility for any other administrative or regulatory approvals that may pertain to this research project, and for ensuring that the authorized research is carried out according to the conditions outlined in the original protocol submitted for ethics review. This Certificate of Approval is valid for the above time period provided there is no change in experimental protocol or consent process or documents.

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Behavioural Research Ethics Board (Beh-REB)

Certificate of Re-Approval

PRINCIPAL INVESTIGATOR	DEPARTMENT	Beh #
Angela Bowen	Nursing	13-284
INSTITUTION (S) WHERE RESEARCH WILL BE CARRIED OUT		
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STUDENT RESEARCHER(S)		
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SASKATCHEWAN HEALTH RESEARCH FOUNDATION (SHRF)		
TITLE:		
Feelings in Pregnancy & Motherhood: Child and Maternal Outcomes		
RE-APPROVED ON	EXPIRY DATE	
31-Jul-2015	30-Jul-2016	

Full Board Meeting

Delegated Review

CERTIFICATION

The University of Saskatchewan Behavioural Research Ethics Board has reviewed the above-named research project. The proposal was found to be acceptable on ethical grounds. The principal investigator has the responsibility for any other administrative or regulatory approvals that may pertain to this research project, and for ensuring that the authorized research is carried out according to the conditions outlined in the original protocol submitted for ethics review. This Certificate of Approval is valid for the above time period provided there is no change in experimental protocol or consent process or documents.

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Behavioural Research Ethics Board (Beh-REB)

Certificate of Re-Approval

PRINCIPAL INVESTIGATOR	DEPARTMENT	Beh #
Angela Bowen	Nursing	13-284

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT

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(CIHR)

SASKATCHEWAN HEALTH RESEARCH
FOUNDATION (SHRF)

TITLE:

Feelings in Pregnancy & Motherhood: Child and Maternal Outcomes

RE-APPROVED ON	EXPIRY DATE
21-Jul-2014	20-Jul-2015

Full Board Meeting

Delegated Review

CERTIFICATION

The University of Saskatchewan Behavioural Research Ethics Board has reviewed the above-named research project. The proposal was found to be acceptable on ethical grounds. The principal investigator has the responsibility for any other administrative or regulatory approvals that may pertain to this research project, and for ensuring that the authorized research is carried out according to the conditions outlined in the original protocol submitted for ethics review. This Certificate of Approval is valid for the above time period provided there is no change in experimental protocol or consent process or documents.

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Certificate of Approval

PRINCIPAL INVESTIGATOR
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CANADIAN INSTITUTES OF HEALTH RESEARCH (CIHR)

TITLE
Feelings in Pregnancy & Motherhood: Child and Maternal Outcomes

ORIGINAL REVIEW DATE	APPROVAL ON	APPROVAL OF:	EXPIRY DATE
23-Aug-2013	23-Aug-2013	Application for Behavioural Research Ethics Review Secondary Use of De-Identified Data from BEH 04-183	22-Aug-2014

Full Board Meeting

Delegated Review

CERTIFICATION

The University of Saskatchewan Behavioural Research Ethics Board has reviewed the above-named research project. The proposal was found to be acceptable on ethical grounds. The principal investigator has the responsibility for any other administrative or regulatory approvals that may pertain to this research project, and for ensuring that the authorized research is carried out according to the conditions outlined in the original protocol submitted for ethics review. This Certificate of Approval is valid for the above time period provided there is no change in experimental protocol or consent process or documents.

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CHAPTER 2: DESCRIPTIVE SUMMARY OF FEELINGS IN PREGNANCY & MOTHERHOOD STUDY DATA

2.1 Introduction

The following thesis is focussed on data collected from a cohort of mothers and their children near the child's third birthday in Saskatchewan, Canada as part of the Feelings in Pregnancy study ([Bowen et al., 2012](#)). These women were interviewed in early pregnancy (T1), late pregnancy (T2), early in the postpartum period (T3), and three years after birth (T4). The Feelings in Pregnancy study is an example of a longitudinal study. Longitudinal studies have an advantage over simple cross-sectional observational studies as temporality can be established between exposures observed at earlier time points and subsequent outcomes particularly when many observations can be made on the same individual over the study period ([Grimes & Schulz, 2002](#); [Song & Chung, 2010](#)). Thus, such studies can provide an opportunity to see changes over time and establish a sequence of events ([IWH, 2015](#)) as well as identify 'the cumulative effects of various life cycle transitions', culture, ethnicity, and other socio-demographic factors on long-term outcomes ([Rajulton, 2001](#); [Smith & Torrey, 1996](#)).

Missing 'patient-reported outcomes' and covariate data are common in longitudinal studies ([Bell & Fairclough, 2014](#)). Missing waves of data or 'unit nonresponse' ([Schafer & Graham, 2002](#)) defined as when the participant missed whole round of data collection are usually more difficult to deal with as compared to missing items when one or more questions in the questionnaire are left unanswered ([Bell & Fairclough, 2014](#); [Ibrahim & Molenberghs, 2009](#)). A special case of wave non-response is *attrition or drop-out* in which the participant leaves the study, never to return ([Schafer & Graham, 2002](#)). Loss of precision and power to detect change are the two most important consequences of missing data ([Bell & Fairclough, 2014](#)).

Data attrition or loss to follow-up is one of the major drawbacks of prospective cohort studies; especially when the missing participants are systematically different from those who continue to participate in the study ([Grimes & Schulz, 2002](#); [Song & Chung, 2010](#)). Population-

based mental health studies also have other inherent methodological issues including limited options for validated measurement tools and the potential for the ‘Hawthorne effect’, in which individuals modify their behaviour in response to repeated contacts with study personnel ([Hammarström et al., 2016](#); [Rajulton, 2001](#)). This chapter provides a summary of the participating mothers in the Feelings in Pregnancy ([Bowen et al., 2012](#)) study. The objective of this analysis was to describe the information collected from the participants during the first prenatal visit and compare information from the mothers 1) who participated in the fourth round of data collection when their children were three years of age, and who were included in subsequent analyses, and 2) those who were lost to follow-up before the fourth visit.

2.2 Methods

Mothers were recruited for the Feelings in Pregnancy study during the second trimester of pregnancy, which was designed to follow these individuals to the time point when their child was five years of age. This thesis focussed on information from first four rounds of data collection, from early pregnancy up to approximately three years after childbirth. The first three rounds of data were collected mainly through face-to-face interviews. However, for the fourth round near the child’s third birthday, mailed out questionnaires and telephone interviews options were provided to fit the individual needs of participants. Mothers were also provided with incentives to encourage participation. Communications with the participants were maintained via birthday cards throughout the study period.

At each study visit information was collected on maternal mental health, maternal high-risk behaviours, socio-demographic factors, and other risk factors described in the peer-reviewed literature. The Edinburgh Postpartum Depression Scale (EPDS) was used to screen mothers during the study for both depression and anxiety ([Cox et al., 1987](#); [Murray & Cox, 1990](#)).

Mothers with total EPDS (Edinburgh Postpartum Depression Scores) scores of ≥ 12 were categorized as depressed ([Choate & Gintner, 2011](#); [Cox et al., 1987](#)). For the present analysis total of all ten EPDS items were used to represent the linear depression scores at T1, T2, T3, and T4. EPDS has also been validated as a useful measure to screen for anxiety (items 3, 4, & 5) in pregnancy and postpartum period ([Matthey et al.\(2013\)](#)). Total scores of item 3, 4, & 5 were used to represent linear anxiety score at T1, T2, T3, and T4.

Mother's education was dichotomized as 'some post-secondary education' and 'less than post – secondary education'. Mother's employment status was dichotomized as 'Yes' vs. 'No'. Annual family income was dichotomized using the annual income of \$40,000 as a cut-off (based on the estimates of low-income cut-off for a family of four in Canada) ([Statcan, 2015](#)). History of exposure to smoking, alcohol, and recreational drug use were transformed to a nominal variable, '0' indicating never exposed, '1' quit and '2' continued exposure. Maternal overall health was measured by asking 'how would you rate your overall health today' and dichotomized by summarizing 'okay', 'fair' & 'poor' categories as 'poor' and then 'good', 'very good', and 'excellent' as 'good'. Most 91.9% (596) reported having good overall health. Maternal relationship status was a nominal variable with options including 'no relationship', 'not satisfied', 'somewhat satisfied', and 'very satisfied'. However, due to relatively few observations in the 'not satisfied' and 'somewhat satisfied/neutral' categories; the variable was re-categorised as 'very satisfied', 'not very satisfied', and 'no relationship'.

Data collected at T1 from mothers who participated in the fourth round of data collection were compared with that from the mothers who were lost to follow-up. To detect any significant differences between these two groups of mothers, chi-square tests and t tests were used for

categorical and linear variables (independent and dependent) respectively ([Dohoo et al., 2012](#)).

Difference were considered statistically significant when $p < 0.05$.

The outcome variables were further checked for patterns and mechanism of missing data ([Zhou et al., 2014](#)). Patterns identify the number of observations which are missing in the data and how do they organize in the data matrix. ([Zhou et al., 2014](#)). Whereas, the mechanism identifies the reason the values are missing and explores the probability of missing data based on the observed data ([Enders, 2010](#); [Zhou et al., 2014](#)). Missing data patterns were identified using ‘misstable’ and ‘mvpattern’ command in STATA 12.0 ([Little, 1988](#); [Weesie, 2001](#)). The mechanism of missing values is categorized into missing completely at random (MCAR), missing at random (MAR) or not missing at random (MNAR) ([Allison, 2003](#); [Little & Rubin, 2014](#)).

Little’s test was used to check the assumption for missing completely at random (MCAR) ([Little, 1988](#)). A non-significant test statistic at $p > 0.05$ indicates that the assumption of MCAR is true. However, for checking MAR, we used the strategy recommended by STATA ([StataCorp, 2013b](#)). The ‘misstable’ procedure with ‘gen(miss)’ was used to compute the mirror variables for the missing component of depression and anxiety variables, followed by logistic regression models to test if the observed variables predicted the missing variable. If the logistic regression models predicted the missing variables, then the values could be assumed to be MAR ([StataCorp, 2013b](#)). There were no tests for statistical significance available to check the assumptions of MNAR. If the variables were neither MCAR nor MAR, they were assumed to be MNAR.

2.3 Results

Mothers were screened for depression and anxiety in early pregnancy, late pregnancy, early postpartum, and at three-years after birth. Of the 648 women recruited and participating

during early pregnancy, 603 (93.1%) completed second round and 594 (91.7%) completed third round. Of the 594 women who completed the third round of data collection, 593 (99.8%) had a live birth. Information about the outcome was not available for the one remaining mother who did not participate in the third round of data collection. The fourth round of data collections, when the child was three years of age was completed by 338/648 (52.2%) mothers, 310 (47.8%) were lost to follow-up despite the best efforts of study personnel to trace them.

The mean (SD) duration of gestation at recruitment was 17 weeks (4.4 weeks). The second measurement was later in the pregnancy at a mean gestation of 30.4 weeks (2.4 weeks). The third measurement was at an average 4.0 weeks (2.0 weeks) after birth, and the fourth measurement was completed when the child was an average age of 36.4 months (1.6 weeks).

2.3.1 Profile of the participants at enrollment

The average age \pm standard deviation of the 648 mothers who participated in early pregnancy (T1) was 28.9 ± 4.8 years. Average \pm standard deviation depression and anxiety scores were 6.8 ± 4.5 and 3.44 ± 2.2 , respectively. Slightly more than one third of participants reported having a prior history of depression, and just over one quarter had a family history of perinatal depression (diagnosis or treatment of depression in the mother or any of the siblings of the participants (Table 2-1).

Table 2-1: Description of the Feelings in Pregnancy study participants at the time of enrollment (N=648).

Variable (N)	Description	Frequency	Percentage
History of depression (648)	Yes	229	35.3
	No	419	64.7
Family history of perinatal depression	Yes	173	26.7
	No	389	60.0
	I don't know or Don't have a mother	86	13.3
Education status at T1 (647)	\leq Grade 12	115	17.8
	\geq Grade 12	532	82.2
Parity at intake (648)	Primigravida	248	38.3

Variable (N)	Description	Frequency	Percentage
	Multigravida	400	61.7
Ethnicity (647)	Caucasian	545	84.2
	Non-Caucasian	102	15.8
Employment at T1 (646)	Yes	503	77.9
	No	143	22.1
Income at T1 (641)	<\$40,000	210	32.8
	>\$40,000	431	67.2
Marital status at T1 (648)	Single/Divorced/Separated	63	9.7
	Married/Common law	585	90.3
Satisfied with relationship with father of baby at T1 (644)	Very satisfied	562	87.3
	Not very satisfied	67	10.4
	No relationship	15	2.3
Overall health at T1 (648)	Excellent/Very good/Good	596	92.0
	Poor/Fair/Okay	52	8.0
Emotional support T1(648)	Yes	635	98.0
	No	13	2.0
Physical abuse at (T1) (648)	Yes	187	28.9
	No	461	71.1
Emotional abuse at (T1) (648)	Yes	338	52.2
	No	310	47.8
Sexual abuse at (T1) (648)	Yes	153	23.6
	No	495	76.4
Smoking at T1 (647)	Yes	76	11.7
	Quit	148	22.9
	Never	423	65.4
Alcohol at T1 (648)	Drink	44	6.8
	Quit	418	64.5
	Never	186	28.7
Drug at T1 (647)	Use	20	3.1
	Quit	111	17.2
	Never	516	79.8
Exercise at T1 (648)	Yes	567	87.5
	No	81	12.5
Neighborhood ratings at T1 (553)	Excellent/Good	430	77.8
	Average/Poor/very poor	123	22.2
Counselling at T1 (648)	Yes	60	9.3
	No	588	90.7

T1 – Early pregnancy.

Most participants were Caucasian, had some post-secondary education, were employed and had an average annual family income greater than \$40,000 (Table 2-1). Most women also reported being very satisfied with their relationship. Almost all of the mothers reported having emotional support; despite the fact that more than a quarter of the women reported having been

physically abused. More than half of participants had faced emotional abuse, and almost a quarter reported having been sexually abused in the past (Table 2-1).

2.3.2 Comparison of mothers who were lost to follow-up as compared to those who participated in fourth round of data collection

The average depression and anxiety scores measured during the first two rounds of data collection from mothers who were lost to follow-up were significantly greater than those who participated in the fourth round of data collection (Table 2-2). Mothers who were lost to follow-up (18.7%) had a higher proportion of screened depressed (EPDS \geq 12) at enrollment as compared to mothers (9.7%) who participated in the fourth round of data collection ($p<0.0001$).

Table 2-2: Comparison summary of the average depression and anxiety scores for the women who were lost to follow up before the fourth round of data collection as compared to those who completed the fourth round of data collection.

Variables	Missing for the fourth round			Participated in the fourth round			*p-value
	Number of observations	Mean (SD)	Range	Number of observations	Mean (SD)	Range	
Depression T1	310	7.7 (4.8)	0 – 27	338	6.0 (3.9)	0 – 21	<0.0001
Depression T2	270	6.8 (4.6)	0 – 28	333	5.7 (4.0)	0 – 25	0.002
Depression T3	256	5.8 (4.5)	0 – 29	338	5.4 (3.8)	0 – 20	0.22
Depression T4	–	–	–	338	4.5 (3.8)	0 – 19	
Anxiety T1	310	3.8 (2.1)	0 – 9	338	3.0 (1.9)	0 – 8	<0.0001
Anxiety T2	270	3.2 (2.1)	0 – 9	333	2.8 (1.8)	0 – 9	0.005
Anxiety T3	256	2.8 (2.1)	0 – 9	338	2.5 (1.9)	0 – 9	0.083
Anxiety T4	–	–	–	338	2.2 (1.8)	0 – 8	

T1 – Early pregnancy, T2 – Late pregnancy, T3 – Early postpartum, T4 – Three years after birth

* p-values computed using one way ANOVA

There were also differences in the age, education, and ethnicity of those who were lost to follow up. Average (SD) age of the mothers who participated in the fourth round of data collection was 29.9 (4.3) years as compared to 28.0 (5.2) years for the mothers who were lost to follow-up ($p<0.0001$) (Table 2-3). About a quarter of the mothers lost to follow-up were less than 25 years of age as compared to about 10% of the mothers who continued to participate in the study ($p<0.0001$) (Table 2-3). Similarly, about a quarter of the mothers lost to follow-up had less

than grade 12 education, as compared to only 8.9% of the mothers who continued to participate in the study ($p<0.0001$) (Table 2-3). Amongst the missing mothers, slightly more than one-fourth of the mothers were Non-Caucasians as compared to only 6.2% among those who participated ($p<0.0001$) (Table 2-3).

Mothers who were lost in follow-up as compared to those who participated in the fourth round of data collection also had poorer overall health at enrollment ($p<0.0001$), had fewer planned pregnancies ($p<0.0001$), and higher proportions were single/divorced or separated ($p<0.0001$) (Table 2-3:). There was no significant difference in the parity status and availability of emotional support reported by both groups of mothers.

Table 2-3: Comparison of mothers who were lost to follow-up and those who participated in the fourth round of data collection at the time of enrollment (T1).

Variable (n)	Description	Frequency (percentage)		p-value*
		Missing (310)	Present 338)	
Comparison of the demographic profile				
Mother's age (648)	<25 years	75 (24.2%)	33 (9.8%)	<0.0001
	25 – 34 years	199 (64.2%)	257 (76.0%)	
	≥35 years	36 (11.6%)	48 (14.2%)	
Education status at T1 (647)	≤ Grade 12	85 (27.5%)	30 (8.9%)	<0.0001
	≥ Grade 12	224 (72.5%)	308 (91.1%)	
Parity at intake (648)	Primigravida	111 (35.8%)	137 (40.5%)	0.22
	Multigravida (>1)	199 (64.2%)	201 (59.5%)	
Ethnicity (647)	Caucasian	228 (73.8%)	317 (93.8%)	<0.0001
	Non-Caucasian	81 (26.2%)	21 (6.2%)	
Employment at T1 (646)	Yes	215 (69.6%)	288 (85.5%)	<0.0001
	No	94 (30.42%)	49 (14.5%)	
Income at T1 (641)	<\$40,000	140 (45.9%)	70 (20.8%)	<0.0001
	≥\$40,000	165 (54.1%)	266 (79.2%)	
Marital status at T1 (648)	Single/Divorced/ Separated	44 (14.2%)	19 (5.6%)	<0.0001
	Married/Common law	266 (85.8%)	319 (94.4%)	
Satisfied with relationship with father of baby at T1 (644)	Very satisfied	254 (82.5%)	308 (91.7%)	0.002
	Not very satisfied	45 (14.6%)	22 (6.5%)	
	No relationship	9 (2.9%)	6 (1.8%)	
Overall health at T1 (648)	Excellent/ Very good/ Good	273 (88.1%)	323 (95.6%)	<0.0001
	Poor/Fair/Okay	37 (11.9%)	15 (4.5%)	
Emotional support T1 (648)	Yes	300 (96.8%)	335 (99.1%)	0.47
	No	10 (3.2%)	3 (0.89%)	

Variable (n)	Description	Frequency (percentage)		p-value*
		Missing (310)	Present 338)	
Comparison of mental health and behavioural profile				
History of depression (648)	Yes	120 (38.7%)	109 (32.3%)	0.09
	No	190 (61.3%)	229 (67.8%)	
Family history of perinatal depression (648)	Yes	84 (27.1%)	89 (26.3%)	0.15
	No	177 (57.1%)	212 (62.7%)	
	I don't know or Don't have a mother	49 (15.8%)	37 (11.0%)	
Smoking at T1 (647)	Yes	60 (19.4%)	16 (4.7%)	<0.0001
	Quit	76 (24.6%)	72 (21.3%)	
	Never	173 (56.0%)	250 (74.0%)	
Alcohol at T1 (648)	Drink	26 (8.4%)	18 (5.3%)	0.19
	Quit	191 (61.6%)	227 (67.2%)	
	Never	93 (30.0%)	93 (27.5%)	
Drug at T1 (647)	Use	15 (4.9%)	5 (1.5%)	<0.0001
	Quit	69 (22.3%)	42 (12.4%)	
	Never	225 (72.8%)	291 (86.1%)	
Exercise at T1 (648)	Yes	269 (86.8%)	298 (88.2%)	0.64
	No	41 (13.3%)	40 (11.8%)	

* p-value is based on a chi-square test for categorical variables and an independent sample t-test for continuous variables.

There were no significant differences in the proportion of participants with a previous history of depression ($p=0.09$) or family history of depression ($p=0.15$) between mothers lost to follow-up and those who participated in the fourth round of data collection (Table 2-3).

On comparing the high-risk behaviours between the two groups of mothers, a higher proportion (19.4% vs. 4.7%) of mothers who were lost to follow-up had smoked in the last month ($p<0.0001$). Similarly, higher proportions (4.8% vs. 1.5%) of mothers lost to follow-up had used recreational drugs in the past one month ($p<0.0001$). However, for alcohol consumption, no significant difference was observed between the two groups ($p=0.19$) (Table 2-3).

2.3.3 Missing data patterns

Six patterns of missing data were identified in the EPDS depression and anxiety scores (Table 2-4).

Table 2-4: Missing data patterns for depression and anxiety scores over the four years from T1 (early pregnancy) to T4 (three years after birth).

Pattern	Frequency (Percentage)	Anxiety (T2)	Depression (T2)	Anxiety (T3)	Depression (T3)	Anxiety (T4)	Depression (T4)
1	333 (51.4%)	Yes	Yes	Yes	Yes	Yes	Yes
2	247 (38.1%)	Yes	Yes	Yes	Yes	No	No
3	31 (4.8%)	No	No	No	No	No	No
4	23 (3.5%)	Yes	Yes	No	No	No	No
5	9 (1.4%)	No	No	Yes	Yes	No	No
6	5 (0.8%)	No	No	Yes	Yes	Yes	Yes

T2 – Late pregnancy, T3 – Early postpartum, T4 – Three years after birth

In total, 45 (7.0%) mothers were lost to follow-up in the second round of data collection.

Most 31 (4.8%) did not participate in the study again; however, 9 (1.4%) missed the second and fourth round of data collection, 5 (0.8%) missed only the second round of data collection and completed the remaining two rounds of data collection (Table 2-4).

In total, 54 (8.3%) mothers were lost to follow-up in the third round of data collection.

Most 31 (4.8%) were those who dropped out after the first round, remaining 23 (3.5%) left the study after the second round of data collection (Table 2-4).

In total, there were 310 (47.8%) mothers who were lost to follow-up for the fourth round of data collection. Most 247 (79.7%) missed only the fourth round of data collection. Thirty-one (4.8%) were those who dropped out after the first round and 23 (3.5%) dropped out after the second round of data collection. The remaining 9 (1.4%) missed second and then participated in the third round to miss the fourth round of data collection (Table 2-4).

Data missing in the second round of data collection were not monotonic. However, the data missing in the third round of data collection were monotonically missing in the fourth round

of data collection. Little's test revealed that data were not MCAR (chi-square distance (df=11) 36.6, p=0.0001).

2.3.4 Checking for Missing at Random (MAR)

The binary variable created with the ‘misstable’ and ‘gen(miss_)’ command was coded ‘1’ for the missing participants and ‘0’ for those who participated in the fourth round of data collection. In total 310 (47.8%) participants were missing from the fourth round of data collection. Logistic regression models were used to assess if the missing outcome data of depression and anxiety were predicted by the observed data (Table 2-5:). Since we had used EPDS to measure both depression and anxiety among prenatal and postnatal mothers, the missing variables thus created for depression and anxiety were identical.

During early and late pregnancy (T1 & T2) visit, a one-unit increase in the depression and anxiety scores significantly increased the odds of missing data at three years after birth (p<0.0001) (Table 2-5).

Table 2-5: Summary of the association between risk factor information collected during the study and missing depression and anxiety outcomes variables (n=648).

Determinants	Missed depression & anxiety scores at T4			
	Odds ratio	Lower	Upper	p-value
Early Pregnancy (T1)				
Depression scores	Continuous	1.1	1.0	1.1 <0.0001
Anxiety	Continuous	1.2	1.1	1.3 <0.0001
Maternal age	<25 vs. 25 – 34	2.9	1.9	4.6 <0.0001
	≥35 vs. 25 – 34	0.9	0.6	1.5 0.89
Gravida status*	Multigravida vs. Primigravida	1.2	0.9	1.7 0.22
Education	Some post-secondary vs. Less than post-secondary	0.3	0.2	0.4 <0.0001
Employed	Yes vs. No	0.4	0.3	0.6 <0.0001
Income	≥\$40,000 vs. <\$40,000/ year	0.3	0.2	0.4 <0.0001
Marital status	Single/ Divorced/ Separated vs. Married/ Common law	2.6	1.5	4.5 0.001
Overall health	Poor vs. Good	2.9	1.6	5.4 0.001
Relationship satisfaction	Not very satisfied vs. Very satisfied	2.4	1.5	4.2 0.001

Determinants	Missed depression & anxiety scores at T4				
	Odds ratio	Lower	Upper	p-value	
No relationship vs. Very satisfied	1.8	0.6	5.2	0.26	
Emotional support	No vs. Yes	3.7	1.0	13.7	0.05
Smoking	Quit vs. Never	1.5	1.0	2.2	0.03
	Smoke vs. Never	5.4	3.0	9.7	<0.0001
Alcohol*	Quit vs. Never	0.8	0.6	1.2	0.33
	Drink vs. Never	1.4	0.7	2.8	0.28
Drug use	Quit vs. Never	2.1	1.4	3.2	<0.0001
	Use vs. Never	3.9	1.4	10.8	0.01
Exercise*	Yes vs. No	0.9	0.6	1.4	0.59
Late pregnancy (T2)					
Depression	Continuous	1.1	1.0	1.1	0.003
Anxiety	Continuous	1.1	1.0	1.2	0.006
Overall health*	Good vs. Poor	0.7	0.4	1.2	0.22
Relationship satisfaction	Not very satisfied vs. Very satisfied	1.8	1.1	2.9	0.01
	No relationship vs. Very satisfied	2.5	1.0	6.5	0.05
Emotional support*	No vs. Yes	0.3	0.1	1.3	0.12
Smoking	Quit vs. Never	2.0	1.1	3.5	0.01
	Smoke vs. Never	3.7	2.1	6.6	<0.0001
Alcohol*	Quit vs. Never	1.2	0.8	1.8	0.33
	Drink vs. Never	0.8	0.4	1.6	0.55
Drug use	Quit vs. Never	2.2	0.9	5.7	0.09
	Use vs. Never	9.1	1.1	74.4	0.04
Exercise*	Yes vs. No	1.0	0.6	1.6	0.94
Early Postpartum (T3)					
Depression*	Continuous	1.0	0.9	1.1	0.23
Anxiety*	Continuous	1.1	0.9	1.2	0.09
Overall health*	Good vs. Poor	0.9	0.5	1.8	0.87
Smoking	Quit vs. Never	1.0	0.4	2.8	0.94
	Smoke vs. Never	3.2	1.8	5.7	<0.0001
Alcohol*	Quit vs. Never	0.6	0.2	1.5	0.25
	Drink vs. Never	0.8	0.6	1.2	0.32
Drug use*	Quit vs. Never	0.33	0.04	3.0	0.32
	Use vs. Never	2.2	0.52	9.33	0.28
Exercise*	Yes vs. No	0.8	0.6	1.2	0.37

*Variables that were not the significant predictors of missing depression and anxiety scores from the fourth round of data collection at p<0.05

Younger (<25 years) mothers at T1 had three times the odds of missing fourth round of data collection as compared to (25–34) year-old mothers (p<0.0001). However, parity of the mother at T1 had no association with the missing the fourth round of data collection (p=0.22). At

T1 mothers who were employed ($p<0.0001$), had some post-secondary education ($p<0.0001$), had an annual family income of $\geq \$40,000$ / year ($p<0.0001$), had lower odds of missing data at three years after birth (Table 2-5). Single/ divorced/ separated ($p=0.001$) mothers at T1 with poor overall health ($p=0.0001$) and no emotional support ($p=0.05$) had higher odds of missing the fourth round of data collection (Table 2-5). Mothers who were either in a not very satisfied relationship or no relationship also had higher odds of missing the fourth round of data collection as compared to mothers who were in a very satisfied relationship ($p=0.003$) (Table 2-5).

Mothers who smoked ($p<0.0001$) or used drugs ($p<0.0001$) in early and late pregnancy (T1 & T2) had higher odds of missing the fourth round of data collection (Table 2-5). However, alcohol consumption at T1 ($p=0.19$) and T2 ($p=0.50$) had no relationship with missing fourth round of data collection.

In the early postpartum period (T3), neither the maternal mental health factors (depression ($p=0.23$) and anxiety ($p=0.09$) scores) nor the maternal high-risk behaviours of alcohol consumption ($p=0.36$) and drug use ($p=0.34$) were significant predictors of missing fourth round of data collection. Only smoking in the early postpartum period significantly increased the odds of missing fourth round of data collection ($p=0.0003$) (Table 2-5).

During pregnancy (T1 & T2) measures of maternal mental health (depression and anxiety) and maternal high-risk behaviours of smoking and drug use (not alcohol consumption) were significant predictors of missing fourth round of data collection. Socio-demographic factors (age, marital status, education, income, employment, emotional support, and relationship satisfaction) at enrollment were also significant predictors of missing fourth round of data collection. Thus, there is evidence that the data missing in the fourth round of the study were

associated with observed maternal mental health, socio-demographic, and high-risk behaviours, especially during the pregnancy.

2.4 Discussion

Almost half of the mothers that started the study were lost to follow-up before the fourth round of data collection when the children were three years of age. The women who were lost to follow-up differed from those who completed the fourth round of data collection based on several of the observed variables. The patterns of missing data were examined to determine the best option for managing the missing data in subsequent analyses.

2.4.1 Mechanisms of missing data

Three types of missingness have been described: missing completely at random (MCAR), missing at random (MAR), and missing not at random (MNAR) ([Rubin, 1976](#)). For the data to be MCAR, complete cases should be a random sample of the study population. Thus, the distribution of missing value is independent of the distribution of both observed and unobserved data ([Little & Rubin, 2014](#)). However, for MAR two assumptions are: 1) missing data depends on the observed covariate data prior to the drop-out, 2) in the presence of observed outcome and covariate data, it should not depend on the unobserved outcome data ([Schafer & Graham, 2002](#); [Young & Johnson, 2015](#)). In other words, for the assumption of MAR to be true the missing data should not be depended on the outcome variable after controlling for other variables in the model ([Allison, 2003](#)).

If the missing data is attributed to unobserved data or only to the unobserved outcome (not to observed covariate data), then the missing data is MNAR ([Groenwold et al., 2012](#); [Ibrahim & Molenberghs, 2009](#); [Tseng et al., 2016](#); [Young & Johnson, 2015](#)). However, it is very difficult to have a completely MNAR data; most of the missing data are partly MAR (dependent

on the observed covariates) ([Groenwold et al., 2012](#)). There is evidence that if reliable covariate information is available from the time point before the drop-out (which is true in almost all longitudinal studies) estimates produced under the assumption of MAR produce more accurate results as compared to methods used to address the assumption of MNAR ([Donders et al., 2006](#); [Groenwold et al., 2012](#); [Rubin et al., 1995](#)).

2.4.2 Methods to deal with missing outcome and covariate data

The most common way to deal with missing data is complete case analysis ([Raghunathan, 2004](#)). If the missing data is termed ‘ignorable’ ([Pigott, 2001](#)) that is either MCAR or MAR, a complete case analysis or listwise deletion will also not bias the estimates ([Allison, 2003](#)). Since in the longitudinal or repeated measures data, individual observations over time on the individual tend to be correlated; thus, multiple imputation (MI) and mixed regression models with maximum likelihood (ML) estimation that use all the data have also been recommended for MCAR and MAR data ([Allison, 2003](#); [Pigott, 2001](#); [Schafer & Graham, 2002](#)).

Various methods of imputation that have been used for longitudinal data include: ‘*last value carried forward*’, ‘*linear interpolation*’, ‘*two longitudinal linear regression*’, and ‘*multiple imputation*’. Multiple imputation (MI) methods are by far the most robust of the methods ([Young & Johnson, 2015](#)). MI utilizes the data from all waves to impute the missed outcome and covariate data ([Schafer & Graham, 2002](#)). However, if the number of missing values are small, simpler methods like last value carried forward can also be used. Multiple imputation methods impute values for all the missing values by creating as many datasets as the number of missing values, and the summary statistics can be computed ([Twisk & de Vente, 2002](#)). There is evidence in the literature that MI methods and complete case analysis with covariate adjustment both

produces precise and unbiased estimates for MCAR and MAR outcome data ([Groenwold et al., 2012](#); [Young & Johnson, 2015](#)).

ML ignores the missing data in the expectation algorithm (EM) of the likelihood function as though they were never observed ([Schafer & Graham, 2002](#)). ‘xt’ procedures in STATA support both ML and restricted maximum likelihood (REML) methods ([Laird & Ware, 1982](#); [Rabe-Hesketh & Skrondal, 2012](#); [StataCorp, 2013a](#)). Maximum likelihood methods have been considered a highly efficient method for the available data ([Duncan et al., 1998](#); [Schafer & Graham, 2002](#)). Even in the situation where data is partially MNAR, bias in estimates is isolated to a subset of analysis model parameters where complete case analysis would have biased the estimates ([Enders, 2010](#)).

2.4.3 Implications for thesis research

Our results indicate that missed outcome data in the FIP study were attributed to observed data prior to the dropout. Thus, we can assume that data were MAR ([Groenwold et al., 2012](#); [Ibrahim & Molenberghs, 2009](#)) as compared to being MCAR. Results also indicate that the average depression and anxiety scores for all rounds of data collection were higher for the missing mothers as compared with non-missing mothers. Thus, there is a chance that the outcome data could be partly missing not at random instead of complete MAR. Under these conditions complete case analysis with covariate adjustment and multiple imputation both produce unbiased estimates ([Groenwold et al., 2012](#); [Schafer & Graham, 2002](#)). Thus, MI seems to be the most appropriate strategy for the drop-out cases in repeated measures data where the underlying mechanism of missingness is both MAR and MNAR, followed by complete case analysis and mixed models if adjustment is made for the baseline covariates ([Groenwold et al., 2012](#))

Given the six patterns identified, our data were missing non-monotonically, and the proportion of participants missing one or more waves of data collection were 48.6%. Another limitation of our data were large time gap (approximately three years) between the third and fourth rounds of data collection which means that there was a need to include the time periods of data collection to inform the residual variance covariance structure to produce unbiased results. Second, imputation of the fourth round of data based on the previous three rounds of data especially after a gap of three years would have produced biased estimates for both depression and anxiety scores as they are proposed to be dependent on other time-varying covariates in the study. Third, it was impossible to impute the child outcome measures that were measured at only the fourth round of data collection we were limited to perform analysis on the participants who completed the fourth round of data collection (pattern 1 and 6) in the analysis. Thus, with such a large proportion of outcome and covariate data missing and a large time gap between the third and fourth round of data collection, multiple imputation based approaches were not recommended. At a hindsight, low coefficient of determinations (r^2) computed after the lagged variable analysis (Chapter 4 – Table 4-5 and Table 4-9) provides additional evidence that MI-based methods could have seriously biased the results of the analyses represented in the subsequent chapters.

2.5 Conclusions

We have used ML based mixed models to model the course of longitudinal depression and anxiety scores using the observed covariates from all rounds of the study. We used linear mixed models with random intercept to model the repeated measures within the individual and an exponential correlation structure and non-integer time in weeks since the first visit to account for non-equidistant time points to account for the missing data in the study ([Dohoo et al., 2012](#); [Kreft](#)

[et al., 1998; Rabe-Hesketh & Skrondal, 2012](#)). We do not assume that we were able to handle the MNAR component of the data loss; however, for MAR component ML-based methods have been widely accepted and produce unbiased estimates. However, the generalizability of our study results is limited to predominantly Caucasian mothers with above average family income, and who have some post-secondary education.

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**CHAPTER 3: DIMENSIONS UNDERLYING THE CBCL AND PATTERN
OF ITEM-FACTOR RELATIONSHIP OF CBCL/1.5 – 5 YEARS
OBSERVED AMONG CANADIAN-THREE-YEAR OLDS**

Abstract

The Child Behaviour Checklist (CBCL) (1.5 – 5 years) is a widely-used measure of behavioural and emotional functioning in preschool children. Factor analytic studies of the preschool CBCL have so far produced mixed results. This study was undertaken to examine the number of underlying dimensions of the CBCL among a cohort of Canadian preschoolers and to measure the reliability of individual subscales. Data from 343 children who completed the fourth round of the Feelings in Pregnancy and Motherhood study (FIP) were analyzed using Mplus7.3. Robust weighted least squares estimator (WLSMV) with polychoric correlation. Weighted root means square residuals (WRMR), root means square error of approximation (RMSEA), and Comparative Fit and Tucker Lewis (CFI, TLI) indices were used to assess the model fit. The original model with seven first-order latent variables and two second-order latent variables did not converge. Six of the seven (except somatic problems) individual first-order latent variables of aggression, attention problems, anxiety/depression, emotionally reactive, withdrawn behaviour, and sleep problems had a good fit to the data (RMSEA<.05, CFI/TLI>0.95/0.95, WRMR<1.0). However, the emotionally reactive subscale was highly correlated with the anxiety/depression subscale (estimated correlation of 1.1). Both the correlated first-order model of the five remaining latent variables (RMSEA=0.03, CFI/TLI=0.95/0.95, WRMR=0.97) and the second-order model had a good fit to the data. In the second-order model aggression and attention problems loaded on externalizing behaviour and anxiety/depression, withdrawn, and sleep problems loaded on internalizing behaviour (RMSEA=0.03, CFI/TLI=0.96/0.96, WRMR=0.96). CBCL (1.5 – 5 years) individual subscales of aggression, attention problems, anxiety/depression, and sleep problems were reliable measures of emotional and behavioural development of three-year-olds in Canada and were, therefore, available for subsequent analyses examining the impact of maternal mental health on early childhood development.

3.1 Introduction

Childhood behaviour problems can be classified as internalizing or externalizing. Early childhood internalizing behaviour problems increased the probability of depression, anxiety, and suicide in teenagers and adults ([Farrington, 1989](#); [Moffitt, 1993](#); [Raine, 2002](#)). Whereas, externalizing behaviour problems in early childhood increase the probability of juvenile delinquency in adolescence and adult crime and violence ([Farrington, 1989](#); [Moffitt, 1993](#); [Raine, 2002](#)). Thus, identifying early childhood behaviour problems is critically important for understanding and preventing behavioural problems later in life ([Liu et al., 2011](#)). However, there is a debate about the taxonomies and criteria for diagnostics used in children ([Hartman et al., 1999](#)). Clinically derived taxonomies have been criticized for their lack of empirical support and empirically derived taxonomies have not provided consistent links between symptoms and specific problem dimensions ([Achenbach, 1995](#); [Quay & Werry, 1979](#)).

Empirically designed and normed under the broad umbrella of classical test theory (CTT), the Child Behaviour Checklist (CBCL) is widely used by researchers, clinicians, and other professionals to measure behavioural and emotional functioning in children ([Lambert et al., 2003](#)). Under classical test theory, raw test scores from all items are summed up. There is no regard to how an individual item was answered. The CBCL represents a major effort towards a quantitative empirically defined taxonomy of childhood psychopathology. The current versions of the CBCL/1.5-5 and C-TRF were published in 2000 in English ([Achenbach & Rescorla, 2000](#)). This was a re-normed version of CBCL/ 2- 3 and only two items out of 99 items were replaced, and six were further qualified ([Konold et al., 2003](#)). However, substantial changes to the factor structure in both number and composition were reported ([Achenbach & Rescorla, 2000](#)). Normative scores for CBCL/1.5-5 have been developed from 700 non-referred girls and boys between 18 - 71 months of age from 40 states across the US using the 1999 national survey

sample of pre-schoolers ([Achenbach & Rescorla, 2000](#)). First-order syndromes were emotionally reactive, anxious/depressed, somatic problems, withdrawn behaviour, sleep problems, aggressive behaviour, and attention deficit. Second-order latent variables were internalizing and externalizing behaviour, and the third order latent variable was total problem scores ([Achenbach & Rescorla, 2000](#)).

Internalizing and externalizing behaviour problem patterns were identified using second-order unweighted least squares (ULS) factor analysis ([Achenbach & Rescorla, 2000](#)). Aggression behaviours and attention problem syndromes loaded on externalizing behaviour, and emotionally reactive, anxious/ depressed, somatic problems, and withdrawn syndromes loaded on internalizing behaviour ([Achenbach & Rescorla, 2000](#)). The sleep problem syndrome did not load well on the either of the second-order latent factors ([Achenbach & Rescorla, 2000](#)). For the first-order syndromes, scores ranging between 93rd to 97th percentile were labelled borderline and above 97th clinical warranting consideration of professional help ([Achenbach & Rescorla, 2000](#)). The borderline clinical range for the internalizing and externalizing behaviours was lowered to approximately 83rd through 90th percentile and clinical range above the 90th percentile ([Achenbach & Rescorla, 2000](#)).

The generalizability of an instrument's syndrome structure across populations, both healthy and unhealthy, termed as 'configural invariance' is an integral component of measurement invariance ([Schmitt & Kuljanin, 2008](#); [Vandenberg & Lance, 2000](#)). Thus, when an instrument developed in one population is applied in another population, it should measure the same constructs in the new society. Konold et al. ([2003](#)) tested the CBCL/1.5–5 syndrome model using CBCL data obtained in the National Institute of Child Health and Development Study of Early Child Care (NICHD SECC) in United States and concluded that the single-factor

(total problem score) and three-factor model (internalizing, externalizing, and sleep) fit the data poorly ([Konold et al., 2003](#)). The seven-factor model fit the data well when it was reduced to six factors by combining the Emotionally Reactive and Anxious/Depressed factors ([Konold et al., 2003](#)). Tan et al. ([2007](#)) replicated the procedures of Achenbach and Rescorla by performing Confirmatory Factor Analyses (CFA) on tetrachoric correlations. They also performed CFA on polychoric correlations. CFAs of both types of correlations supported the seven-syndrome model among a sample of Australian girls adopted from China ([Tan et al., 2007](#)).

Factor analytic studies of the preschool CBCL have thus produced somewhat mixed results. To date, no peer-reviewed papers have been identified which examined the configural invariance among Canadian preschoolers. Thus, this study was undertaken to examine the number of underlying dimensions of the CBCL and the pattern of item-factor relationship among Canadian preschoolers. The second objective of this analysis was to measure the reliability (accuracy and precision) of the model thus constructed and report the item difficulty parameters of the individual syndromes. The resulting model was used in a subsequent analysis to explore risk factors for psychopathology in preschoolers from the Canadian province of Saskatchewan.

3.2 Methods

3.2.1 Study sample

The study sample was part of longitudinal ‘Feelings in Pregnancy and Motherhood’ (FIP) study Canadian women who were recruited in early pregnancy (T1) (17 weeks \pm SD 4.4) and observed for children outcomes during early postpartum (T3) (4 weeks \pm SD 2.0 weeks after birth) and three-years after birth (T4) (36.4 months \pm SD 1.6 weeks) ([Bowen et al., 2012](#)). Three hundred and thirty-eight mothers (333 singleton pregnancies and five twin pregnancies)

completed the fourth phase of data collection when their children were three-years-old. Data from these 343 children (333 singleton births and ten twin births) were included in this analysis.

3.2.2 CBCL data collection tool

The CBCL was a paper and pencil survey which was completed by the child's primary caregivers to describe the child's functioning over the last two months. Each caregiver indicated how often their child displayed emotional or behavioural problems by endorsing one of three item response options: 0 '*Not true*', 1 '*Somewhat or Sometimes True*', or 2 '*Very True or Often True*'. Thus, total scores can range between 0 – 200. All surveys were scored by members of the assessment team and scores for each item were entered into SPSS. Based on the guide for manual computation of the scores, syndrome-specific total scores for aggressive behaviours, attention problems, anxious/depressed, emotionally reactive, somatic problems, withdrawn behaviour and sleep problems were computed; followed by computation of internalizing and externalizing behaviour scores for each participant ([Achenbach & Rescorla, 2000](#)). These scores were further used for the preliminary factor analysis.

The rationale underlying factor analysis applies to continuous and categorical variables alike. Factor analysis of continuous observed variables and continuous latent variables using full information maximum likelihood function was called Confirmatory Factor analysis (CFA) ([Long, 1983](#)); whereas, the analysis of ordered categorical (ordinal, Likert scale) observed variables and continuous latent variables using limited information methods was called Item Factor Analysis (IFA) ([Mislevy, 1986](#); [Reise et al., 1993](#)). IFA models within the item response theory framework were specifically developed for categorical responses ([Lord, 1980](#); [Wirth & Edwards, 2007](#)). The objective of IFA like CFA is to confirm hypothesized factor structure and obtain estimates for each parameter of the measurement model (i.e., factor loadings, factor

variances and covariance, indicator error variance, and possibly error covariance) that produce a predicted variance–covariance matrix that resembles the sample variance–covariance matrix as closely as possible ([Edwards, 2010](#); [Hoffman, 2014](#); [Muthén, 1984](#)). However, limited information methods do not use the original data but create a ‘tetrachoric’ (for the binary observed variables) or ‘polychoric’ (for categorical observed variables) variance-covariance matrix which is used as input data ([Muthén, 1983](#); [Muthén, 1984](#)).

In the case of complex models, it could be more effective to begin by fitting only portions of the model initially, and then use the resulting parameter estimates as starting values in the larger solution ([Brown, 2006](#); [Hoffman, 2014](#); [Pandolfi et al., 2009](#)). In CFA, we assess ‘measurement invariance’ also known as ‘factorial invariance’ or ‘measurement equivalency’ which measures the extent to which the psychometric properties of the observed indicators are transportable or generalizable across groups. In IFA/IRT, lack of measurement invariance is known as ‘differential item functioning’. Hence, from here forward we will only use the term Item Factor Analysis (IFA) for reporting our methods and results. Item factor analysis was performed using Mplus vs7.3 ([Muthén & Muthén, 2014](#)).

3.2.3 CBCL item structure

The CBCL is 100 item scale; data from 343 children pertaining to 67 of the 100 items of the CBCL scale were included in the analysis (Figure 3-1). The remaining 33 items were labelled as others and were used to compute total problem score, which was the total of the scores obtained for the child ([Achenbach & Rescorla, 2000](#)).

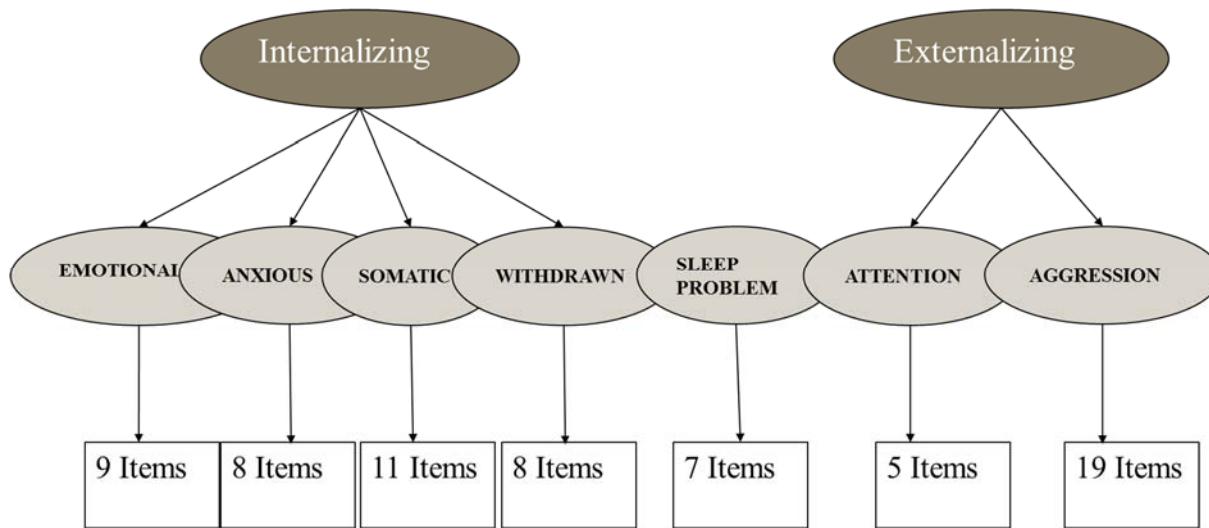


Figure 3-1: Item distribution and structure of the seven first-order latent variables and two second-order latent variables of CBCL 1.5 – 5 years as described by the developers ([Achenbach & Rescorla, 2000](#)).

3.3 Missing data

There were 14 missing data points from the 22,981 total CBCL (1.5 – 5 year) data points collected in this study, representing only 0.02% of all data points used in the IFA. The missing data had no systematic pattern across participants or items i.e., missing data were observed across 12 different items, and 12 subjects had at least one missing data point. Little's MCAR test (chi-square (119) = 84, p-value = 0.99) was not significant ([Little, 1988](#)). Hence, the data were considered to be missing completely at random (MCAR) and manual imputation by median scores was initiated thereby utilizing the full capacity of the Mplus program to perform Item Factor Analysis.

3.4 Multivariate normality

Multivariate normality was checked by Doornik Hansen Chi-square test ($\chi^2 (14) - 1.34 e^{+05}$, p-value <0.0001) and variables with high kurtosis scores were identified ([Doornik & Hansen, 2008](#)). Eight items were found to have high kurtosis scores (values>25) (item 39 (Headaches), item 45 (Nausea), item 46 (Twitches), item 67 (Unresponsive to affection), item 70

(Little affection), item 71 (Little interest), item 90 (Sad), and item 93 (Vomits)) and were removed from the analysis ([Brown, 2006](#); [Hoffman, 2014](#)). Initial removal of these items with high kurtosis scores also resolved the issues of empty cells and highly negative correlations between the pairs of items.

3.5 Estimation methods

Because there were categorical observed items and continuous latent variables, robust weighted least squares estimator (WLSMV) with polychoric correlations and delta parameterization was used for the item-level IFAs ([Jöreskog, 1994a](#); [Muthén & Muthén, 1998 - 2012](#); [Muthén, 1983](#)). For the second-order model, model identification (anchoring) was achieved by fixing the marker item factor loading to 1, and freeing the factor loadings of the first-order latent factors on to the second-order latent factors, and fixing the factor variance and factor mean of the second-order latent factors to one and zero respectively ([Hoffman, 2014](#)). This was done to allow the computation of correlation between the second-order latent factors.

WLSMV estimator in Mplus first computes a sample correlation matrix based on the data (tetrachoric, polychoric) and then fits the model based on the correlation matrix independent of the input data, thereby estimating the model parameters directly ([Muthén & Muthén, 1998 - 2012](#)). The goal is to have the predicted correlation matrix similar to the observed matrix ([Brown, 2006](#)). Additional information on polychoric correlation methods is provided in Appendix 3-A).

3.6 Empty cells

Mplus polychoric correlation matrices for CBCL were analyzed in the item level IFAs ([Muthén & Muthén, 1998 - 2012](#)). Several item pairs evidenced at least one ‘zero frequency’ cell in the 3x3 polychoric table. One of the options that have been used is dichotomization of the item

scores to ‘zero’ and ‘one or two’ to reduce the number of empty cells in the tetrachoric correlation matrix ([Achenbach & Rescorla, 2000](#); [Pandolfi et al., 2009](#)). The second option is to retain the original data structures (Likert) and check for lack of convergence due to empty cells in the polychoric matrix after every iteration of the model ([Konold et al., 2003](#)). Comparison of the tetrachoric and polychoric matrices revealed a similar proportion of empty cells; however, items corresponding to the empty cells were slightly different. So, it was decided to keep the original Likert scale data for further analysis and deal with the items with empty cells during the IFA.

3.7 Model structure tested

The initial IFA of the complete second-order CBCL model with correlated second-order internalizing and externalizing behaviours and sleep problems after the removal of the above-mentioned highly kurtotic items did not converge (Figure 3-1). Similarly, the first-order correlated seven individual syndrome model (Figure 3-2) of aggressive behaviour, attention problems, anxious/depressed, emotionally reactive, somatic problems, withdrawn behaviour, and sleep problems did not converge.

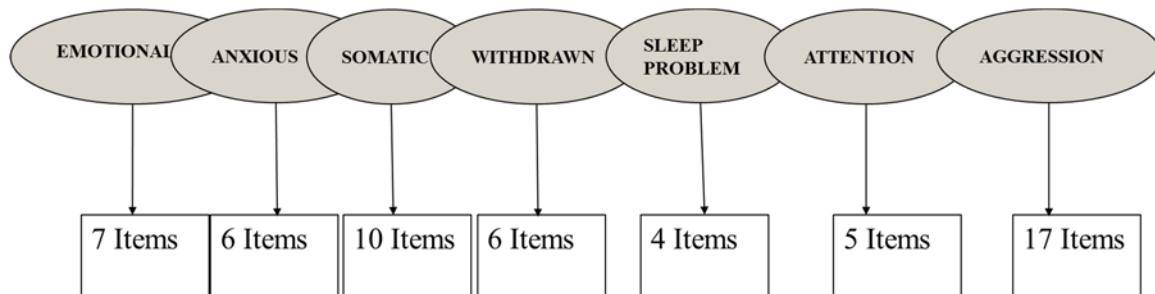


Figure 3-2: First-order individual syndrome scales after the removing highly kurtotic items that were used to test individual model fit.

Hence, we used the three-step strategy as suggested by Pandolfi ([2009](#)). First, item scores within each of the first-order syndromes of aggressive behaviour, attention problems,

anxious/depressed, emotionally reactive, somatic problems, withdrawn behaviour, and sleep problems scales were examined to evaluate the fit of the items with the underlying latent factors. Items loading poorly (<0.2) or which were not significant ($p>0.05$) were removed ([Geiser, 2012](#); [Harrington, 2009](#); [Pandolfi et al., 2009](#)). Item correlation based on the modification indices were used to improve the fit ([Bollen, 1989](#); [Byrne, 2013](#); [Byrne, 1989](#); [Kline, 2015](#)). In the second step, all the individual syndromes that were a good fit were included in a model to understand the correlation structure of these re-structured syndromes ([Pandolfi et al., 2009](#)). The use of the correlated model structure is consistent with previous IFA studies on the measurement structure of CBCL ([De Groot et al., 1994](#); [Dedrick et al., 1997](#); [Tan et al., 2007](#)).

Finally, a second-order model structure was constructed based on the estimated correlations of the factor latent variables from step 2 and tested to evaluate the existence of higher order model structure as proposed by the authors and then to assess the fit to the data.

Model fit statistics were computed and compared from step 2 and 3 using ‘Difftest’ which is a chi-square test of the difference between two nested models ([Asparouhov et al., 2006](#); [Muthén & Muthén, 1998 - 2012](#)). The second-order model is more restricted with more degrees of freedom and is nested in the first-order model. If the chi-square test is not-significant ($p>0.05$), this indicated that constraining the parameters of the nested model (2nd order) did not significantly worsen the fit of the model. Hence, 2nd order model was considered to have a better fit ([Hoffman, 2014](#); [Muthén & Muthén, 1998 - 2012](#)).

3.8 Assessing model fit

For each item to be retained as a potential candidate for each factor variable, we applied the same criteria as the authors including: factor loadings must be significant ($p<0.10$),

standardized loadings exceeded 0.2, and the sign of the loadings was positive ([Achenbach & Rescorla, 2000](#)).

Due to the categorical nature of our data, a residual based fit index - weighted root mean square residual (WRMR) was used to measure the absolute fit of the models. It measures the weighted average differences between the sample and estimated population variance and covariance ([Muthén & Muthén, 1998 - 2012](#); [Yu, 2002](#)). WRMR evaluated the hypothesis that observed and predicted matrices match. The recommended upper limit is 0.9/1 ([Brown, 2006](#); [Hu & Bentler, 1999](#); [Marsh et al., 2004](#); [Yu, 2002](#)).

Root mean square error of approximation (RMSEA) is an absolute index that assesses the extent to which a model fits the population covariance matrix as compared to the hypothesized parameter estimates ([Browne et al., 1993](#); [Steiger & Lind, 1980](#)). It is sensitive to the number of parameters, but insensitive to sample size. RMSEA has a known distribution permitting the calculation of confidence intervals and a p-value ([Muthén & Muthén, 1998 - 2012](#)). An RMSEA value of ‘0’ indicates perfect fit and the recommended upper value is 0.05 ([Brown, 2006](#); [Hu & Bentler, 1999](#)). The confidence interval of RMSEA indicates the precision of the RMSEA point estimate ([Muthén & Muthén, 1998 - 2012](#)).

The Comparative Fit Index (CFI) and Tucker-Lewis Index (TLI) evaluated the fit of the model as compared to the baseline model ([Bentler, 1990](#); [Bentler & Bonett, 1980](#); [Tucker & Lewis, 1973](#)). The base model was one in which the co-variances among all input indicators are fixed to zero ([Hoffman, 2014](#)). CFI has a range of possible values from 0.0 to 1.0; whereas, TLI can have values greater than 1.0. Values closer to 1.0 indicate a good fit ([Hu & Bentler, 1999](#)). Hu & Bentler ([1999](#)) suggests the cut- off value of >0.95 for CFI & TLI.

However, WRMR, RMSEA, and CFI/TLI are only meaningful if the model is over-identified which means that the number of input parameters in variance – covariance matrix exceeds the number of freely estimated model parameters (factor loadings, factor correlations) ([Brown, 2006](#)). For a just-identified model, a minimum of three items are required for each latent variable for the computation of one unique set of parameters that perfectly fit the input matrix. Hence, the goodness of model fit evaluation does not apply as, by nature, the model has a perfect fit ([Brown, 2006](#); [Geiser, 2012](#)).

Other model evaluation methods included the identification of localized areas of strain with standardized residuals >1.96 , modification indices – a critical value of 3.84 or greater (reflects significant change in the model if the fixed or constrained parameter was freely estimated), interpretability, size and statistical significance of the model's parameter estimates (standardized factor correlations >1.0 , negative factor variances or negative indicator error variance) ([Brown, 2006](#); [Hoffman, 2014](#)).

3.9 Model output and reliability measures

Observed dependent variables were referred to as ‘factor indicators’ or ‘items’. and the continuous latent variables were referred to as ‘factors’ or ‘latent trait’ ([Yang & Kao, 2014](#)). IRTs were a collection of logistic regression models for ordered categorical factor indicators that attempted to explain item response in terms of item parameters and person’s trait (ability/latent variable) ([Edwards, 2010](#); [Edwards & Wirth, 2009](#); [Muthén & Muthén, 1998 - 2012](#); [Yang & Kao, 2014](#)).

Latent trait (θ), factor loadings (FL), thresholds (t), item characteristic curves (ICCs) and item information curves (ICs) were part of the IRT model output using Mplus and were used to describe the scale parameters and measure reliability. Additional information on these parameters

is provided in Appendix 3-B- Detailed description of item response theory-based model parameters and methods used to compute them.

Factor loadings for each item were the assessment of the relationship of the variable with the underlying latent trait and could be interpreted as standardized regression coefficients ([Brown, 2006](#); [Hoffman, 2014](#)). A threshold or cut-off was the expected value of the latent response variable at which an individual transitioned from a value of ‘0’ to ‘1’ of the categorical outcome variable and were used to compute the same number of ‘Item Difficulty’ or ‘location’ parameters ([Baker, 2001](#); [Hoffman, 2014](#)). Item difficulty describes how difficult it was to achieve a 50% probability of a correct response for a specific item given the respondent’s level of the latent trait ([Bauer & Hussong, 2009](#); [Yang & Kao, 2014](#)). Thus, the location of the curve on the ‘x-axis’ measures the difficulty ([Baker, 2001](#); [Hoffman, 2014](#)).

Item Discrimination (also called ‘slope’ of the curve) determines how well items identify the person at different levels of the latent trait; steeper slopes translate into better discrimination at a given theta (latent trait) level ([Baker, 2001](#); [Yang & Kao, 2014](#)). Unstandardized factor loadings can be used to compute the discrimination parameter ([Hoffman, 2014](#); [Yang & Kao, 2014](#)). For an item to be discriminatory, it should have a high slope and narrow base, which translates into an item that had the ability to identify a specific characteristic (also referred to as ‘shape’ parameter) ([Baker, 2001](#)). In our case, each item was measured on the three-point Likert scale; 0 ‘*Not true*’, 1 ‘*Somewhat or Sometimes True*’, or 2 ‘*Very True or Often True*’. Hence, each of the items would have two difficulty parameters and one discrimination parameter.

ICCs were the graphical presentation of the location, slope, and shape parameters of the items on the latent trait and were an estimate of the probability that a patient will endorse a

particular response option ([Yang & Kao, 2014](#)) (Figure 3-3). Test characteristic curve (TCC) was obtained by summing each ICC across the latent trait continuum ([Baker, 2001](#)).

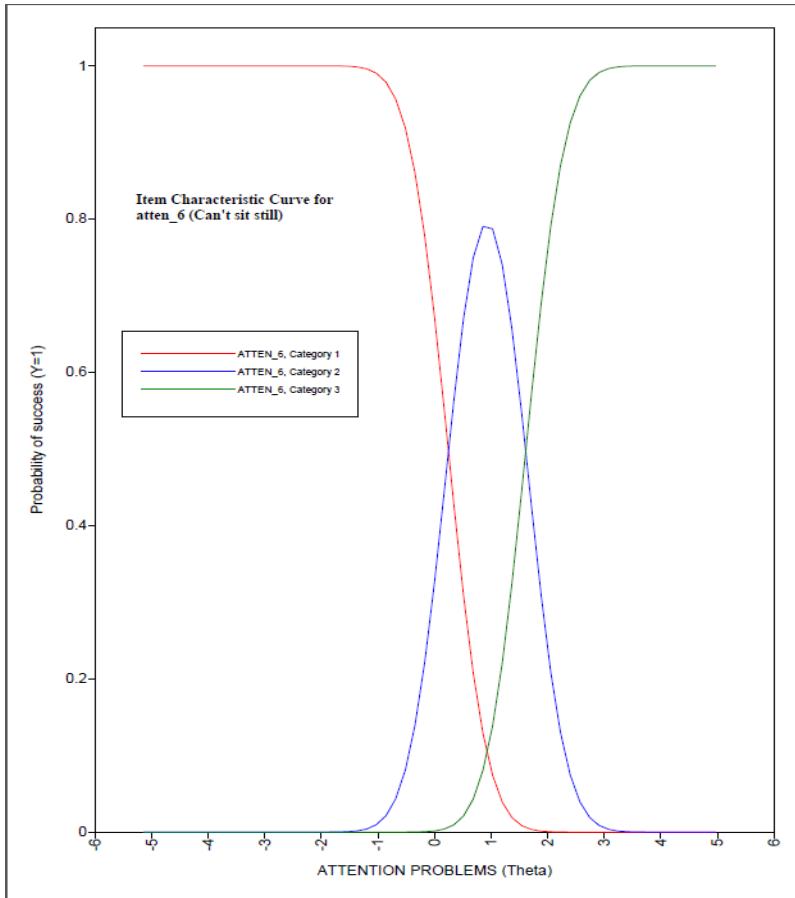


Figure 3-3: Sample Item Characteristic Curve (ICC) for item 6 (Can't sit still) loading on the attention deficit subscale indicating good discrimination (shape and slope) properties and item with relatively high difficulty as the item span between -1 and +3 on the trait scale.

Information, the inverse of precision with which a parameter could be estimated, can be used to compute reliability estimates for items and sum of items ([Baker, 2001](#); [Hoffman, 2014](#)). Information curves (ICs) represents the information against the continuous latent trait and data can be extracted from Mplus to obtain information ([Baker, 2001](#); [Hoffman, 2014](#)). Reliability of the scale could be computed from the information using the formula (information/ (information +1)). Thus for test information function of 4, computed reliability is 0.8 (4/ (4+1)) ([Hoffman,](#)

[2014](#)). Test information scores of less than 4, indicate that the scale is not reliable ([Hoffman, 2014](#)).

Standardized item factor loadings (p-values) and residual variances from individual syndromes, first-order correlated factor structure models, and second-order correlated models were reported. In addition, item difficulty parameters and the test information (reliability) of individual syndromes were reported.

3.10 Results

Data from 343 children with a mean age 36.6 months \pm SD 3.8 were included in this analysis. Slightly more than half (180, 52.5%) were girls. Most children (324, 94.5%) were reported to be in very good to excellent health. Both parents were Caucasian (300, 87.5%) for most children and 9% (31) of the parents reported being mixed Caucasian. Most participants 88.6% (304) were part of families with an annual income greater than \$40,000 CAD.

3.10.1 Step 1: Item factor analysis of individual behavioural syndromes

Because each item can have a minimum score of ‘0’ and a maximum score of ‘2’, the total item score possible for internalizing behaviour was 72 points, for externalizing behaviour was 48 points; observed scores ranged up to 29 for internalizing behaviour and up to 39 for externalizing behaviour.

Table 3-1: Mean (standard deviation), median (interquartile range) and range^a of the observed first-order and second-order latent variables and maximum scores possible based on the original scale ([Achenbach & Rescorla, 2000](#)).

	Observed Syndromes						
	Emotionally reactive	Anxious/depressed	Somatic problems	Withdrawn behaviour	Sleep problems	Attention problems	Aggressive behaviour
Maximum scores possible	18	16	22	16	14	10	38
Range of scores observed^a	0-10	0-8	0-7	0-8	0-11	0-8	0-32
Mean (SD)	1.9 (1.8)	1.7 (1.7)	1.5 (1.6)	1.0 (1.2)	2.8 (2.5)	1.8 (1.6)	8.3 (5.7)
Median (IQR)	1.0 (1.0, 3.0)	1.0 (0.0, 3.0)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	2.0 (1.0, 4.0)	1.0 (1.0, 3.0)	8.0 (4.0, 12.0)
	Internalizing behaviour				Externalizing behaviour		
Maximum scores possible	72				48		
Range of the scores observed	0-29				0-39		
Mean (SD)	6.2 (4.7)				10.2 (6.8)		
Median (IQR)	5.0 (2.0, 9.0)				10.0 (5.0, 14.0)		

^aRange reported as (minimum, maximum).

3.10.1.1 Emotionally reactive

The original model was built with eight of the nine items; item 46 (Twitches) (removed initially due to kurtosis (30.9)), had a poor fit (RMSEA >0.05, CFI/TLI <0.9, WRMR >1.0). Item 97 (Whining) (FL = 0.4, residual variance = 0.9) was further removed due to low standardized factor loadings to improve the fit. The final model that best fit the data were without items 46 and 97, and it included correlations between item 82 (Moody) and item 79 (Shifts between sad and excited) (estimate (standard error) - 0.64 (0.084)), as well as between item 92 (Upset by new) and item 21 (Disturbed by change) (estimate (standard error) - (0.43 (0.09))). The final seven item model was over-identified (22 free parameters) and fit the data reasonably well (RMSEA = 0.036, CFI/TLI = 0.98/0.97, WRMR = 0.64) (Appendix 3-C - Table 1 & Table 2, Figure 3-4).

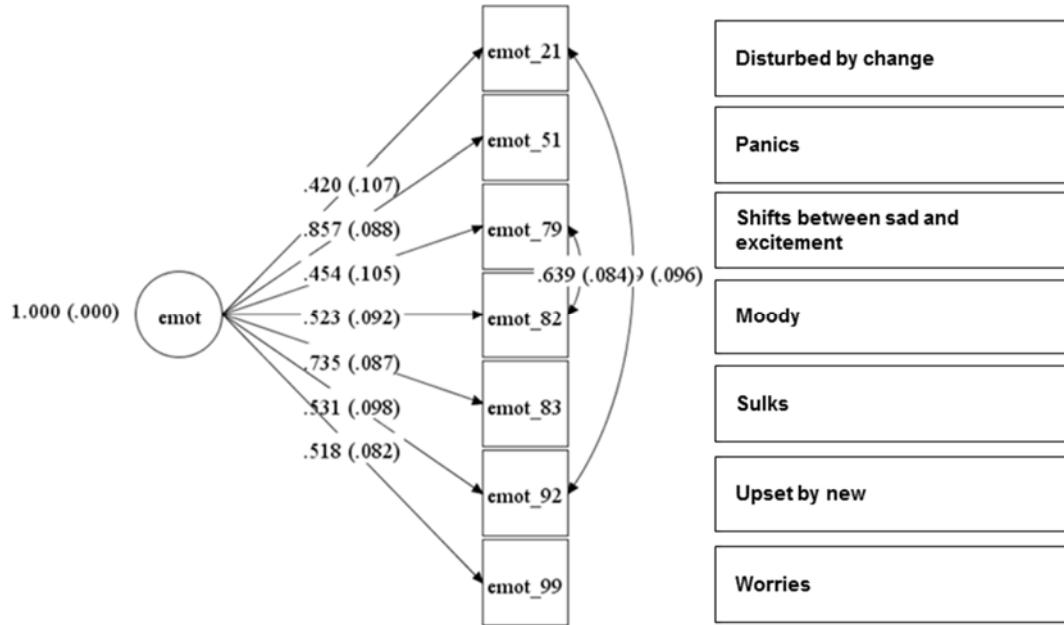


Figure 3-4: Summary of item standardized factor loadings (standard error) and item correlations (standard error) for the emotionally reactive latent variable. ‘emot’ represents the latent variable emotionally reactive. Unidirectional arrows represent the factor loadings of items on the latent variable, and bi-directional arrows represent the correlations amongst the items.

3.10.1.2 Anxious/depressed behaviour

The original model, built with seven of the eight items (item 90 (Sad) removed due to kurtosis scores of 26.6), had a reasonable fit ($\text{RMSEA} = 0.05$ (0.02 – 0.08), $\text{CFI}/\text{TLI} > 0.95$, $\text{WRMR} < 0.9$). Items 43 (Looks unhappy) and 68 (Self-conscious) were sequentially removed based on low factor loadings and very high residual variance ($\text{FL} = 0.3$, residual variance = 0.9 for both). The final model had five uncorrelated items. Item 33 (Feelings hurt) had negative threshold values. This indicated that mothers who indicated their children reported feeling hurt were less likely to report their child being anxious which might also be the reason for low standardized factor loadings. However, the final model with five of the eight items was over-identified (14 free parameters) and fit the data reasonably well ($\text{RMSEA} = 0.04$, $\text{CFI}/\text{TLI} = 0.98/0.97$, $\text{WRMR} = 0.56$) (Appendix 3-C - Table 1 & Table 2, Figure 3-5).

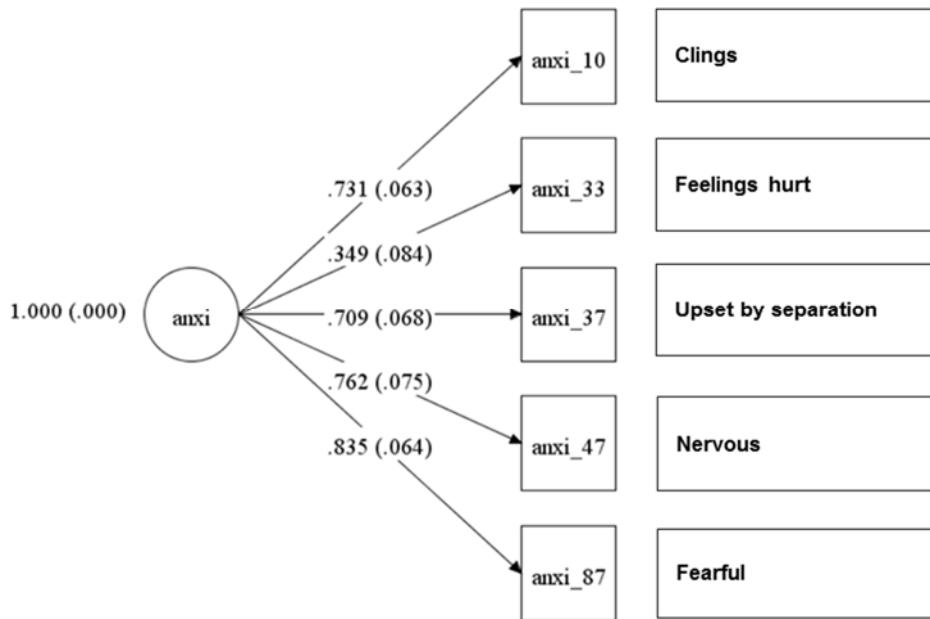


Figure 3-5: Summary of item standardized factor loadings (standard error) and item correlations (standard error) for the anxious/depressed latent variable. ‘anxi’ represents the latent variable anxious/depressed and unidirectional arrows represent the factor loadings of items on the latent variable.

3.10.1.3 Somatic problems

The original model built after the removal of the highly kurtotic items; item 39 (Headaches), item 45 (Nausea), and item 93 (Vomits) had a poor fit ($\text{RMSEA} = 0.16$, $\text{CFI}/\text{TLI} = 0.57/0.41$, $\text{WRMR} = 2.33$). Item 19 (Diarrhoea) did not have significant factor loading. Items 7 (Can’t stand things out of place) and 86 (Too concerned with neatness and cleanliness) had negative standardized factor loadings and items 1 (Aches) and 52 (Painful bowel movements) had high modification indices. Hence these items were sequentially removed and correlation added in an attempt to improve the model fit parameters. The resultant four item model was over-identified (10 free parameters) and was the best fitting model; although the model still did not fit the data well ($\text{RMSEA } 0.11$, $\text{CFI}/\text{TLI} = 0.68/0.04$, $\text{WRMR} = 0.94$) (Appendix 3-C – Table 1 & Table 2, Figure 3-6). Any further attempts to improve the model fit resulted in under-identified

scale (less than three items on the scale). Hence it was decided to remove the somatic problem scale from further analysis.

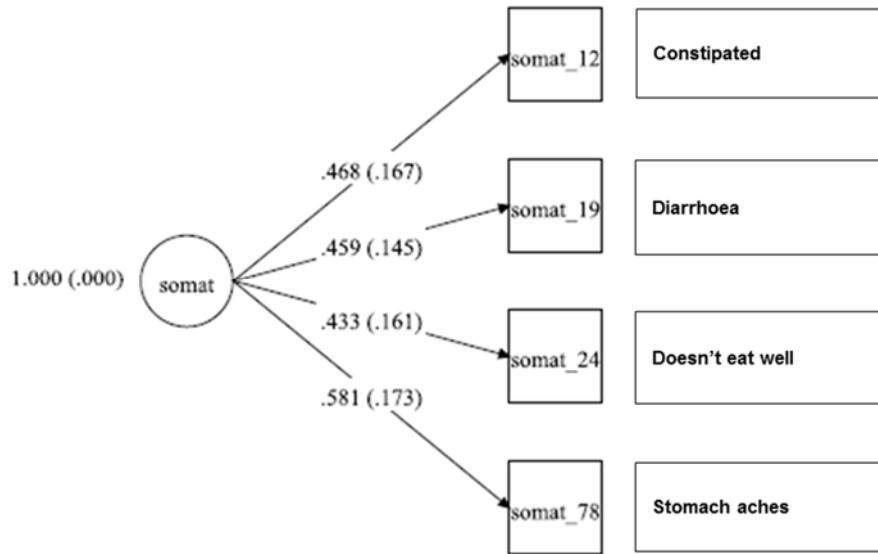


Figure 3-6: Summary of item standardized factor loadings (standard error) and item correlations (standard error) for the somatic problems latent variable. ‘somat’ represents the latent variable somatic problems and unidirectional arrows represent the factor loadings of items on the latent variable.

3.10.1.4 Withdrawn behaviour

Out of the eight items in the original scale, three variables, including item 67 (Unresponsive to affection), item 70 (Little affection), and item 71 (Little interest), were removed due to high kurtosis values. The base model without the three items had a poor population fit index ($\text{RMSEA} = 0.06$), although other fit indices ($\text{CFI}/\text{TLI} = 0.99/0.98$ and $\text{WRMR} = 0.6$) indicated a good fit. There was no way of improving the fit of the model, without making it just-identified (i.e., only three items remaining in the scale). Hence, this five-item scale was overidentified (15 free parameters) and considered the best fit model for withdrawn behaviour (Appendix 3-C – Table1 & Table 2, Figure 3-7).

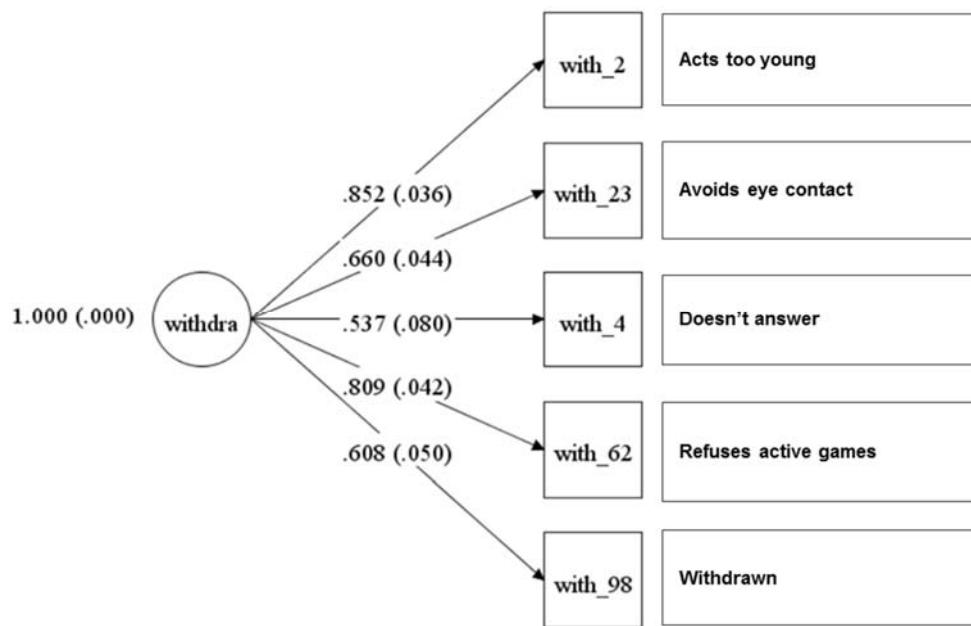


Figure 3-7: Summary of item standardized factor loadings (standard error) and item correlations (standard error) for the withdrawn behaviour latent variable. ‘withdra’ represents latent variable withdrawn behaviour and unidirectional arrows represent the factor loadings of items on the latent variable.

3.10.1.5 Sleep problems

The original sleep scale with seven items had a poor fit (RMSEA 0.119, CFI/TLI = 0.9/0.85, and WRMR = 1.3). Items with high modification index and correlated with multiple items were removed; item 64 (Resists bed) and item 74 (Sleep little). The final five item model included correlated items 48 (Nightmares) and 84 (Talks, cries in sleep) and was over-identified (16 free parameters). Model fit parameters (RMSEA = 0.05, CFI/TLI = 0.99/0.97, WRMR = 0.5) indicated a good fit (Appendix 3-C – Table 1 & 2, Figure 3-8).

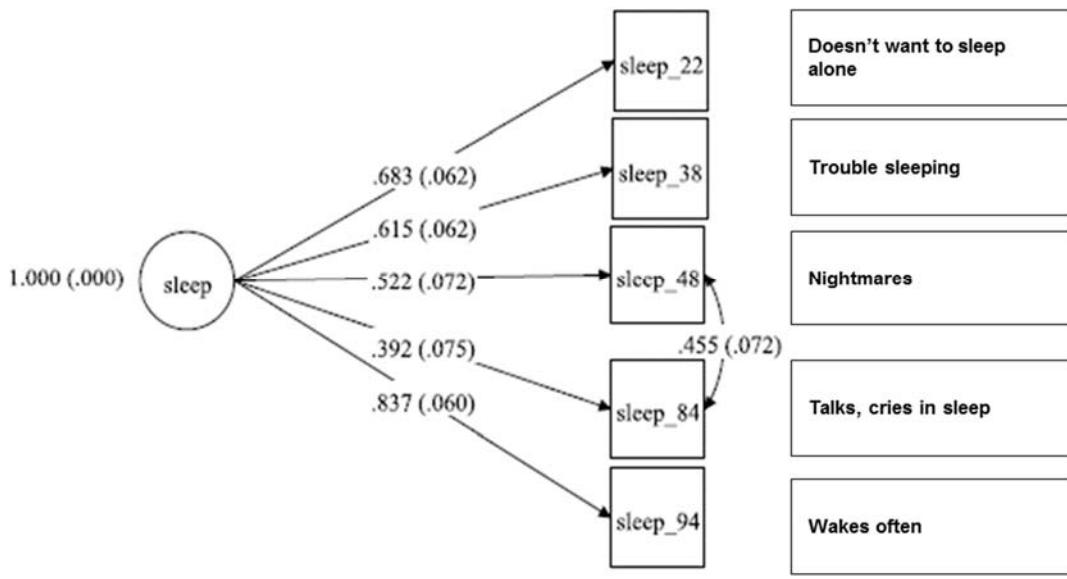


Figure 3-8: Summary of item standardized factor loadings (standard error) and item correlations (standard error) for the sleep problem latent variable. ‘sleep’ represents the latent variable sleep problems. Unidirectional arrows represent the factor loadings of the items on the latent variable, and bidirectional arrow represents correlations between the items.

3.10.1.6 Aggressive behaviour

One of the largest scales in the CBCL, aggressive behaviour initially had 19 items. The base model with all the 19 items had a poor fit ($\text{RMSEA} = 0.072$, $\text{CFI}/\text{TLI} = 0.923/0.913$, $\text{WRMR} = 1.31$). Items 8 (Can’t stand waiting), 15 (Defiant), 18 (Destroys others), 27 (Lacks guilt) and 88 (Uncooperative) were removed based on the modification indices. Items that were negatively correlated included: items 35 (Fights) and 16 (Demands met) (estimate (std. error) -0.51(0.14)), items 81 (Stubborn) and 40 (Hits others) ((estimate (std. error) -0.50(0.12))), and items 96 (Wants attention) and 40 (Hits others) ((estimate (std. error) -0.4(0.1))); their exclusion improved the model fit. The final fourteen item model with correlations was over-identified (45 free parameters) and model fit parameters ($\text{RMSEA} = 0.05$, $\text{CFI}/\text{TLI} = 0.97/0.96$, and $\text{WRMR} = 0.9$) indicated a good fit (Appendix 3-C – Table 1 & 2, Figure 3-9).

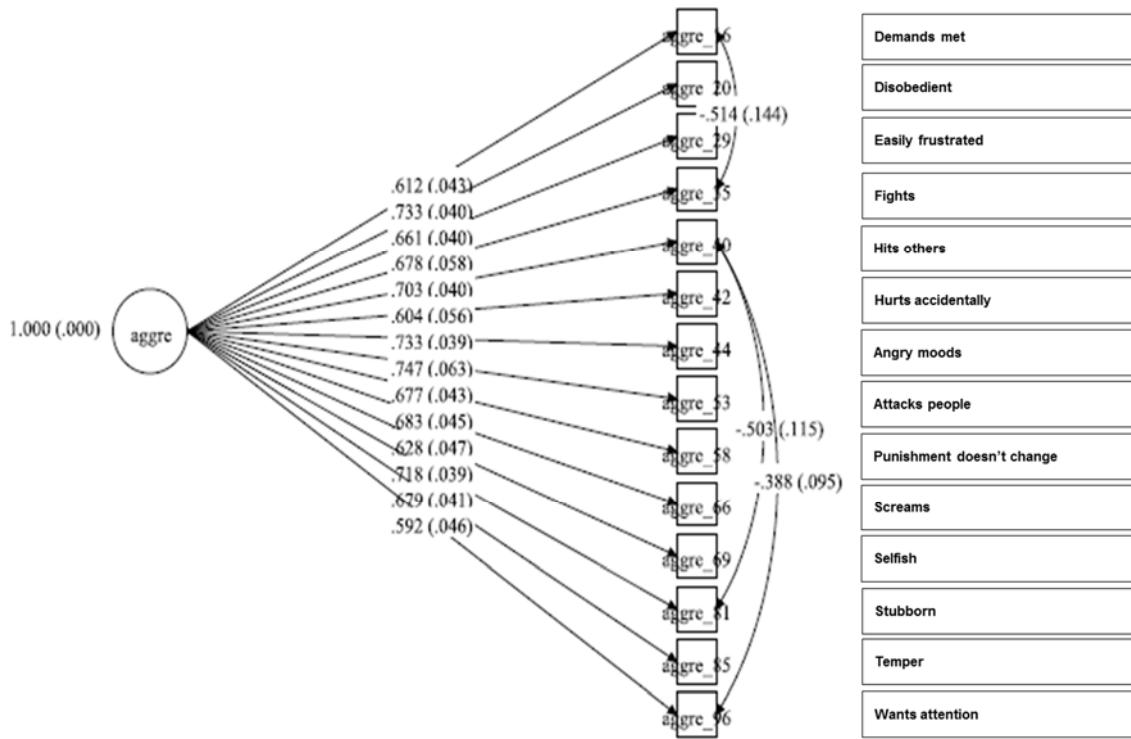


Figure 3-9: Summary of item standardized factor loadings (standard error) and item correlations (standard error) for the aggressive behaviour latent variable. ‘aggre’ represents the latent variable aggression. Unidirectional arrows represent the factor loadings of the items on the latent variable, and bidirectional arrows represent the correlation between items.

3.10.1.7 Attention problems

The original scale with all the five items fit the data well ($\text{RMSEA} = 0.0$, $\text{CFI}/\text{TLI} = 1.0/1.0$, $\text{WRMR} = 0.3$); however, item 56 (Clumsy) had to be removed from the model due to no significant factor loadings ($p\text{-value} = 0.1$). The final model with four items was over-identified (12 free parameters) and the model fit parameters ($\text{RMSEA} = 0.0$, $\text{CFI}/\text{TLI} = 1.0/1.0$, $\text{WRMR} = 0.07$) indicated a good fit to the data (Appendix 3-C – Table 1 & Table 2, Figure 3-10).

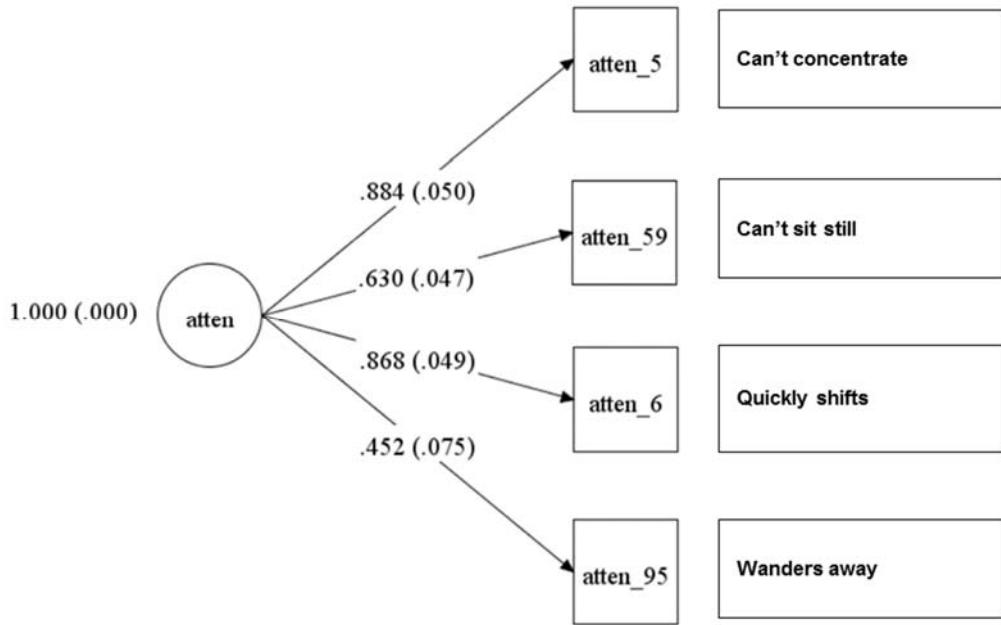


Figure 3-10: Summary of item standardized factor loadings (standard error) and item correlations (standard error) for the attention problem latent variable. ‘atten’ represents the latent variable attention problems, and unidirectional arrows represent the factor loadings of items on the latent variable.

3.10.2 Step 2: First-order correlated model

Each of these six remaining models for anxious, emotionally reactive, withdrawn behaviour, sleep problems, aggressive behaviour, and attention problems were further assessed in a correlated first-order model to assess the correlations between the latent variables. However, the model terminated with a warning and thus fit parameters and estimates were unreliable due to negative PSI matrix indicating highly correlated latent variables. Anxious and emotionally reactive had an estimated correlation coefficient of 1.06 indicating that it was impossible to statistically distinguish between the two scales (Table 3-2). This resulted in poor fit, and negative residual variances also called a Heywood case, which made the parameters in-admissible. Based on modification indices and the estimated correlation matrix, items in the emotionally reactive subscale were also highly correlated with the aggressive behaviour, anxiety, and attention

problems latent variables. The Heywood case could not be corrected through parameter fixation or setting the negative variance to zero ([Geiser, 2012](#)).

Table 3-2: Estimated correlation matrix for the six first-order latent variables of aggressive behaviour, attention problems, emotionally reactive, anxious, sleep problems, and withdrawn behaviour from the first-order correlated model structure

	Aggressive behaviour	Anxious/ Depressed	Attention problems	Emotionally reactive	Sleep problems	Withdrawn behaviour
Aggressive behaviour	1.00					
Anxious/ Depressed	0.51	1.00				
Attention problems	0.69	0.30	1.00			
Emotionally reactive	0.71	1.06	0.37	1.00		
Sleep problems	0.42	0.72	0.38	0.49	1.00	
Withdrawn behaviour	0.26	0.49	0.16	0.41	0.59	1.00

As suggested by Konold et al., ([2003](#)) merging of the emotionally reactive and anxiety subscales was also attempted. However, due to the high correlation of emotionally reactive scale items with items on anxiety, aggressive behaviour, and attention deficit subscales any attempt to improve the fit and avoid having a negative PSI matrix resulted in the loss of a large number of items from anxiety, emotionally reactive, aggressive subscales, and withdrawn behaviour subscales. Hence, the emotionally reactive subscale was removed from further analysis.

The first-order model of the remaining five subscales of anxious, sleep problems, withdrawn behaviours, aggressive behaviour, and attention problems achieved over-identification and terminated normally (Appendix 3-D – Figure 1). However, the model did not have a reasonable fit (RMSEA=0.03, CFI/TLI=0.94/0.94, WRMR=1.1). Item 22 (Doesn't want to sleep alone) was removed due to correlations with items in aggressive behaviour and anxious subscales recognizing that correlations across the latent variables were not allowed ([Geiser, 2012](#)). The

final model had a reasonable fit ($\text{RMSEA} = 0.03$, $\text{CFI}/\text{TLI} = 0.95/0.95$, $\text{WRMR} = 0.97$) (Appendix 3-C: Table 1 & 3, Appendix 3-D: Figure 1). Estimated correlation matrixes indicated that aggressive behaviours and attention problems had moderate correlation and could be combined into one second-order latent variable (Table 3-3). Similarly, estimated correlation matrix for re-specified anxious, sleep problems, and withdrawn behaviours showed moderate correlations and could be combined into another second-order latent variable (Table 3-3).

Table 3-3: Estimated correlation matrix for the five remaining first-order latent variables of aggressive behaviour, attention problems, anxious, sleep problems, and withdrawn behaviour.

	Aggressive behaviour	Attention problems	Anxious/depressed	Sleep problems	Withdrawn behaviour
Aggressive behaviour	1.00				
Attention problems	0.69	1.00			
Anxious/depressed	0.50	0.31	1.00		
Sleep problems	0.45	0.38	0.67	1.00	
Withdrawn behaviour	0.66	0.52	0.76	0.46	1.00

3.10.3 Step 3: Second-order correlated model

A second-order correlated model with aggressive behaviours and attention problems loading on externalizing behaviours and anxiety, sleep problems, and withdrawn behaviours loading on internalizing behaviour was examined. Items 16 (Demands met) 62 (Refuses active games) and 98 (Withdrawn) were removed due to highly correlated items with the aggression and anxious/depressed subscale and unmeasurable residual variance for the aggression subscale. The second-order model achieved a reasonable fit ($\text{RMSEA} = 0.03$, $\text{CFI}/\text{TLI} = 0.96/0.96$, $\text{WRMR} = 0.965$) (Appendix 3-C: Table 1 & Table 4, Appendix 3-D: Figure 3). However, this resulted in a withdrawn subscale that was just-identified. Chi-square test of difference of model fit (difftest) between the first-order and second-order model was not significant, hence indicating

that the constraints in the more restricted second-order model did not significantly worsen the fit. Thus, the second-order model with anxious, sleep problems, and withdrawn behaviour loading on to internalizing behaviour and aggressive behaviour and attention problem loading on to externalizing behaviour was the best fitting model (Appendix 3-D: Figure 3). No out of range parameter estimates were observed. All factor loadings were statistically significant (p -value <0.05) (Appendix 3-C: Table 1 & Table 3).

Table 3-4: Estimated correlation matrix for the first-order and second-order latent variables

	Aggressive behaviour	Attention problems	Anxious/ depressed	Sleep problems	Withdrawn behaviour	Internalizing behaviour	Externalizing behaviour
Aggressive behaviour	1.00						
Attention problems	0.69	1.00					
Anxious/ depressed	0.48	0.33	1.00				
Sleep problems	0.46	0.33	0.69	1.00			
Withdrawn behaviour	0.36	0.26	0.54	0.52	1.00		
Externalizing behaviour	0.99	0.70	0.48	0.47	0.37	1.00	
Internalizing behaviour	0.57	0.40	0.84	0.82	0.64	0.57	1.00

The estimated correlation between internalizing and externalizing factors (0.57) was statistically significant (p -value <0.0001), thus supporting the possibility of another higher order underlying the two domains (Table 3-4).

The sample mean estimated from the factor scores for aggressive behaviour was 0.03, for attention problems was 0.05, for anxious/depressed was 0.04, sleep problems was 0.04, and withdrawn behaviour was 0.03. The estimated means for externalizing and internalizing behaviour were 0.04 and 0.07, respectively. The residual variance for aggressive behaviour was 0.02 ($p=0.9$), attention problem was 0.50 ($p<0.0001$), anxious was 0.30 ($p=0.05$), sleep problem

was 0.33 ($p=0.01$), and withdrawn behaviour was 0.59 ($p<0.0001$). The residual variances for internalizing and externalizing were not computed because their factor variances were fixed to one and factor means were fixed to zero.

The probability plot for aggressive behaviour shows that items 20 (Disobedient), 29 (Easily frustrated), and 85 (Temper) were not ‘difficult’ based on the probability of correct response greater than 50% ($\text{Pr}(Y=1) > 0.5$). Similarly, item 59 (Quickly shifts) from the attention subscale and item 33 (Feelings hurt) from the anxiety subscale were not difficult ($\text{Pr}(Y=1) > 0.5$) (Appendix 3-D: Figure 3). The rest of the items were difficult (probability of correct response less than 50%), and thus the total scale might not be a reliable measure to screen children with borderline disorders (Appendix 3-D: Figure 3).

All the subscales except for withdrawn behaviour were reliable (test information scores greater than four and computed reliability of greater than 80%) (Appendix 3-D: Figure 4). Computed reliability for anxious behaviour was 95.6%, for sleep problems was 83.9%, for aggressive behaviour was 94.4%, and for attention problems was 87.5%. For withdrawn behaviour, the test information score was 2.6 and computed reliability was 72.2%, indicating that the withdrawn subscale was not reliable (Appendix 3-D: Figure 4). This could be because it was a just-identified model (only three items on the subscale). From the item difficulty plots, all the three retained items were difficult (probability of correct response less than 50%). To improve the reliability, the test requires more items which are lower on the difficulty scale (i.e., right of the distribution).

3.11 Discussion

This was one of the first studies to validate the CBCL 1.5 – 5 years in Canadian preschoolers. Overall the second-order model with five syndrome scores of aggressive

behaviours, attention problems loading on the externalizing behaviour, and anxiety problems, sleep problems, and withdrawn behaviour loading on the internalizing behaviour had a good fit. The two second-order factors of internalizing and externalizing behaviour also showed a moderate level of correlation (0.57) indicating the presence of third order latent variable which could explain the cognitive development in these children. Emotionally reactive syndrome scales fitted well neither in the correlated first-order model nor in the re-specified scale of anxious and emotionally reactive subscales combined. Similar issues of poor model fit have been observed by Konold TR, et al., ([2003](#)). CBCL 1.5 – 5 years is a large scale with 67 items loading onto seven first-order and two second-order factors. The purpose of this analysis was to identify the dimensions of the CBCL, which best fit data from the ‘Feelings in Pregnancy and Motherhood’ study. The results from this analysis were then used in Chapter 6 of this thesis to understand and identify the predictors of the emotional and behavioural development among three-year-olds.

The initial loss of items from the analysis due to insufficient variance in this sample could have biased the estimates of several polychoric correlations. Item omission is not unprecedented in IFAs of instruments within the Achenbach System of Empirically Based Assessment ([Ivanova et al., 2007](#); [Pandolfi et al., 2009](#)). This omission might have resulted in a re-specified but more parsimonious model which was then further used to identify the determinants of the cognitive and behavioural development of preschoolers. However, an attempt was made to retain the original structure of the data for the analysis by using polychoric correlations. We also used the IFA/IRT methods that have been recommended for ordered categorical (Likert scale) data ([Hoffman, 2014](#); [Muthen, 1983](#)).

We acknowledge the relatively small sample size and issues pertaining to generalization. However, the sample size was sufficient to evaluate each syndrome scale separately and further

support the second-order and plausibly third-order model latent factor structure ([Pandolfi et al., 2012](#)).

One of the strengths of the study was the very small number of missing items. We deliberated the use of both manual imputations with median values using all the remaining data as well as computer generated multiple imputation methods in Mplus 7.3 ([Muthén & Muthén, 2014](#)). However, with multiple imputation in Mplus, we could not compare the nested models using chi-square test or use modification indices to improve model fit ([Muthén & Muthén, 1998 - 2012](#)). Modification indices are part of the model outputs in Mplus and are the proportional change in the chi-square value of the model fit with the changes proposed by the program to improve model fit ([Muthén & Muthén, 1998 - 2012](#)). Hence, due to the extremely small number of missing values that were MCAR, we decided to use manual imputation by median scores thereby utilizing the full capacity of the Mplus program to perform Item Factor Analysis.

Development of competing measurement models have been the cornerstone of development in psychometrics ([Cano & Hobart, 2011](#)). Future replication studies may provide a better fit or allow the development of adaptive models to measure a specific trait. One of the methods to validate the re-specified model is to apply it to a longitudinal sample. Since FIP is a longitudinal study in which children were measured a second time at five years of age, there is a potential opportunity to validate this re-specified model in future.

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3.13 Appendices

3.13.1 Appendix 3-A: Detailed description of the polychoric correlation method used with WLSMV estimator in Mplus.

Polychoric correlation estimates the correlation between two theorised normally distributed continuous latent variables, developed from two observed ordinal variables ([Jöreskog, 1994b](#); [Muthén & Muthén, 1998 - 2012](#)). WLSMV estimator in Mplus computes a sample correlation matrix based on the data (tetrachoric, polychoric) and then fits the model based on this correlation matrix independent of the input data. ([Muthén & Muthén, 1998 - 2012](#)). The goal is to have the predicted correlation matrix similar to the observed matrix ([Brown, 2006](#)). So, the model is fitted in a way that would have been done if the observed variables had been continuous. No factor score estimation is involved, and the parameters are estimated directly ([Muthén & Muthén, 1998 - 2012](#)). The maximum value of the correlation between two categorically scored items is often downwardly biased ([Farrington & Loeber, 1997](#); [Muthén, 1989](#)) which results in downwardly biased factor loadings ([Hartman et al., 1999](#)). However, the use of polychoric correlations instead of the input data overcomes the issue of downwardly biased estimates and provides an accurate estimate of the pairwise correlations ([Babakus et al., 1987](#)). Mplus produces this polychoric correlation as a part of the output ([Muthén & Muthén, 1998 - 2012](#)).

3.13.2 Appendix 3-B- Detailed description of item response theory-based model parameters and methods used to compute them.

The latent trait denoted by theta (θ), on a transformed scale, has a mean of zero (0) and standard deviation of 1 with an arbitrary range that will cover the latent trait that is being measured ([Yang & Kao, 2014](#)). Thus, a theta for depression can range from -6 to +6 ([Yang & Kao, 2014](#)) Values close to -6 represent less severe depression, and those closer to 6 represent more severe depression ([Yang & Kao, 2014](#)).

Factor loadings for each item are an assessment of the relationship of the variable with the underlying latent trait and could be interpreted as standardized regression coefficients ([Brown, 2006](#); [Hoffman, 2014](#)).

A threshold is the expected value of the latent response variable at which an individual transition from a value of ‘0’ to ‘1’ of the categorical outcome variable when the latent trait value is ‘zero’. They are same as intercepts with an opposite sign also called as ‘Greene’s intercepts’ or ‘cut points’ ([Edwards & Wirth, 2009](#); [Embreton & Reise, 2000](#); [Greene, 2012](#); [Hoffman, 2014](#)). For k number of categories in the observed Likert scale of the outcome variable, (k-1) thresholds are provided ([Edwards & Wirth, 2009](#); [Embreton & Reise, 2000](#); [Hoffman, 2014](#)). Thresholds are used in the computation of the same number of ‘Item Difficulty’ or ‘location’ parameters ([Baker, 2001](#); [Hoffman, 2014](#)).

Item difficulty describes ‘how difficult [it] is to achieve 50% probability of correct response for a specific item given the respondent’s level of the latent trait’ ([Bauer & Hussong, 2009](#); [Yang & Kao, 2014](#)). Thus, the location of the curve on the ‘x-axis’ with a range of -3 to +3 (most commonly used) measures the difficulty ([Baker, 2001](#); [Hoffman, 2014](#)). Mplus provides the graphical output of difficulty parameters called Item Characteristic Curves (ICCs), from which difficulty parameters can be obtained ([Hoffman, 2014](#)). The ICC is an estimate of the

‘probability that a patient will endorse a particular response’ ([Baker, 2001](#); [Bauer & Hussong, 2009](#); [Yang & Kao, 2014](#)). The theta value of zero (0) indicates a 50% probability that a person will endorse a certain response option. For example, a depressed person with theta greater than zero would have more than 50% chance of endorsing an option ‘all the time’ as compared to ‘no’ or ‘sometimes’.

Item Discrimination (also called ‘slope’ of the curve) determines how well items identify the person at the different level of the latent trait; steeper slopes translate into better discrimination at a given theta (latent trait) level ([Baker, 2001](#); [Yang & Kao, 2014](#)). Theoretically values range from $-\infty$ to $+\infty$; however, items with negative values are problematic as they suggest that respondents with increasing levels or latent trait scores are less likely to endorse more severe options ([Yang & Kao, 2014](#)). This could only occur if the item poorly discriminates between those with high and low levels of latent trait ([Yang & Kao, 2014](#)). Unstandardized factor loadings can be used to compute the discrimination parameter ([Hoffman, 2014](#)). For an item to be discriminatory, it should have a high slope and narrow base, i.e., the item can identify a specific characteristic (can also be referred as ‘shape’ parameter) ([Baker, 2001](#)). In our case, each item is measured on a three-point Likert scale; 0 ‘*Not true*’, 1 ‘*Somewhat or Sometimes True*’, or 2 ‘*Very True or Often True*’. Hence, each of the items will have two difficulty parameters and one discrimination parameter.

Information curves obtained from Mplus measures the information of the scale ([Baker, 2001](#); [Hoffman, 2014](#)). Thus, the amount of information obtained from an individual item in the scale (item information functions) though small can be used to compute the scale information functions (also called test information function) ([Yang & Kao, 2014](#)). In general, the item information functions tends to look bell-shaped with the amount of information increasing as the

item difficulty increases at lower ability levels ([Baker, 2001](#)). However, if the difficulty is low, the information would be highest at higher ability levels. The greater the number of items in the scale, the greater is the information provided by the scale and higher reliability ([Hoffman, 2014](#)).

Reliability of the scale is computed by (information/ information +1). Thus for test information function of 4, computed reliability is 0.8 (4/ 4+1) ([Hoffman, 2014](#)). Test information scores of less than 4, indicate that the scale is not reliable ([Hoffman, 2014](#)). However, there were no published methods for measuring the reliability of the second-order factors in IFA since there are no observed items for these factors. However theoretically test information is the total of the item's information. Hence, we should be able to compute the internalizing and externalizing behaviour test information by summing the item information scores for all the items under them. However, because thetas are on a difference scale of each item, summation at best would be an estimate ([Hoffman, 2014](#)).

3.13.3 Appendix 3-C: Tables

3.13.3.1 Table 1: Model fit parameters for individual syndromes in the CBCL model as well as for the first-order and second-order model structure for the syndromes retained by IFA (N = 343).

Model	RMSEA	CFI	TLI	WRMR
Anxiety ^a	0.04 (0.0 – 0.09)	0.99	0.97	0.56
Emotionally reactive ^b	0.04 (0.0 – 0.07)	0.98	0.97	0.64
Somatic problems ^c	0.11 (0.05 – 0.18)	0.68	0.04	0.9
Withdrawn behaviour ^d	0.06 (0.01 – 0.11)	0.99	0.98	0.6
Sleep problems ^e	0.05 (0.0 – 0.11)	0.99	0.97	0.5
Aggressive behaviour ^f	0.05 (0.04 – 0.03)	0.97	0.96	0.92
Attention problems ^g	0.00 (0.0 – 0.43)	1.00	1.01	0.07
Six syndrome scale first-order model (without somatic problems)	0.04 (0.03 – 0.04)	0.92	0.92	1.13
Five syndrome scales first-order model (without somatic problems and emotionally reactive) ^h	0.03 (0.02 – 0.04)	0.95	0.95	0.97
Five syndrome scales second-order model ⁱ	0.03 (0.02 – 0.04)	0.96	0.96	0.96

RMSEA – Root Mean Square Error of Approximation, CFI – Comparative Fit Index, TLI – Tucker Lewis Index, WRMR – Weighted Root Mean Square Residual

a – Without item 90 (Sad), item 43 (Looks unhappy), and item 68 (Self-conscious).

b – Without item 46 (Twitches) and item 97(Whining). Correlation between items 82 and 79 as well as item 92 and 21.

c – Did not had a good fit, due to empty cell in the correlation matrix. So the syndrome scale was eliminated from further analysis. Variables removed are item 1(Aches), item 7 (Can't stand things out of place), item 39(Headaches), item 45(Nausea), item 52 (Painful bowel moments), item 86(Too concerned with neatness and cleanliness), and item 93(Vomits).

d – Without item 67 (Unresponsive to affection), item 70 (Little affection), and item 71 (Little interest).

e – Without item 64 (Resists bed) and item 74 (Sleeps little). Correlation between item 84(Talks and cries in sleep) and 48 (Nightmares).

f – Without item 8 (Can't stand waiting), item 15 (Defiant), item 18 (Destroys others), item 27 (Lacks guilt) and item 88 (Uncooperative). Correlation between item 35 (Fights) and 16 (Demands met), item 81(Stubborn) with item 40 (Hits others), and item 96 (Wants attention) with item 40 (Hits others).

g – Without item 56 (Clumsy) due to nonsignificant factor loadings.

h – Without item 22 (Doesn't want to sleep alone).

i - Without items 16 (Demands met) and 62 (Refuses active games).

Chi-square difftest in Mplus was not significant (χ^2 (5.2, df = 4, p-value 0.27). Hence the second-order model fit the data well.

3.13.3.2 Table 2: Standardized model estimates (factor loadings), their level of significance, coefficient of determination and the residual variance for all the items retained in the final models for each of the individual syndromes of emotionally reactive, anxiety, somatic problems, withdrawn behaviour, sleep problems, aggressive behaviour and attention problems (N = 343).

Individual syndromes of behaviours	Estimate	p-value	R ² (p-value)	Residual variance
Emotionally reactive				
Item 21 (Disturbed by change)	0.42	<0.001	0.18 (0.05)	0.82
Item 51 (Panics)	0.86	<0.0001	0.74 (<0.0001)	0.82
Item 79 (Shifts between sad and excitement)	0.45	<0.0001	0.21 (0.031)	0.79
Item 82 (Moody)	0.52	<0.0001	0.27 (0.004)	0.73
Item 83 (Sulks)	0.74	<0.0001	0.54 (<0.0001)	0.46
Item 92 (Upset by new)	0.53	<0.0001	0.28 (0.007)	0.72
Item 99 (Worries)	0.52	<0.0001	0.27 (0.002)	0.73
Anxious/ Depressed				
Item10 (Clings)	0.73	<0.0001	0.53 (<0.0001)	0.47
Item 33 (Feelings hurt)	0.35	<0.0001	0.12 (<0.0001)	0.88
Item 37 (Upset by separation)	0.71	<0.0001	0.50 (<0.0001)	0.49
Item 47 (Nervous)	0.76	<0.0001	0.58 (<0.0001)	0.42
Item 87(Fearful)	0.84	<0.0001	0.69 (<0.0001)	0.30
Somatic problems				
Item 12 (Constipated)	0.47	0.005	0.22 (0.162)	0.78
Item 19 (Diarrhea)	0.46	0.002	0.21 (0.114)	0.78
Item 24 (Doesn't eat well)	0.43	0.007	0.18 (0.178)	0.81
Item 78 (Stomach aches)	0.58	0.001	0.34 (0.093)	0.66
Withdrawn behaviour				
Item 2 (Acts too young)	0.85	<0.0001	0.73 (<0.0001)	0.27
Item 4 (Avoids eye contact)	0.54	<0.0001	0.29 (0.001)	0.71
Item 23 (Doesn't answer)	0.66	<0.0001	0.44 (<0.0001)	0.56
Item 62 (Refuses active games)	0.81	<0.0001	0.65 (<0.0001)	0.35
Item 98 (Withdrawn)	0.61	<0.0001	0.37 (<0.0001)	0.63

Individual syndromes of behaviours	Estimate	p-value	R² (p-value)	Residual variance
Sleep problems				
Item 22 (Doesn't want to sleep alone) ^	0.68	<0.0001	0.47 (<0.0001)	0.53
Item 38 (Trouble sleeping)	0.62	<0.0001	0.38 (<0.0001)	0.62
Item 48 (Nightmares)	0.52	<0.0001	0.27 (<0.0001)	0.73
Item 84 (Talks, cries in sleep)	0.39	<0.0001	0.15 (<0.0001)	0.85
Item 94 (Wakes often)	0.84	<0.0001	0.70 (<0.0001)	0.29
Aggressive behaviour				
Item 16 (Demands met) *	0.61	<0.0001	0.37 (<0.0001)	0.63
Item 20 (Disobedient)	0.73	<0.0001	0.54 (<0.0001)	0.46
Item 29 (Easily frustrated)	0.66	<0.0001	0.44 (<0.0001)	0.56
Item 35 (Fights) *	0.68	<0.0001	0.46 (<0.0001)	0.54
Item 40 (Hits others) #\\$	0.70	<0.0001	0.49 (<0.0001)	0.51
Item 42 (Hurts accidentally)	0.60	<0.0001	0.36 (<0.0001)	0.64
Item 44 (Angry moods)	0.73	<0.0001	0.54 (<0.0001)	0.46
Item 53 (Attacks people)	0.75	<0.0001	0.56 (<0.0001)	0.44
Item 58 (Punishment doesn't change)	0.68	<0.0001	0.46 (<0.0001)	0.54
Item 66 (Screams)	0.68	<0.0001	0.47 (<0.0001)	0.53
Item 69 (Selfish)	0.63	<0.0001	0.39 (<0.0001)	0.61
Item 81 (Stubborn) #	0.72	<0.0001	0.52 (<0.0001)	0.48
Item 85 (Temper)	0.68	<0.0001	0.46 (<0.0001)	0.54
Item 96 (Wants attention) \\$	0.59	<0.0001	0.35 (<0.0001)	0.65
Attention problems				
Item 5 (Can't concentrate)	0.88	<0.0001	0.78 (<0.0001)	0.22
Item 6 (Can't sit still)	0.87	<0.0001	0.75 (<0.0001)	0.25
Item 59 (Quickly shifts)	0.63	<0.0001	0.39 (<0.0001)	0.60
Item 95 (Wanders away)	0.45	<0.0001	0.20 (<0.0001)	0.79

*#\\$ Correlated items in the aggression subscale.

^ Removed from the first-order correlated model due to correlations with the aggression and anxiety subscale.

3.13.3.3 Table 3: Standardized model estimates (factor loadings) for the final correlated first-order model with anxious, sleep problems, withdrawn behaviour, aggressive behaviour, and attention problems (N=343).

Individual syndromes of behaviours	Estimate	p-value	R ² (p-value)	Residual variance
Anxious/ Depressed				
Item10 (Clings)	0.57	<0.0001	0.32 (<0.0001)	0.68
Item 33 (Feelings hurt)	0.56	<0.0001	0.32 (<0.0001)	0.68
Item 37 (Upset by separation)	0.64	<0.0001	0.41 (<0.0001)	0.59
Item 47 (Nervous)	0.90	<0.0001	0.80 (<0.0001)	0.19
Item 87(Fearful)	0.77	<0.0001	0.59 (<0.0001)	0.41
Withdrawn behaviour				
Item 2 (Acts too young)	0.51	<0.0001	0.26 (0.003)	0.74
Item 4 (Avoids eye contact)	0.50	<0.0001	0.25 (0.002)	0.75
Item 23 (Doesn't answer)	0.57	<0.0001	0.33 (0.001)	0.67
Item 62 (Refuses active games) ^	0.74	<0.0001	0.55 (0.001)	0.45
Item 98 (Withdrawn) ^	0.58	<0.0001	0.33 (0.007)	0.67
Sleep problems				
Item 38 (Trouble sleeping)	0.67	<0.0001	0.48 (<0.0001)	0.55
Item 48 (Nightmares)	0.66	<0.0001	0.44 (<0.0001)	0.56
Item 84 (Talks, cries in sleep)	0.48	<0.0001	0.23 (<0.0001)	0.77
Item 94 (Wakes often)	0.64	<0.0001	0.41 (<0.0001)	0.59
Aggressive behaviour				
Item 16 (Demands met) ^*	0.62	<0.0001	0.38 (<0.0001)	0.62
Item 20 (Disobedient)	0.74	<0.0001	0.55 (<0.0001)	0.45
Item 29 (Easily frustrated)	0.68	<0.0001	0.46 (<0.0001)	0.54
Item 35 (Fights) *	0.64	<0.0001	0.41 (<0.0001)	0.59
Item 40 (Hits others) #\\$	0.67	<0.0001	0.45 (<0.0001)	0.55
Item 42 (Hurts accidentally)	0.61	<0.0001	0.38 (<0.0001)	0.63
Item 44 (Angry moods)	0.71	<0.0001	0.51 (<0.0001)	0.49
Item 53 (Attacks people)	0.76	<0.0001	0.58 (<0.0001)	0.42

Individual syndromes of behaviours	Estimate	p-value	R² (p-value)	Residual variance
Item 58 (Punishment doesn't change)	0.67	<0.0001	0.45 (<0.0001)	0.55
Item 66 (Screams)	0.65	<0.0001	0.42 (<0.0001)	0.58
Item 69 (Selfish)	0.67	<0.0001	0.45 (<0.0001)	0.55
Item 81 (Stubborn) #	0.71	<0.0001	0.51 (<0.0001)	0.50
Item 85 (Temper)	0.66	<0.0001	0.46 (<0.0001)	0.56
Item 96 (Wants attention) \$	0.64	<0.0001	0.40 (<0.0001)	0.60
Attention problems				
Item 5 (Can't concentrate)	0.86	<0.0001	0.74 (<0.0001)	0.26
Item 6 (Can't sit still)	0.84	<0.0001	0.71 (<0.0001)	0.29
Item 59 (Quickly shifts)	0.67	<0.0001	0.45 (<0.0001)	0.55
Item 95 (Wanders away)	0.51	<0.0001	0.26 (<0.0001)	0.74

*#\$ Correlated items in the aggression subscale.
^ Removed from the second-order correlated model due to correlations with the aggression and anxiety subscale.

3.13.3.4 Table 4: Standardized model estimates (factor loadings) for the final second-order model with anxious, sleep problems, and withdrawn behaviour loading on internal and aggressive behaviour and attention problems loading on externalizing behaviour (N=343).

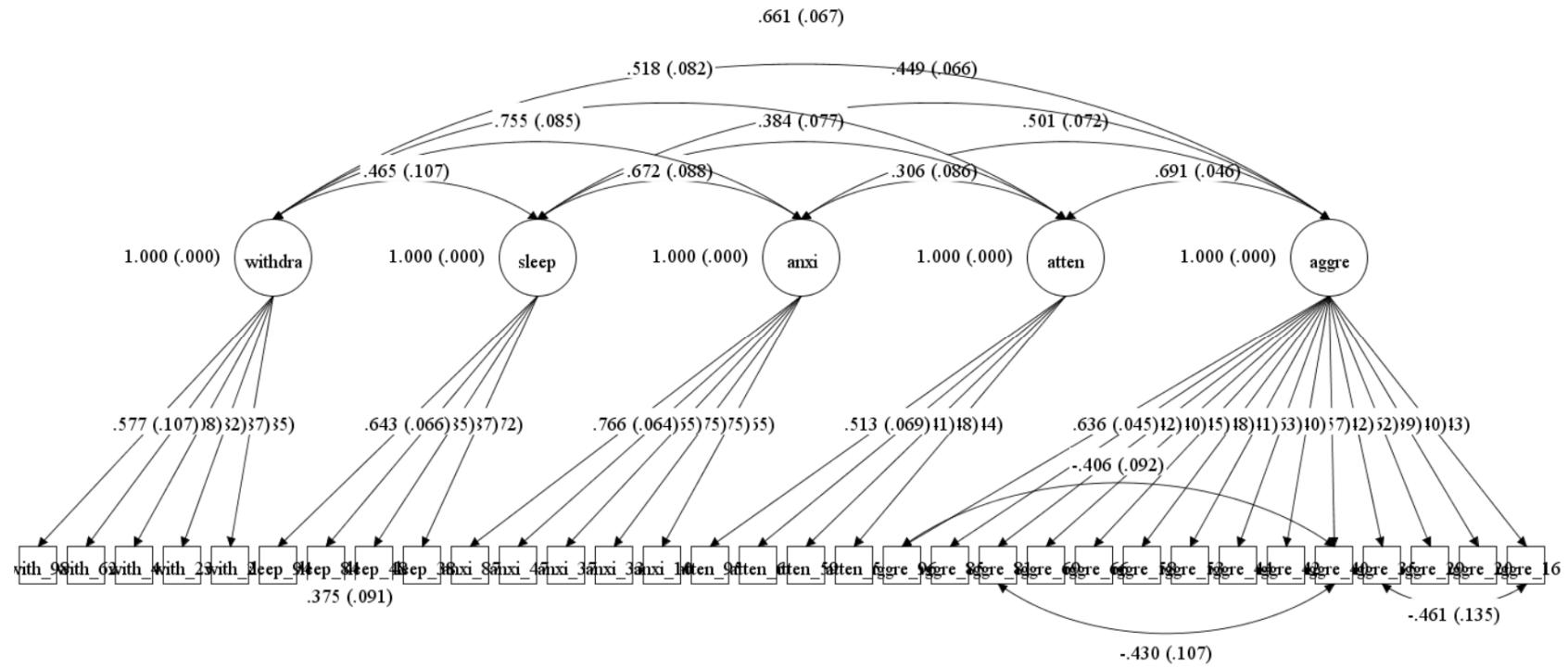
2 nd order latent variables	1 st order latent variables	Observed Variable	Std. estimates	Std. errors	p-value	Residual variance
Internalizing Behaviour	Anxious/ Depressed		0.86	0.86	<0.0001	0.26 (0.09)*
		Item 10 (Clings)	0.55	0.55	<0.0001	0.70
		Item 33 (Feelings hurt)	0.54	0.54	<0.0001	0.71
		Item 37 (Upset by separation)	0.65	0.65	<0.0001	0.58
		Item 47 (Nervous)	0.91	0.91	<0.0001	0.18
		Item 87 (Fearful)	0.78	0.78	<0.0001	0.39
	Sleep Problems		0.82	0.82	<0.0001	0.32 (0.01)*
		Item 38 (Trouble sleeping)	0.66	0.66	<0.0001	0.56
		Item 48 (Nightmares)	0.67	0.67	<0.0001	0.55
		Item 84 (Talks, cries in sleep)	0.48	0.48	<0.0001	0.77
		Item 94 (Wakes often)	0.64	0.64	<0.0001	0.59
	Withdrawn Problems		0.54	0.54	<0.0001	0.71 (<0.0001)*
		Item 2 (Acts too young)	0.69	0.69	<0.0001	0.51
		Item 4 (Avoids eye contact)	0.55	0.55	<0.0001	0.93
		Item 23 (Doesn't answer)	0.27	0.27	0.05#	0.70
Externalizing Behaviour	Aggression		0.97	0.98	<0.0001	0.05 (0.73) *
		Item 20 (Disobedient)	0.74	0.74	<0.0001	0.45
		Item 29 (Easily frustrated)	0.67	0.67	<0.0001	0.55
		Item 35 (Fights)	0.65	0.65	<0.0001	0.58
		Item 40 (Hits others)	0.68	0.68	<0.0001	0.53
		Item 42 (Hurts accidentally)	0.61	0.61	<0.0001	0.63
		Item 44 (Angry moods)	0.71	0.71	<0.0001	0.50
		Item 53 (Attacks people)	0.78	0.78	<0.0001	0.39
		Item 58 (Punishment doesn't change)	0.68	0.68	<0.0001	0.54
		Item 66 (Screams)	0.66	0.66	<0.0001	0.57

		Item 69 (Selfish)	0.66	0.66	<0.0001	0.56
		Item 81 (Stubborn)	0.72	0.72	<0.0001	0.48
		Item 85 (Temper)	0.66	0.66	<0.0001	0.57
		Item 96 (Wants attention)	0.64	0.64	<0.0001	0.59
Attention Problems			0.71	0.71	<0.0001	0.49 (<0.0001)*
		Item 5 (Can't concentrate)	0.86	0.86	<0.0001	0.27
		Item 6 (Can't sit still)	0.85	0.85	<0.0001	0.54
		Item 59 (Quickly shifts)	0.68	0.68	<0.0001	0.28
		Item 95 (Wanders away)	0.49	0.49	<0.0001	0.76

*p-values of the residuals of the latent variables
Removal of the item results in under-identified withdrawn behaviour scale and results in poor model fit.

3.13.4 Appendix 3-D: Figures

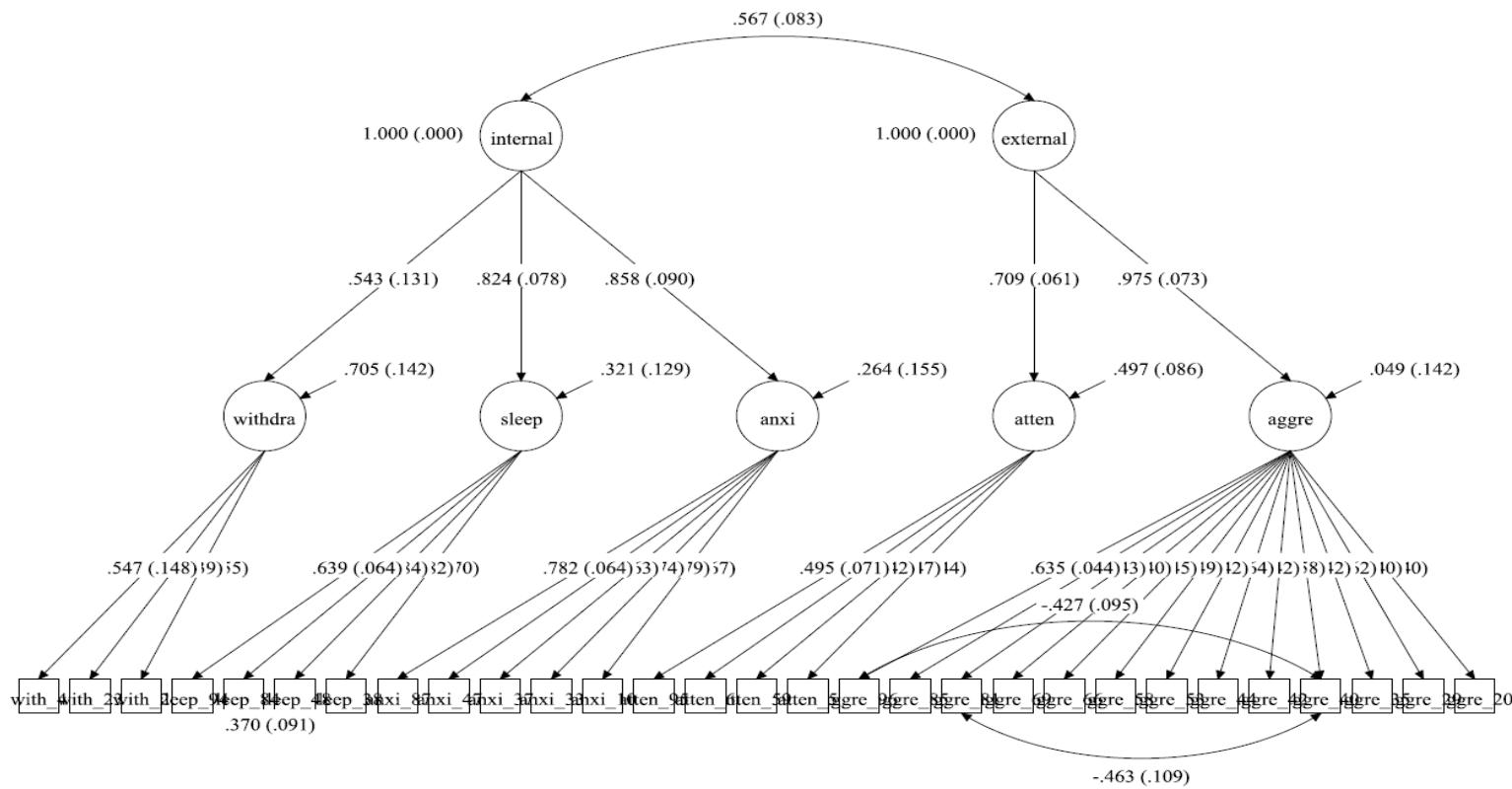
3.13.4.1 Figure 1: First-order correlated model structure using five syndrome scales of withdrawn, sleep problems, anxious, attention problems and aggressive behaviours.



withdra – refers to 1st order latent trait withdrawn behaviour, sleep – refers to 1st order latent trait sleep problems, atten – refers to 1st order latent trait attention problems, anxi – refers to 1st order latent trait anxious/depressed, and aggre – refers to 1st order latent trait aggressive behaviour. Values from the 2nd order latent traits to 1st order latent traits and from 1st order latent traits to observed items are the standardized factor loadings and their standard errors. Small arrows pointing toward first-order latent traits are the residual variances and their standard errors. Arrow pointing towards the items with the aggressive behaviour subscale and sleep problems subscale are the correlated items in the model with their standardized estimates and standard error

All the standardized factor loadings for the items and the first-order latent factors are tabulated in Appendix 3-C: Table 3.

3.13.4.2 Figure 2: Second-order correlated model structure for Child Behavioural Check List 1/5-5 years.



internal & external – 2nd order latent trait indicating internalizing behaviour and externalizing behaviour.

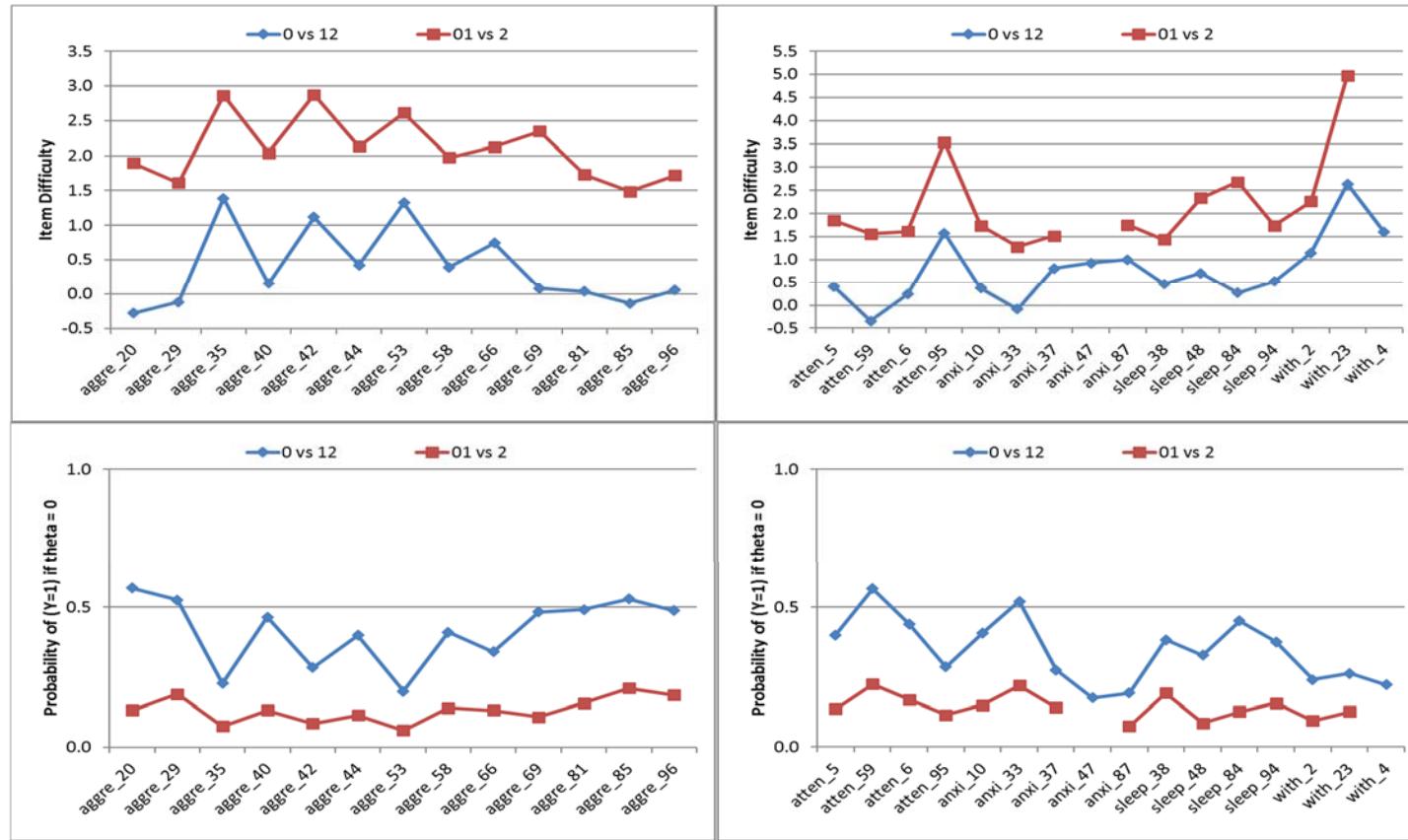
withdra – refers to 1st order latent trait withdrawn behaviour, sleep – refers to 1st order latent trait sleep problems, atten – refers to 1st order latent trait attention problems, anxi – refers to 1st order latent trait anxious/depressed, and aggre – refers to 1st order latent trait aggressive behaviour. Values from the 2nd order latent traits to 1st order latent traits and from 1st order latent traits to observed items are the standardized factor loadings and their standard errors. Small arrows pointing toward first-order latent traits are the residual variances and their standard errors.

Arrow pointing towards the items with the aggressive behaviour subscale and sleep problems subscale are the correlated items in the model with their standardized estimates and standard error, which are as follows:

Items 84 (Talks and cries in sleep) and 48 (Nightmares) = 0.37 (0.09), items 81 (Stubborn) and 40 (Hits others) = -0.46(0.11), items 96 (Wants attention) and 40 (Hits others) = -0.43(0.09)

All the standardized factor loadings for the items and the first-order latent factors are tabulated in Appendix 3-C: Table 4

3.13.4.3 Figure 3: Plots showing the item difficulty parameters computed from the unstandardized thresholds from the model output as well as the probability of success ($\text{Pr}(Y=1)$) in giving a correct response when factor mean (theta) is zero.



0 =Not true, 1=Somewhat or Sometimes True, 2=Very True or Often True.

Item difficulty can be computed from unstandardized thresholds and factor loadings by the formula:

$$= (\text{item threshold} - \text{item loading} * \text{mean}(\text{Factor})) / (\text{item loading} * \text{SD}(\text{Factor variance})).$$

Probability of success ($Y=1$) when factor mean = 0, can be computed from thresholds by the given formula:

$$= 1 - (\text{exponentiated}(\text{threshold}) / (1 + \text{exponentiated}(\text{threshold})))$$

3.13.4.4 Figure 4: Test information curves for anxious, sleep problems, and withdrawn behaviour loading on the internalizing behaviour.

Test information scores of 4 or more translates into reliability score of 0.8 or more.

Reliability of anxious behaviour is $(22*100/23) = 95.6\%$

Reliability of sleep problems is $(5.2*100/6.2) = 83.9\%$

Reliability of withdrawn behaviour is $(2.6*100/3.6) = 72.2\%$

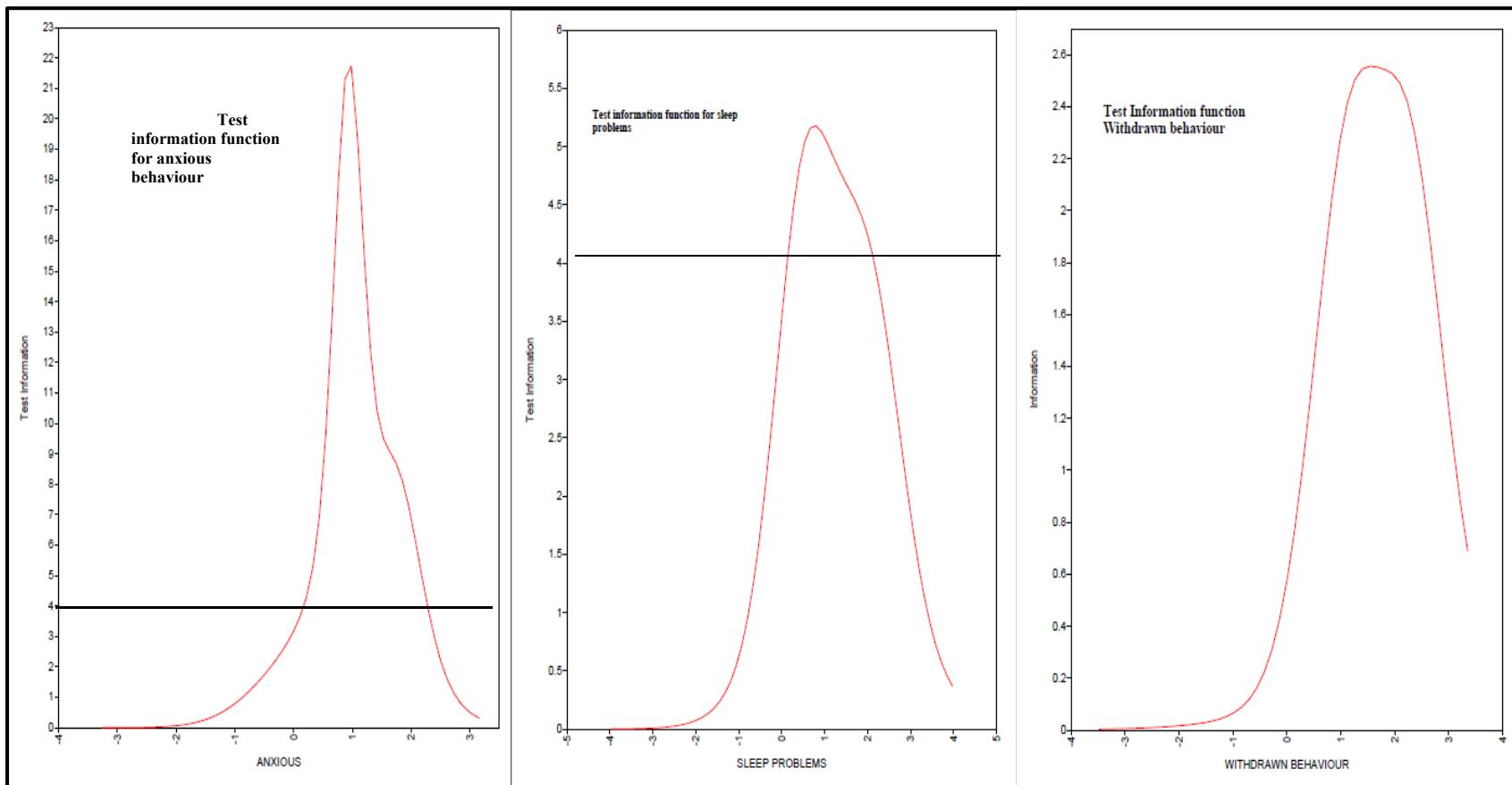
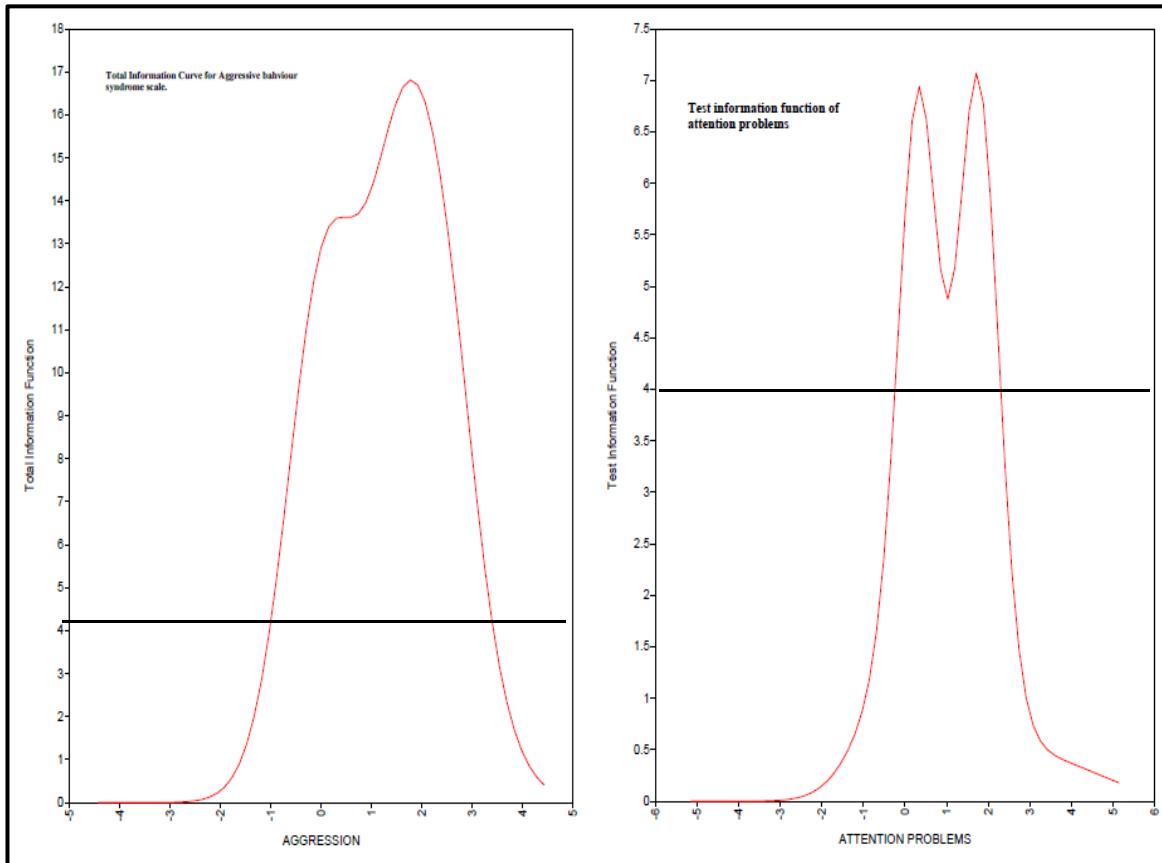


Figure 4 (continued): Test Information curves for aggressive behaviour and attention problems loading on the externalizing behaviour in the final model.

Test information scores of 4 or more translates into reliability score of 0.8 or more.

Reliability of aggressive behaviour was $(17*100/18) = 94.4\%$

Reliability of attention problems was $(7*100/8) = 87.5\%$



**CHAPTER 4: TIME COURSE AND FACTORS ASSOCIATED WITH
MATERNAL DEPRESSION AND ANXIETY – FROM PREGNANCY TO
THREE YEARS POSTPARTUM**

4.0 Abstract

Approximately 3.5 million people were diagnosed with mood and anxiety disorders in 2009 – 2010 in Canada. Across the globe, only a few studies have examined the persistence of symptoms of depression beyond the first postpartum year. The primary goal of this study was to examine the course of depression and anxiety scores in women from early pregnancy to three years postpartum and to identify predictors of depression and anxiety scores across this period. The Edinburgh Postnatal Depression Scale (EPDS) was used to screen mothers for depression and anxiety. Linear mixed models with random intercept and an exponential correlation structure were used to build the models. Data from 333 singleton pregnancies who completed all the four rounds of Feelings in Pregnancy & Motherhood study were included in the analysis. Most (55% (11/20)) mothers who screened positive for depression during the fourth round of data collection were new cases that had no prior history of being positive in the earlier three rounds. Contrary to depression, most (77% (52/68)) mothers who were screened positive for anxiety during the fourth round of data collection had screened positive at least once during the previous three rounds of data collection. Average marginal depression scores during early pregnancy were 6.1 (95% CI 5.8 – 6.5), during late pregnancy were 5.7 (95% CI 5.3-6.1), during early postpartum were 5.4 (95% CI 5.1-5.8), and three years after birth were 4.4 (95% CI 4.0-4.7). Similarly, average marginal anxiety scores during early pregnancy were 3.0 (95% CI 2.8–3.2), during late pregnancy were 2.7 (95% CI 2.5-2.9), during early postpartum were 2.5 (95% CI 2.3-2.7), and three years after birth were 2.2 (95% CI 2.0-2.4). History of depression moderated changes in depression and anxiety scores at different times during and following pregnancy. The effect of the history of depression on anxiety scores was partially mediated by stress in early pregnancy.

4.1 Introduction

Depression and anxiety were the fourth and fifth most common diagnosis among Canadians in 2008 respectively and are the most frequently reported disorders by the women of reproductive age ([Kessler et al., 2012](#); [Martini et al., 2015](#)). Across the globe, a few studies have examined the persistence of symptoms of depression beyond the first postpartum year ([Beeghly et al., 2002](#); [Evans et al., 2001](#); [Horwitz et al., 2007](#); [Matthey et al., 2013](#)), second postpartum year ([Campbell, 1995](#); [Horowitz & Goodman, 2004](#); [McLennan et al., 2001](#); [Murray & Cooper, 1997](#); [Small et al., 1994](#)), and up to the fourth postpartum year ([Kumar & Robson, 1984](#)).

Although previous research on the course of depression is relatively consistent, research on the course of anxiety in the perinatal period is not. At least one study has concluded that there was a general decline in depression and anxiety scores between pregnancy and eight months postpartum ([Evans et al., 2001](#)). Others have reported that anxiety scores increase up to the late pregnancy period ([Da Costa et al., 1999](#)) through to the early postpartum period ([Stuart et al., 1998](#)). To our knowledge, none of the studies has prospectively examined the persistence of anxiety through pregnancy up to three years postpartum.

A systematic review conducted by WHO identified a spectrum of socio-demographic, obstetric, psychological, and behavioural factors that have significant effects on postpartum depression ([Stewart, 2003](#)). However, limited information is available on whether these factors have an effect on longitudinal depression scores or whether the effect differs at various times during the perinatal period. Similarly, a systematic review on anxiety disorders in pregnancy was unable to make any conclusions about risk factors of prenatal anxiety due to the lack of comparable data and conflicting findings ([Goodman, 2014](#)). Some of the reported risk factors for anxiety were single marital status, low socio-economic status, and first parity ([Goodman, 2014](#)). However, role of child rearing (breastfeeding) and child bearing (birth order, type of birth)

practices, maternal high-risk behaviour (smoking, alcohol use, and drug abuse), child factors (sex of the child, overall health of the child) on both longitudinal depression and anxiety scores in mothers was lacking.

Hence, the current study described the time course and changes in depression and anxiety from the pregnancy period through three years after childbirth among Canadian mothers. The study examined the association of previously recognised risk factors for postpartum depression with longitudinal depression and anxiety scores from pregnancy to three years postpartum. In addition, we also investigated the importance of previously observed depression and anxiety scores at each time on later depression and anxiety scores. We hypothesized that family and previous history of maternal depression and anxiety were significantly associated with longitudinal depression and anxiety. We further hypothesized that the effects of previous and family history of perinatal depression and anxiety were mediated through prenatal maternal stress and high-risk behaviours.

4.2 Methods

The Feelings in Pregnancy and Motherhood (FIP) study was a longitudinal study of Canadian women who were screened for depression, anxiety, and mood problems at early pregnancy, late pregnancy, early postpartum, and three-years after birth ([Bowen et al., 2012](#)). The outcomes of interest for this analysis were maternal depression and anxiety scores measured from pregnancy to three years postpartum and changes in these outcomes from pregnancy through the three-year postpartum period.

4.2.1 Time course of data collection

Mothers were recruited during the second trimester of pregnancy. The mean duration of gestation at recruitment and the first data collection point was 17 weeks \pm SD (4.4 weeks)

labelled as ‘early pregnancy or T1’. The second measurement, labelled as ‘late pregnancy or T2’, was later in the pregnancy at a mean gestation of 30.4 weeks \pm SD 2.4 weeks. The third measurement was at an average four weeks \pm SD 2.0 weeks after birth, and the fourth measurement was completed at an average age of 36.4 months \pm SD 1.6 weeks; these time points were labelled as ‘early postpartum or T3’ and ‘three years after birth or T4’, respectively. Thus, the average time gaps between the consecutive time points (in weeks) were 13.7 weeks \pm SD 3.8 (between 1st and 2nd), 13 weeks \pm SD 2.8 (between 2nd and 3rd) and 154 weeks \pm SD 16.5 (between 3rd and 4th).

For the first three measurements, face-to-face interviews were conducted by the two trained research associates. For the fourth data collection point, three years after birth, telephone interviews or mail surveys were added as contact options recognizing that some mothers had moved or could not easily meet with the investigators.

In total, 648 mothers were recruited for the study. Retention rate was 93% (603/648) for T2, 91.7% (594/648) for T3, and 52.2% (338/648) for T4. Of the 338 mothers who completed the fourth round of data collection, five twin pregnancies were excluded from this analysis. Hence, data from 333 mothers, with a singleton pregnancy, who completed the fourth round of data collection were considered for this analysis.

4.2.2 Measures of depression and anxiety

The Edinburgh Postnatal Depression Scale (EPDS) was used to screen mothers for depression and anxiety ([Cox et al., 1987](#); [Murray & Cox, 1990](#)). The sensitivity of the scale ranges from 73% to 100% and specificity from 68% to 96% in pregnancy and postpartum women ([Buist et al., 2002](#); [Cox & Holden, 2003](#); [Rush, 2000](#)). The EPDS scale has ten items, and each item has four responses scored from 0 to 3. Therefore, the EPDS has a total maximum

score of 30. Higher scores indicated more severe symptoms. For longitudinal analysis, the total EPDS score for each time point of the study was used. However, for descriptive analysis, most widely used cut-off of at least 12 was used to dichotomize the depression variable ([Bergink et al., 2011](#); [Choate & Gintner, 2011](#); [Cox et al., 1987](#)).

EPDS has also been validated as a useful measure to screen for anxiety (items 3, 4, & 5) in pregnancy and postpartum period ([Matthey et al.\(2013\)](#)). Total anxiety scores could range from 0 to 9. Two cut-off score values of four ([Phillips et al., 2009](#)) and six ([Matthey, 2008](#)) have been proposed. However, no cut-off has been widely accepted. For descriptive analysis, the more sensitive cut-off of four was used. However, total EPDS-3A scores were used for the longitudinal analysis.

4.2.3 Independent variables

Questionnaires were completed which contained information on mood changes, high-risk behaviours (smoking, alcohol, recreational drug abuse), family history of perinatal depression, medical and obstetric history, socio-economic status, stressors, childcare arrangements, relationship with the father of the child, and supports available to the mother. These questionnaires were originally developed based on extensive literature review and clinical observations of two of the authors and had been previously used in various studies ([Bowen et al., 2012](#); [Bowen et al., 2009](#)).

The child's birth weight, birth length, one- and five-minute 'Apgar' (Appearance, Pulse, Grimace, Activity, and Respiration) scores, type of birth, and any neonatal or birth complications were abstracted from hospital discharge records after obtaining permission from the mother. Information about initiation of breastfeeding was collected at T3 (four weeks after birth), and duration of breastfeeding was requested from the mother at T4 (three years after birth).

Information regarding any subsequent pregnancy, miscarriage, or birth was also obtained from the mother at T4 (three years after birth). Birth order was computed and transformed into an ordinal variable (1st, 2nd, and 3rd or more). Family income was dichotomized using the annual income of \$40,000 as a cut-off (based on the estimates of low-income cut-off for a family of four in Canada in 2009 ([Statcan, 2015](#)). Covariates describing maternal attributes, labour, and neonatal information and the time points when the information was collected were summarized (Table 4-1).

Table 4-1: Summary of the covariates considered in model building, data type, and coding, and periods during which each variable was available for analysis.

Variable	Description of Variable	Pregnancy		Postpartum	
		T1	T2	T3	T4
Maternal socio-demographic-behavioural information					
Age (years)	Centered around mean (29 years) And categorized as: >35 years, 25 – 34 years, and <25 years		✓		
Overall health	Excellent/Good vs. Fair/Poor	✓	✓	✓	✓
Pregnancy intention	Planned vs. Unplanned	✓			
Marital Status	Single/divorced/widowed vs. Married/common law	✓			✓
Satisfaction with the partner relationship	Not very satisfied, Very satisfied, No relationship	✓	✓	✓	✓
Education	Some postsecondary vs. Less than postsecondary	✓			✓
Ethnic background	Caucasian vs. Non-Caucasian	✓			
Gravida	Multigravida vs. Primigravida	✓			
Employment	Employed vs. Non-employed	✓			✓
Family Income	≥\$40,000 - <\$40,000	✓	✓	✓	✓
History of depression	Yes vs. No	✓			
History of perinatal depression & treatment during current pregnancy	Diagnosed and pharmaceutical treatment, Diagnosed and non-pharmaceutical treatment, No diagnosis	✓			✓
Family history of perinatal depression	Yes vs. No		✓		
Availability of emotional support	Yes vs. No	✓	✓	✓	✓
History of abuse	Yes vs. No	✓	✓	✓	✓
History of counselling	Yes vs. No	✓	✓	✓	✓
Affective Liability Scores	Continuous				✓

Variable	Description of Variable	Pregnancy		Postpartum	
		T1	T2	T3	T4
History of exercise	Yes vs. No	✓	✓	✓	✓
Smoking	Smoke, Quit, Never	✓	✓	✓	✓
Alcohol	Consume, Quit, Never	✓	✓	✓	✓
Recreational drug use	Use, Quit, Never	✓	✓	✓	✓
Labor & neonatal information					
Length of gestation	Centered around mean (39.3 weeks) and categorized as: ≥41 weeks (post-term), 37 – 41 weeks (term), ≤37 weeks (pre-term)			✓	
Sex of baby	Female vs. Male			✓	
Birth weight	Large for gestational age, Small for gestational age, Appropriate for gestational age			✓	
Apgar score (one minute)	≥7 vs. <7			✓	
Breastfeeding	Yes vs. No			✓	✓
Type of birth	Caesarian section, Assisted (forceps/vacuum), Spontaneous			✓	
Complications during birth	Yes vs. No			✓	
Complications in neonatal period	Yes vs. No			✓	
T1 – Early pregnancy (17 +/- 4.4 weeks), T2 – Late pregnancy (30.4 +/- 2.4 weeks), T3 – Early postpartum (4 +/- 2 weeks after birth), T4 – Late postpartum (36.4 +/- 1.6 weeks)					

4.2.4 Model building strategy

Since both depression and anxiety were measured using the EPDS scale, it was likely that the depression and anxiety scores at a specific time point would be highly correlated. Hence, depression and anxiety were considered separately in the analysis of risk factors for maternal mental health. However, for the lagged variable analysis the effects of lagged (previous) depression and anxiety scores on the subsequent depression scores were checked. Similarly, the effects of lagged (previous) depression and anxiety scores on the subsequent anxiety scores were checked.

4.2.5 Selection of the methods of estimation

The outcome data were balanced (same number of measures for each participant), uniform (time points measured across the participants were approximately the same) but were not equidistant (i.e., the time gap between the study time points were not the same) with four measurements for each participant. Linear mixed models were used with a random intercept to account for repeated measures within individual mothers and an exponential correlation structure to account for the non-equidistant time points. The correlation structure was tested against models with an exchangeable (compound symmetry) and unstructured correlation structures and chosen based on the lowest AIC ([Dohoo et al., 2012](#)).

4.2.6 Unconditional analysis and model building

Independent variables were screened prior to building a multivariable model by examining the unconditional associations between each risk factor and outcomes. Variables with an unconditional p-value <0.2 based on the type 3 Wald test were retained for consideration in building the final model ([Dohoo et al., 2012](#)). Continuous risk factors were checked for linearity ([Dohoo et al., 2012](#)). All ranked categorical and continuous variables were checked for collinearity. Where variables were highly correlated ($\rho \geq 0.9$), the variable with fewer missing values or that was most biologically relevant was retained ([Dohoo et al., 2012](#)).

Sequential manual stepwise backward selection was used to develop the main effects model, retaining only variables where p-value <0.05 . Potential confounders were assessed based on a $>20\%$ change in regression coefficients of interest. Biologically relevant interactions, including interactions between significant risk factors and study time points, were considered and retained and reported in the final model if $p <0.05$. Variable significance was checked by type 3 Wald test ([Dohoo et al., 2012](#)). Significant predictors and other predictors of interest were

checked for mediation effects based on *a priori* hypothesis using ‘binary_mediation’ command in STATA 12.0 ([Baron & Kenny, 1986](#); [Fairchild & MacKinnon, 2009](#); [Kenny, 2008](#); [Kenny, 2009](#); [Kenny, 2013](#); [MacKinnon, 2011](#); [StataCorp](#)). The normality of the residuals and the assumption of homogeneity of variances, or equal variance across all levels of independent variable, were tested by plotting standardized residuals versus fitted values ([Dohoo et al., 2012](#)).

Grand marginal means with 95% confidence intervals were computed based on the final model and plotted to illustrate the overall change in depression and anxiety scores across the study time points. Variance partition coefficients (VPC) were computed for the null models and final models to assess the change in the proportion of total variation between mothers explained by the predictors in the models ([Dohoo et al., 2012](#)).

4.2.7 Lagged variable models

In lagged response models, responses at previous time points were treated as covariates to evaluate whether the depression/anxiety scores at previous time points influenced subsequent depression/anxiety scores (Table 4-2). Lagged variables are labelled starting with the preceding measurement that is closest in time with increasing values reflecting variables that were measured in the more distant past. Lagged variable models are also known as ‘transition models’ ([Rabe-Hesketh & Skrondal, 2012](#)) as the regression coefficients reflect the average relative differences (or transitions) between previous measurements and the current time under study.

Table 4-2: Summary of the lagged variables available for analysis for each time point assessed in the models using linear regression.

Outcome variable	1st lag variable	2nd lag variable	3rd lag variable
Model 1 T4 Three years after birth	T3 Early postpartum	T2 Late pregnancy	T1 Early pregnancy
Model 2 T3 Early postpartum	T2 Late pregnancy	T1 Early pregnancy	
Model 3 T2 Late pregnancy	T1 Early pregnancy		

Because of the unequal times between observations, the effect of the lagged variables was examined separately using linear regression for each measure of depression and anxiety (Table 4-2). We also checked the effects of lagged anxiety variables on the subsequent time period depression scores and vice versa. Finally, both lagged depression, and anxiety variables were considered together in building final lagged models for depression and then for anxiety scores to identify the measure (depression or anxiety) and time point(s) that best predicted each outcome of interest. Only lagged variables with p-value <0.05 were retained in the final model. Change in the values of the estimates, 95% confidence interval, and the percentage of the variance in the outcome variable as explained by the significant lagged variables in the models were reported.

4.3 Results

Most of the mothers were Caucasian (313/333, 94%), were employed at the time of conception (284, 85%), and had some postsecondary education (303, 91%). Most (263, 79%) had an annual family income of more than \$40,000 at T1 and continued to have an annual family income of more than \$40,000 at T4 (247, 94%).

Most (306, 92%) were in a committed relationship at the time of conception. Of them, 304 (91%) were very satisfied with their relationship at the time of enrollment, 261(86%) continued to be very satisfied with their relationship with the partner at T4. In our study population, 79 (24%) reported being physically abused during the pregnancy. Stress during early pregnancy (T1) was very common (302, 91%), and decreased only slightly at T2 (292, 88%), and then again at T3 (260, 78%).

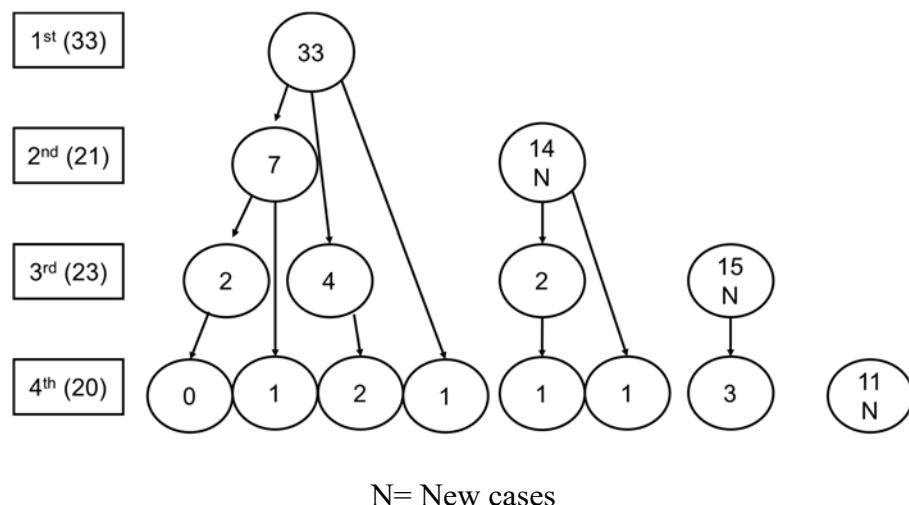
4.3.1 Descriptive statistics for depression and anxiety

Complete data were available for 333 singleton pregnancies at three years after birth (Table 4-3).

Table 4-3: Summary of the depression and anxiety scores for study participants (N=333).

	T1 - Early pregnancy (333)	T2 - Late pregnancy (328)	T3 - Early postpartum (333)	T4 – Three years after birth (333)
Depression (EPDS)				
Median (Minimum, Maximum)	5.0 (0 – 21)	5.0 (0 – 25)	5.0 (0 – 20)	4.0 (0 – 19)
Mean + SD	6.0 + 4.0	5.7 + 4.0	5.4 + 3.8	4.5 + 3.8
Anxiety (EPDS-3A)				
Median (Minimum, Maximum)	3.0 (0 – 8)	3.0 (0 – 9)	2.0 (0 – 9)	2.0 (0 – 8)
Mean + SD	3.0 + 2.0	2.7 + 1.8	2.5 + 2.0	2.2 + 1.7
EPDS – Edinburgh Postnatal Depression Scores				
EPDS-3A – Three item (3, 4, 5) scale to measure anxiety				
Early pregnancy – 17 + 4.4 weeks of gestation, Late pregnancy – 30.4 + 2.4 weeks of gestation, Early postpartum – 4 + 2.0 weeks after birth, and Late postpartum – 36.4 + 1.6 weeks after birth				

At T1, EPDS scores ≥ 12 indicating depression were identified in 33 (10%) of the mothers. There were 21 (6%) mothers with EPDS scores of ≥ 12 at T2, 23 (7%) at T3, and 20 (6%) were screened positive for depression at T4 (Figure 4-1).

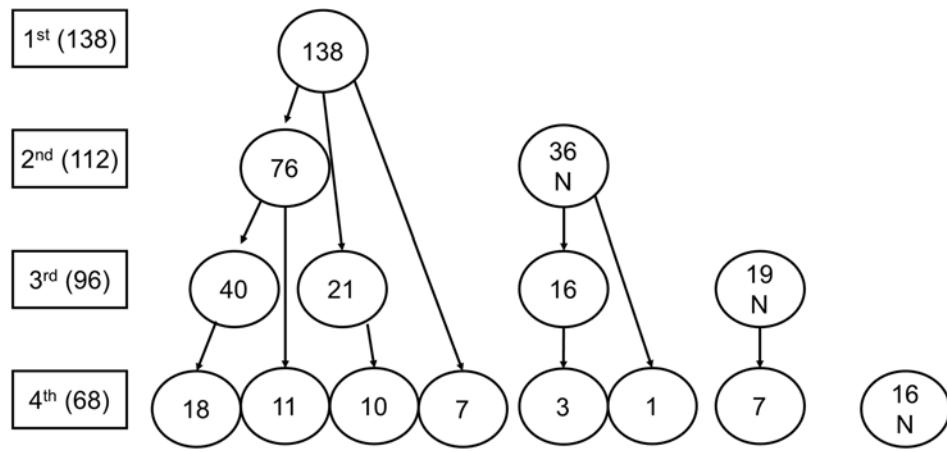


N= New cases

Figure 4-1: Flow chart summarizing the number of mothers screened positive for depression and their status during subsequent time points. Mothers who were screened positive for the first time at later time points were labelled as a new (N) case at that time point.

Of the 33 mothers screened positive at T1, 16 (48.5%) never screened positive during any of the subsequent three study points, only seven (21%) continued to have EPDS scores ≥ 12 at T2, six (18%) screened positive at T3 and four (12%) screened positive at T4 (Figure 4-1). Those screened positives in pregnancy (T1 and T2) only contributed 25% (5/20) of cases that were positive at T4. Most 55%, (11/20) of the cases that screened positive at T4 were new cases that had no prior history of being positive in the earlier three rounds.

Similarly, 138 (41%) of participants had EPDS – 3A scores ≥ 4 consistent with anxiety at T1; 112 (34%) screened positive at T2, 96 (29%) screened positive at T3, and 68 (20%) screened positive at T4 (Figure 4-2). Contrary to depression, most 77% (52/68) of the cases who were screened positive for anxiety at T4 (fourth round of data collection) had screened positive during pregnancy (T1/T2) or T3.



N= New cases

Figure 4-2: Flow chart summarizing the number of mothers screened positive for anxiety and their status during the subsequent time points. Mothers who were screened positive for the first time at later time points were labelled as a new (N) case at that time point.

4.3.2 Factors associated with depression (EPDS) scores from early pregnancy (T1) to three years postpartum (T4)

Study time points, family history of perinatal depression, history of depression, physical abuse during pregnancy, overall health of the mother, stress at T1, T2, and T3, pregnancy complications, birth complications, breastfeeding initiated, any subsequent pregnancy, emotional support, affective lability scores, maternal and child overall health, partner satisfaction with relationship, total number of pregnancy at T4, and recreational drug use were unconditionally associated ($p<0.2$) with depression scores (Appendix 4-A).

In the final multivariable model, stress at T3, a not very satisfied relationship with the father of the child/partner (vs. very satisfied), and higher affective lability scores (at T4) were associated with increase in the average depression scores across all study time points (

Table 4-4). The presence of emotional support and being multigravida was associated with lower average depression scores across all study time points. The association between relationship satisfaction with the father of the child and depression scores was confounded by recreational drug abuse and stress at T2 (

Table 4-4).

Table 4-4: Estimated difference in depression measured as EPDS scores from early pregnancy (T1) to three years after birth (T4) associated with factors retained in the final multivariable model that did not contribute to an interaction term.

Independent variable		Change in depression scores	95% CI Lower	95% CI Upper	p-value
Stress at T3	Yes vs. No	0.8	0.2	1.4	0.01
Stress at T2 ^c	Yes vs. No	0.7	-0.1	1.5	0.07
Emotional support	Yes vs. No	-3.4	-5.7	0.9	0.01
Satisfaction with relationship	Very satisfied vs. No relationship	-0.2	-1.5	1.2	0.82
	Not very satisfied vs. No relationship	1.8	0.4	3.3	0.01
Affective Lability Scores at T4	Per unit of score	0.1	0.13	0.2	<0.0001

Independent variable		Change in depression scores	95% CI Lower	95% CI Upper	p-value
Parity at T4	Multigravida vs. Primigravida	-0.8	-1.5	-0.1	0.02
Recreational drug abuse ^c	Quit vs. Never used	0.1	-0.9	1.0	0.91
	Use vs. Never used	0.9	-0.7	2.6	0.27
<i>Interaction between study time points and history of depression*</i>					0.01
<i>Interaction between history of depression and stress at T1*</i>					0.004
C - confounders with respect to satisfaction level with the father of the child or partner					
Early pregnancy (T1) – 17 ± 4.4 weeks of gestation, Late pregnancy (T2) – 30.4 ± 2.4 weeks of gestation, Early postpartum (T3) – 4 ± 2.0 weeks after birth, and (T4) Three year after birth– 36.4 ± 1.6 weeks after birth					
* Estimates for pairwise combinations of interaction terms are presented in Tables 4-5 & 4-6.					

The final multivariable model for depression scores at each time point also included a significant interaction between history of depression and the study time points ($p=0.01$) (Table 4-4, Figure 4-3). As a result, the difference in EPDS scores between study time points varied for those with and without the history of depression. For those with a history of depression, EPDS scores were significantly lower at T2, T3, and T4 as compared to T1 (Table 4-5, Figure 4-3). For those with no history of depression, EPDS scores at T4 were significantly lower than for T1, T2, and T3 (Table 4-5, Figure 4-3).

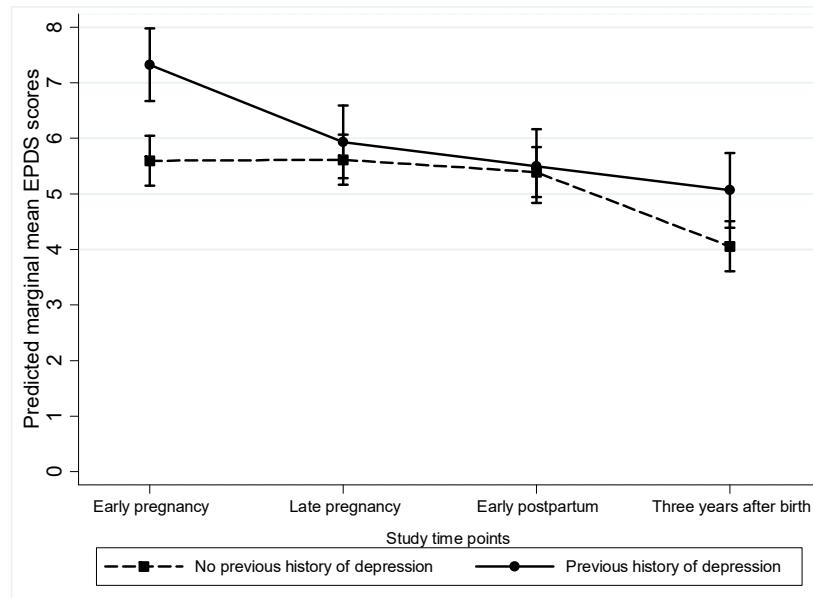


Figure 4-3: Plot of interaction effects of reported history of depression and study time points on average predicted EPDS scores.

Because of the significant interaction, the effect of the history of depression also varied depending on the study time point. Average predicted depression scores were significantly lower during early pregnancy (T1) ($p<0.0001$) and three years after birth (T4) ($p=0.015$) for mothers with no history of depression as compared to mothers with a history of depression (Table 4-5, Figure 4-3), but there was no significant difference based on history of depression at T2 ($p=0.43$) or T3 ($p=0.79$).

Table 4-5: Estimated pairwise differences in depression measured as EPDS scores from T1 to T4 time points associated with interaction effects between the history of depression and study time points in the final multivariable model.

Interaction between time points and history of depression		Change in depression scores (β)	95% CI		p-value
			Lower	Upper	
Differences between time points for mothers with a history of depression					
History of depression at T2 vs.	History of depression at T1	-1.4	-2.2	-0.6	0.001
History of depression at T3 vs.	History of depression at T1	-1.8	-2.7	-0.9	<0.0001
History of depression at T4 vs.	History of depression at T1	-2.3	-3.1	-1.4	<0.0001
History of depression at T3 vs.	History of depression at T2	-0.4	-1.2	0.4	0.28
History of depression at T4 vs.	History of depression at T2	-0.9	-1.7	-0.02	0.05
History of depression at T4 vs.	History of depression at T3	-0.4	-1.3	0.4	0.32
Differences between time points for mothers with no history of depression					
No history of depression at T2 vs.	No history of depression at T1	0.02	-0.5	0.6	0.95
No history of depression at T3 vs.	No history of depression at T1	-0.2	-0.8	0.4	0.48
No history of depression at T4 vs.	No history of depression at T1	-1.5	-2.1	-0.9	<0.0001
No history of depression at T3 vs.	No history of depression at T2	-0.2	-0.8	0.3	0.42
No history of depression at T4 vs.	No history of depression at T2	-1.6	-2.1	-0.9	<0.0001
No history of depression at T4 vs.	No history of depression at T3	-1.3	-1.9	-0.7	<0.0001
Differences between mothers with and without the history of depression at each time point					
History of depression at T1 vs.	No history of depression at T1	1.7	0.9	2.5	<0.0001
History of depression at T2 vs.	No history of depression at T2	0.3	-0.5	1.1	0.43
History of depression at T3 vs.	No history of depression at T3	0.1	-0.7	0.9	0.79
History of depression at T4 vs.	No history of depression at T4	1.0	0.2	1.8	0.02
T1 – 17 \pm 4.4 weeks of gestation, T2 – 30.4 \pm 2.4 weeks of gestation, T3 – 4 \pm 2.0 weeks after birth, and T4 – 36.4 \pm 1.6 weeks after birth					

There was also a significant interaction between stress at T1 and history of depression in the final multivariable model for depression ($p=0.004$) (Table 4-6, Figure 4-4). As a result, the association between history of depression and the average EPDS scores across all time points varied for those who did and did not report stress at T1. For women who reported stress at T1, those with a history of depression had slightly higher EPDS scores ($p<0.0001$) than for those who did not report a history of depression (Table 4-6, Figure 4-4a). Whereas for women who did not report stress at T1, there was no difference in the EPDS scores associated with the history of depression ($p=0.13$) (Table 4-6, Figure 4-4a).

Table 4-6: Estimated pairwise differences in depression measured as EPDS scores from early pregnancy to three years postpartum associated with interaction effects between the history of depression and stress at T1 in the final multivariable model.

Interaction effect of stress at T1 and reported history of depression		Change in depression scores (β)	95% CI		p-value
			Lower	Upper	
History of depression and Stress at T1 vs.	No history of depression and Stress at T1	0.9	0.4	1.5	<0.0001
History of depression and No stress at T1 vs.	No history of depression and No stress at T1	-1.9	-4.4	0.6	0.13
History of depression and Stress at T1 vs.	History of depression and No stress at T1	4.1	1.7	6.5	0.001
No history of depression and Stress at T1 vs.	No history of depression and No stress at T1	1.2	0.3	2.1	0.008
History of depression and Stress at T1 vs.	No history of depression and No stress at T1	2.1	1.2	3.1	<0.0001
History of depression and No stress at T1 vs.	No history of depression and Stress at T1	-3.1	-5.5	-0.7	0.01
T1 (Early pregnancy) – 17 ± 4.4 weeks of gestation,					

Similarly, the association between stress at T1 and EPDS scores varied for those who did and did not report a history of depression. For women with a history of depression, those who reported being stressed at T1 had EPDS scores that were an average of four points higher ($p<0.0001$) than mothers who did not report stress at T1 (Table 4-6, Figure 4-4b). However, in

the absence of the history of depression, mothers who reported being stressed at T1 had only a one-point average difference in depression scores ($p=0.008$) as compared to those who did not report being stressed (Table 4-6, Figure 4-4b).

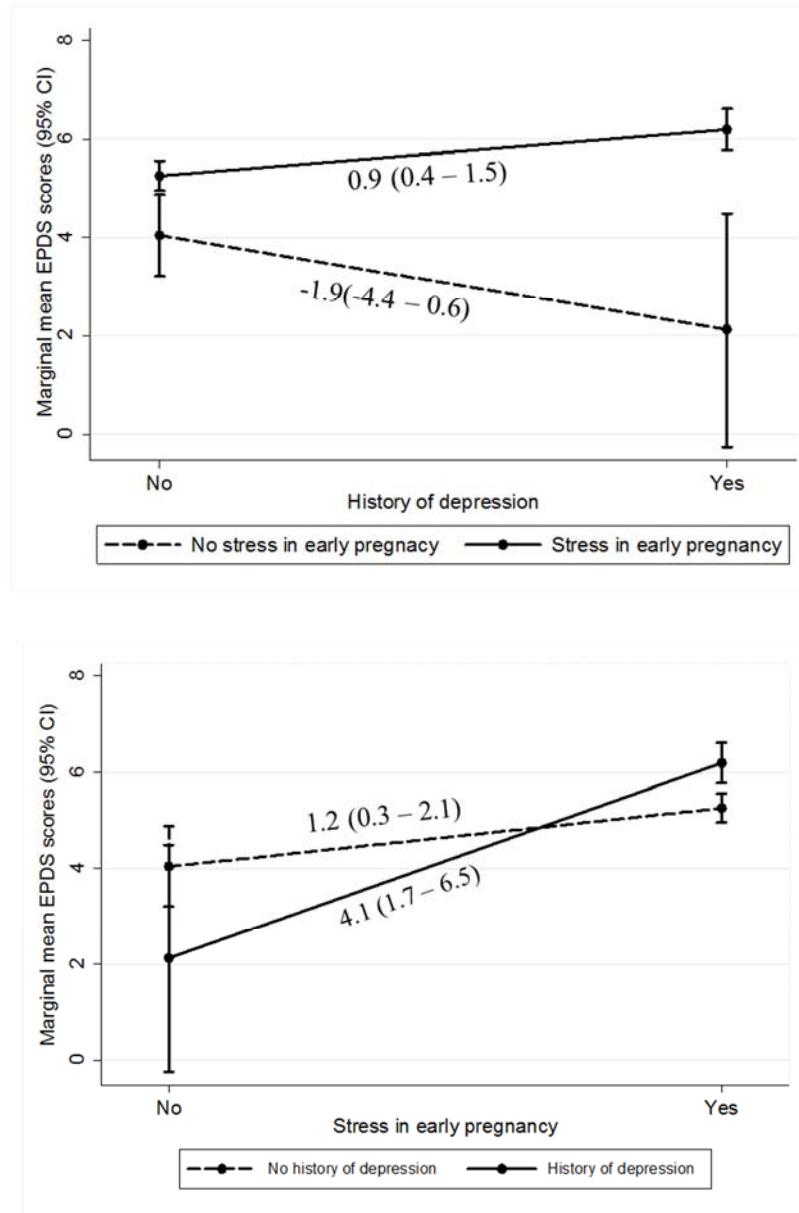


Figure 4-4: Plots of interaction effects of reported history of depression and stress at T1 on average predicted EPDS scores. The difference in EPDS scores based on a history of depression is reported for women with and without stress at early pregnancy (T1) (4a) and based on stress in early pregnancy (T1) for women with and without a history of depression (4b).

Overall, an average decline in the depression scores from T1 to T4 was observed during the study period (Figure 4-5). The total variance for the null model was 16.3, included a between mother variance of 5.2 (95% CI 4.0 – 6.7), and overall error variance of responses within mother of 10.4 (95% CI 9.4 – 11.4) and exponential error variance among residuals was 0.8 (95% CI 0.7 – 0.9). Total variance for the final model was 12.1, a reduction of 25.7%. Between mother, the variance was reduced to 1.6 (95% CI 0.9 – 2.8) due to the terms included in the final model, a decline of 68%. Whereas, overall error variance of responses within mother was 9.6 (95% CI 8.6 – 10.7) a decline of 7.3%. The exponential error variance among residuals in the final model for depression was 0.8 (95% CI 0.8 – 0.9).

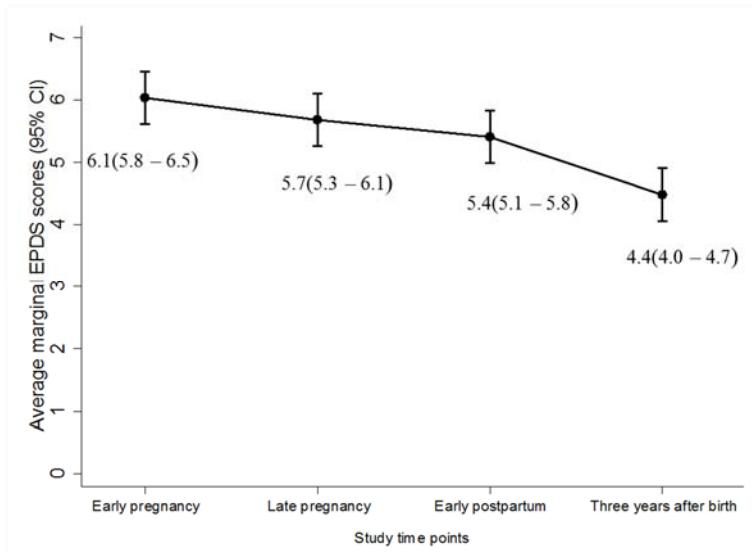


Figure 4-5: Plot of marginal mean predicted EPDS scores with 95% CI for each study time point from early pregnancy (T1) to three years after birth (T4).

4.3.3 Prediction of current depression scores by previous depression scores

Depression scores measured at T1 ($p<0.0001$), T2 ($p<0.008$), and T3 ($p<0.0001$) time points were significant positive predictors of depression scores at the T4 time point (Table 4-7). Similarly, T1 ($p<0.0001$) and T2 ($p<0.0001$) depression scores were significant positive

predictors of depression scores at the T3, and T1 ($p<0.0001$) depression score was a significant positive predictor of the T2 depression scores (Table 4-7).

Table 4-7: The association between previous depression and anxiety scores (lagged variables) and subsequent measures of depression measured as predicted change in EPDS scores for every unit increase in lagged variable with 95%CI.

	Lagged predictor variables of interest			R^2
	Early postpartum (T3)	Late pregnancy (T2)	Early pregnancy (T1)	
Outcome	Depression	Depression	Depression	
Depression scores measured at:	1 st lag	2 nd lag	3 rd lag	
Late postpartum (T4)	0.2 (0.1 – 0.3) **	0.2 (0.05 – 0.3) *	0.2 (0.1 – 0.3) **	21.4%
Early postpartum (T3)		1 st lag 0.2 (0.1 – 0.4) **	2 nd lag 0.2 (0.1 – 0.4) **	18.6%
Late pregnancy (T2)			1 st lag 0.4 (0.3 – 0.5) **	19.3%
Outcome	Anxiety	Anxiety	Anxiety	
Depression scores measured at:	1 st lag	2 nd lag	3 rd lag	
Late postpartum (T4)	0.5 (0.3 – 0.7) *	0.3 (-0.01 – 0.6)	0.4 (0.2 – 0.6) *	14.6%
Early postpartum (T3)		1 st lag 0.5 (0.2 – 0.7) *	2 nd lag 0.4 (0.2 – 0.7) *	15.4%
Late pregnancy (T2)			1 st lag 0.8 (0.6 – 1.0) **	16.0%

Significant at $p<0.05$, **Significant at $p<0.0001$
 R^2 = the percentage of the total variance in the dependent variables explained by the lagged variables

4.3.4 Prediction of current depression scores by previous anxiety scores

T1 ($p=0.001$) and T3 ($p=0.02$) anxiety scores were significant positive predictors of depression scores at the T4 time point (Table 4-7). T2 anxiety scores ($p=0.06$) were not significantly associated with depression scores at the T4 time point. Similarly, T1 ($p<0.0001$) and T2 ($p=0.001$) anxiety scores were significant positive predictors of depression scores at the

T3 time point, and T1 ($p<0.0001$) anxiety scores were a significant positive predictor of depression scores at the T2 time point (Table 4-7).

4.3.5 Prediction of current depression scores by simultaneous evaluation of both previous depression and anxiety scores

After consideration of both previous depression and anxiety scores (lagged depression and lagged anxiety variables) in the models for depression scores at each study time; only previous depression scores (early pregnancy (T1) ($\beta=0.2$, 95% CI 0.1 – 0.3, $p<0.0001$), late pregnancy (T2) ($\beta=0.2$, 95% CI (0.05 – 0.3), $p=0.008$), and early postpartum (T3) ($\beta=0.2$, 95% CI 0.1 – 0.3, $p<0.0001$) remained significant predictors of depression scores at T4 ($R^2=21.4\%$). Previous anxiety variables were no longer the significant predictors at T4 after accounting for concurrent depression measures.

Similarly, after consideration of both early and late pregnancy depression and anxiety scores, only early pregnancy (T1) depression ($\beta=0.2$, 95% CI 0.1 – 0.4, $p<0.0001$) and late pregnancy (T2) depression ($\beta=0.2$, 95% CI 0.1 – 0.4, $p<0.0001$) were significant predictors for the early postpartum (T3) depression scores ($R^2=18.6\%$). Only the early pregnancy (T1) depression ($\beta=0.4$, 95% CI 0.3 – 0.5, $p<0.0001$) variable remained as a significant predictor of T2 depression in the combined model ($R^2= 19.3\%$).

4.3.6 Factors associated with anxiety scores from early pregnancy to three years postpartum

Study time points, history of depression, family history of perinatal depression, any pregnancy-related complications, education status of the mother during early pregnancy (T1) and three years after birth (T4), physical abuse during pregnancy, sex of the child, birth order of the child, stress at T1, T2, and T3, initiation of breastfeeding, affective lability scores, emotional support (T4), overall health of the mother at T4, any subsequent pregnancy, relationship

satisfaction with partner at T4, and longitudinal history of drug abuse during the study period were unconditionally associated ($p<0.2$) with anxiety scores (Appendix 4-B).

Table 4-8: Estimated difference in anxiety scores from early pregnancy to three years postpartum associated with factors retained in the final multivariable model that did not contribute to an interaction term.

Independent variables		Difference in anxiety scores (β)	95% CI		p-value
			Lower	Upper	
Stress at T3	Yes vs. No	0.4	0.1	0.7	0.02
Education at T1	Some postsecondary vs. Less than postsecondary	-0.5	0.6	3.5	0.04
Affective Lability Scores at T4	Continuous	0.1	0.1	0.1	<0.0001
<i>Interaction between study time points and history of depression *</i>					0.04
<i>Interaction term of history of depression and stress at T1*</i>					0.004
T1 – 17 \pm 4.4 weeks of gestation, T2 – 30.4 \pm 2.4 weeks of gestation, T3 – 4 \pm 2.0 weeks after birth, and T4 – 36.4 \pm 1.6 weeks after birth					
* Estimates for pairwise combinations of interaction terms are presented in Tables 4-9 & 4-10.					

In the final multivariable model, stress at T3, education status of the mother at T1, and affective lability scores (T4) were independent significant predictors of anxiety scores (Table 4-8). Stress at T3 and higher affective lability scores were associated with higher anxiety scores. Women with some postsecondary education were more likely to have lower anxiety scores than women with less education.

There was a significant interaction between history of depression and the study time points ($p=0.04$) in the final model for anxiety scores (Table 4-9, Figure 4-6). As a result of this interaction, the difference in anxiety scores between time points varied based on whether or not there was a history of depression. For those with a history of depression, anxiety scores were lower at each of T2, T3, and T4 as compared to T1 ($p<0.0001$) (Table 4-9, Figure 4-6). For those without a history of depression, anxiety scores were lower at T4 as compared to T1 ($p<0.0001$),

T2 ($p<0.0001$), and T3 ($p=0.001$) (Table 4-9, Figure 4-6). Similarly, anxiety levels were lower at T3 as compared to T1 ($p=0.01$) for those without a history of depression.

Table 4-9: Estimated pairwise differences in anxiety measured as EPDS-3A scores from early pregnancy to three years postpartum associated with interaction effects between history of depression and study time points in the final multivariable model.

Interaction between time point and history of depression	Difference in anxiety scores (β)	95% CI		p-value
		Lower	Upper	
Differences between study time points for mothers with a history of depression				
History of depression at T2 vs. History of depression at T1	-0.7	-1.1	0.3	<0.0001
History of depression at T3 vs. History of depression at T1	-0.9	-1.3	-0.5	<0.0001
History of depression at T4 vs. History of depression at T1	-1.0	-1.4	-0.6	<0.0001
History of depression at T3 vs. History of depression at T2	-0.2	-0.6	0.2	0.31
History of depression at T4 vs. History of depression at T2	-0.3	-0.7	0.1	0.10
History of depression at T4 vs. History of depression at T3	-0.1	-0.5	0.3	0.52
Differences between study time points for mothers with no history of depression				
No history of depression at T2 vs. No history of depression at T1	-0.1	-0.4	0.1	0.38
No history of depression at T3 vs. No history of depression at T1	-0.3	-0.6	-0.1	0.01
No history of depression at T4 vs. No history of depression at T1	-0.8	-1.1	-0.5	<0.0001
No history of depression at T3 vs. No history of depression at T2	-0.2	-0.5	0.02	0.08
No history of depression at T4 vs. No history of depression at T2	-0.7	-0.9	-0.4	<0.0001
No history of depression at T4 vs. No history of depression at T3	-0.5	-0.7	-0.2	0.001
Differences between mothers with and without history of depression at each time point				
History of depression at T1 vs. No history of depression at T1	0.9	0.5	1.3	<0.0001
History of depression at T2 vs. No history of depression at T2	0.3	-0.1	0.7	0.10
History of depression at T3 vs. No history of depression at T3	0.4	-0.03	0.7	0.07
History of depression at T4 vs. No history of depression at T4	0.7	0.3	1.1	0.001
T1 (Early pregnancy) – 17 ± 4.4 weeks of gestation, T2 (Late pregnancy) – 30.4 ± 2.4 weeks of gestation, T3 (Early postpartum) – 4 ± 2.0 weeks after birth, and T4 (Three years after birth) – 36.4 ± 1.6 weeks after birth				

Also because of this interaction, the effect of the history of depression on anxiety scores varied between study time points (Table 4-9, Figure 4-6). Anxiety scores were significantly lower for mothers with a history of depression as compared to mothers without a history of depression only at T1 ($p<0.0001$) and T4 ($p=0.001$) (Table 4-9, Figure 4-6). There were no significantly different anxiety scores for mothers with and without a history of depression at T2 ($p=0.10$) and T3 ($p=0.07$).

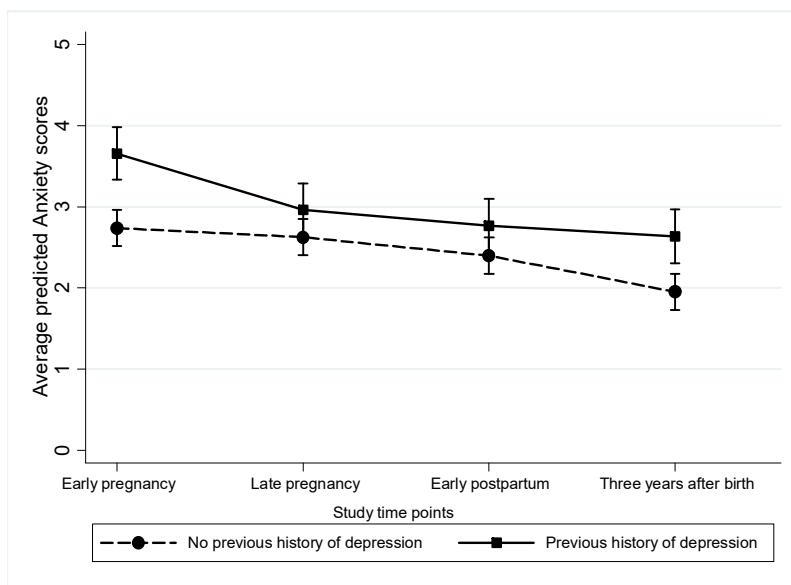


Figure 4-6: Plot of interaction effects of reported history of depression and study time points on average predicted anxiety scores

There was also a significant interaction between stress at T1 and history of depression in the model for anxiety scores. In the final multivariable model, reported stress at T1 modified the association between the history of depression and the anxiety scores (Table 4-10, Figure 4-7).

For women that reported stress at T1, those with history of depression anxiety scores that were 0.7 units higher ($p<0.0001$) as compared to mothers with no history of depression (Table 4-10, Figure 4-7a). However, for those who did not report stress at T1, history of depression was

associated with anxiety scores that were 1.4 units lower ($p=0.05$) as compared to mothers with no history of depression (Table 4-10, Figure 4-7a).

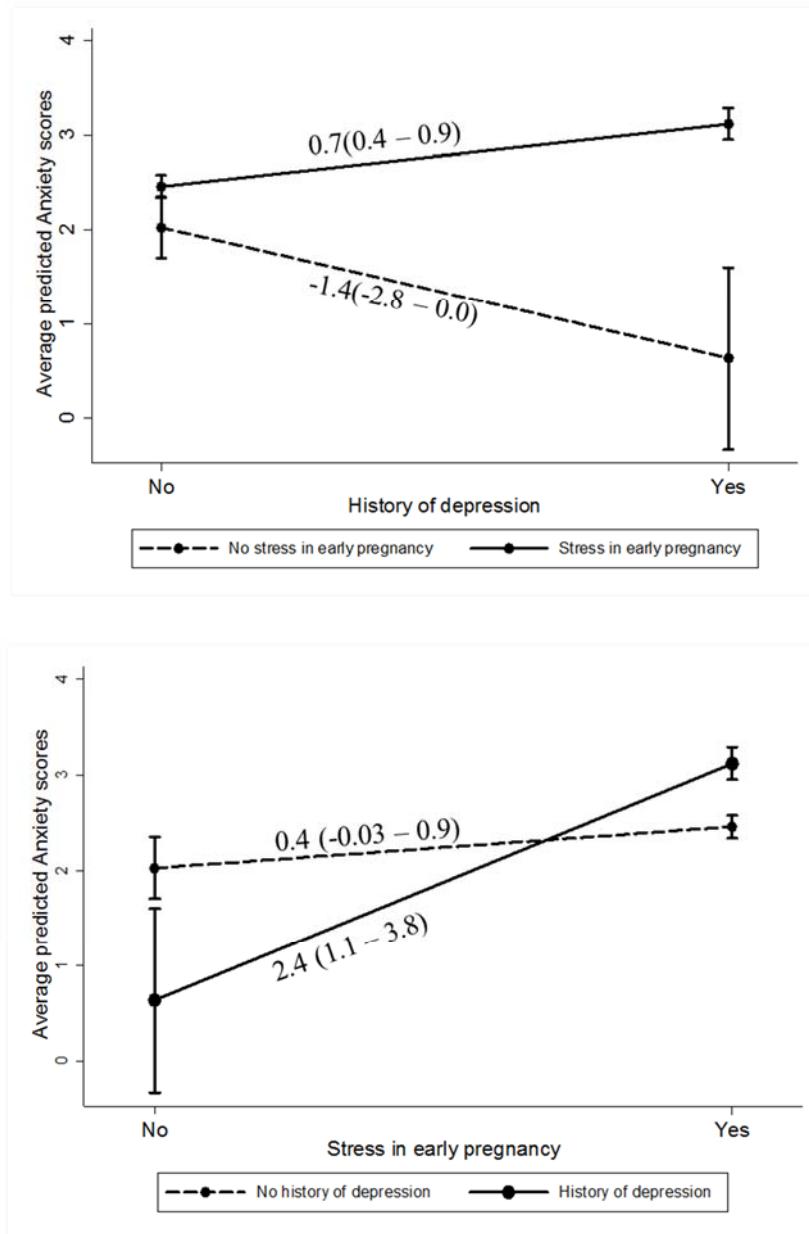


Figure 4-7: Plot of interaction effects of reported history of depression and stress at T1 on average predicted anxiety scores. The difference in anxiety scores based on history of depression is reported for women with and without stress at T1 (7a) and based on stress at T1 for women with and without history of depression (7b).

In the presence of history of depression, stress at T1 was associated with an increase of 2.4 points in the anxiety scores ($p<0.0001$) as compared to mothers who had no stress at T1 (Table 4-10, Figure 4-7b). However, for women without a history of depression, stress at T1 had no significant association with anxiety scores ($p=0.07$) (Table 4-10, Figure 4-7b).

Table 4-10: Estimated pairwise differences in anxiety measured as EPDS-3A scores from early pregnancy to three years postpartum associated with interaction effects between history of depression and stress at T1 in the final multivariable model.

Independent variables		Difference in anxiety scores (β)	95% CI		p-value
			Lower	Upper	
History of depression and Stress at T1 vs.	No history of depression and Stress at T1	0.7	0.4	0.9	<0.0001
History of depression and No stress at T1 vs.	No history of depression and No stress at T1	-1.4	-2.8	0.0	0.05
History of depression and Stress at T1 vs.	History of depression and No stress at T1	2.4	1.1	3.8	<0.0001
No history of depression and Stress at T1 vs.	No history of depression and No stress at T1	0.4	-0.03	0.9	0.07
History of depression and Stress at T1 vs.	No history of depression and No stress at T1	1.1	0.6	1.6	<0.0001
History of depression and No stress at T1 vs.	No history of depression and Stress at T1	-1.8	-3.2	-0.5	0.007
T1 (Early pregnancy) – 17 \pm 4.4 weeks of gestation					

Stress at T1 was a partial mediator with respect to the association between history of depression and anxiety scores after controlling for other covariates in the model. This means that history of depression was significant predictor for stress at T1 ($p <0.0001$). Approximately, 23% of the effect of the total effect of history of depression on anxiety scores was mediated through stress in early pregnancy.

History of depression → Stress at T1 → Anxiety scores over time

Overall average predicted anxiety scores from the final model for all participants declined from T1 to T4 (Figure 4-8).

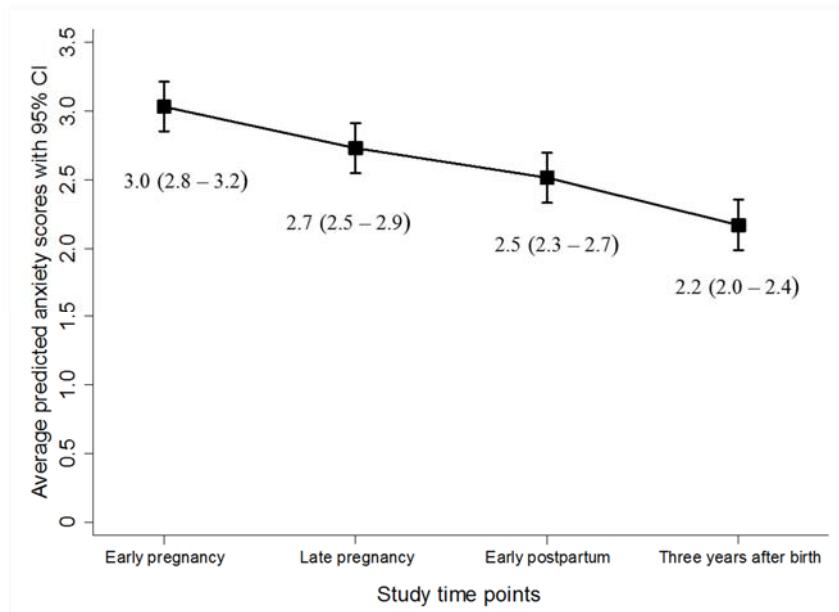


Figure 4-8: Plot of marginal mean predicted anxiety scores with 95% CI for each study time point from early pregnancy (T1) to three years postpartum (T4).

Total variance for the null model was 4.4, and included variance between mothers of 1.3 (95% CI 1.04 – 1.7) and the overall error variance of responses within mother of 2.2 (95% CI 2.0 – 2.5) and exponential error variance among residuals was 0.8 (95% CI 0.7 – 0.9). Total variance was reduced to 3.7 after including the fixed effects in the final model, a reduction of 16.3%. Between mother variance was reduced to 0.8 (95% CI (0.6 – 1.0)), a reduction of 41.5%, and overall within mother variance was reduced to 2.1 (95% CI 1.9 – 2.3) a reduction of 5.6%. The exponential error variance among residuals in the final model for anxiety was 0.8 (95% CI 0.7 – 0.9).

4.3.7 Prediction of current anxiety scores using previous anxiety scores

Both anxiety scores measured at T1 ($p < 0.0001$) and T3 ($p < 0.0001$) were significant predictors of anxiety scores at T4; however, anxiety measured at T2 ($p = 0.27$) was not. Anxiety scores measured at T1 ($p < 0.0001$) and T2 ($p < 0.0001$) were significant predictors of anxiety

scores at T3, and anxiety measured at T1 ($p < 0.0001$) was a significant predictor of anxiety scores at T2 (Table 4-11).

Table 4-11: The association between previous depression and anxiety scores (lagged variables) and subsequent anxiety scores measured as predicted change in EPDS-3A scores for every unit increase in the lagged variable with 95%CI.

Lagged predictor variables of interest				
	Early postpartum (T3)	Late pregnancy (T2)	Early pregnancy (T1)	R ²
Outcome	Anxiety	Anxiety	Anxiety	
Anxiety scores measured at:	1 st lag	2 nd lag	3 rd lag	
Late postpartum (T4)	0.2 (0.1 – 0.3) **	0.1 (-0.1 – 0.2)	0.3 (0.2 – 0.4) **	23.6%
Early postpartum (T3)		0.3 (0.2 – 0.4) **	0.3 (0.2 – 0.4) **	24.7%
Late pregnancy (T2)			0.5 (0.4 – 0.6) **	25.7%
Outcome	Depression	Depression	Depression	
Anxiety scores measured at:	1 st lag	2 nd lag	3 rd lag	
Late postpartum (T4)	0.1 (0.1 – 0.2) *	0.04 (-0.01 – 0.1)	0.1 (0.1 – 0.2) **	22.3%
Early postpartum (T3)		0.1 (0.1 – 0.2) **	0.1 (0.1 – 0.2) **	19.7%
Late pregnancy (T2)			0.2 (0.1 – 0.5) **	20.3%

*Significant at $p < 0.05$, **Significant at $p < 0.0001$

R² = the percentage of the total variance in the dependent variables explained by the lagged variables

4.3.8 Prediction of current anxiety scores using previous depression scores

Both depression scores measured at T1 ($p < 0.0001$) and T3 ($p = 0.001$) were significant predictors of anxiety scores at T4. T1 ($p < 0.0001$) and T2 ($p < 0.0001$) depression scores were also significant predictors of anxiety scores at T3, and T1 ($p < 0.0001$) depression scores was a significant predictor of anxiety scores at T2 (Table 4-11).

4.3.9 Prediction of current anxiety scores by simultaneous evaluation of both previous anxiety and depression scores

When both lagged depression, and anxiety variables were considered together, only the T1 depression (0.1, 95% CI (0.1–0.2), p<0.0001) and T3 anxiety scores (0.3, 95% CI (0.2 – 0.4), p<0.0001) remained as significant predictors of anxiety scores at T4. These two variables explained 24.4% (R^2 value) of the total variance in the anxiety scores at T4.

Early pregnancy (T1) anxiety (0.3, 95% CI (0.1 – 0.4), p=0.008) and late pregnancy (T2) anxiety (0.3, 95% CI (0.1 – 0.4), p=0.008) scores remained the only significant predictors for early postpartum (T3) anxiety scores, and explained 24.7 % of the total variance of early postpartum anxiety (T3) scores. Early pregnancy (T1) anxiety scores (0.4, 95% CI (0.2-0.6), p<0.0001) remained the only significant predictor of T2 anxiety scores in the combined models and explained 25.7% of the total variance of anxiety scores measured at T2.

4.4 Discussion

In our sample, the percentage of mothers who reported symptoms of depression ranged from 6% to 10%, lowest in the late postpartum period (T4) and highest in the early pregnancy (T1) period. This is consistent with the reported percentage of women who develop depression during pregnancy in Canada ([MDSC, 2009](#)). Other studies from across the developed world have reported similar risks for depression from the first to the third year postpartum ([Giallo et al., 2014](#); [Matthey et al., 2000](#); [O'Hara & Swain, 1996](#)). A systematic review by Bennett and colleagues found the prevalence of depression in pregnancy to be 7.4% in the first trimester, 12.8% in the second trimester, and 12.0% in the third trimester ([Bennett et al., 2004](#)). Others have reported that approximately 12% to 16% women experience postpartum depression ([Leung & Kaplan, 2009](#)).

Anxiety was more common than depression in the study participants. The proportion of mothers screened positive for anxiety during the study ranged from 41% in the early pregnancy period (T1) to 29% in the late postpartum period (T4). Although the information available regarding the prevalence of anxiety in pregnancy in Canada is limited, the percentage of the woman affected by anxiety disorder in any given year in Canada is about 16% ([PHAC, 2002](#)). A study of a large community sample in England, reported a prevalence of 21% of clinically significant anxiety symptoms during early pregnancy ([Heron et al., 2004](#)). A systematic review summarizing prevalence of maternal anxiety reported estimates ranging between 2.6% to 39% during pregnancy and 3.7% to 20% in the postpartum period ([Leach et al., 2015](#)). The rates reported in our study were consistent with that reported in the systematic review.

The results of the present study extend and confirm a number of existing findings concerning changes in maternal depression and anxiety scores during and after pregnancy. In our study, average predicted depression and anxiety scores both declined from pregnancy up to three years after birth. Although the existing literature supports the declining course of depression in the perinatal period, there were less consistent reports regarding the course of anxiety in the perinatal period. An earlier study based in the United Kingdom reported a similar decrease in the mean depression and anxiety scores from pregnancy to eight months postpartum ([Heron et al., 2004](#)). A decreasing risk of depression from pregnancy through two years postpartum was also reported by Dipietro, et al. ([2008](#)). Similar results for anxiety were reported by Martini et al. with highest prevalence of anxiety (21.2%) in first trimester followed by a progressive decrease to 6.4% up to four months postpartum ([2013](#)). Others have reported that the prevalence of anxiety was highest in the immediate postpartum period followed by decline later in the postpartum period ([Dennis et al., 2013; Figueiredo & Conde, 2011; Paul et al., 2013](#)).

For depression measured at three years after birth (T4) period, early postpartum (T3) period, and late prenatal (T2) period, previous depression scores were significant predictors; indicating, that the postpartum depression is preceded by antepartum depression. However, for anxiety measured at three years after birth (T4), both previous depression and anxiety scores were significant predictors. Various observation studies had earlier stated that prenatal depression and anxiety scores were significant predictors of postpartum depression and anxiety scores respectively ([O'Hara & Swain, 1996](#)). To our knowledge, this is the one study that examines and quantifies the influence of previous time point depression and anxiety measures on subsequent depression and anxiety scores. Postpartum depression and anxiety were preceded by antepartum depression and anxiety in this study. Previous depression scores accounted for 18% to 21% of variability in the subsequent depressions scores, and previous anxiety scores accounted for 23% to 26% of the variability in the subsequent anxiety scores. Thus, we can conclude that to prevent the development of chronic maternal depression, all time periods, including those during pregnancy and early postpartum, were important and sensitive.

Also, for depression scores measured three-years after birth (T4), early (T1) and late (T2) pregnancy were equally sensitive time periods. However, for anxiety, early pregnancy (T1) was relatively more sensitive time period as compared to the late pregnancy (T2). Based on a systematic review, the most consistently reported risk factors for antepartum depression were lifetime risk of depression, antepartum anxiety, unintended pregnancy, relationship issues, life stress, lack of social support, and domestic violence ([Lancaster et al., 2010](#)). However, Records & Rice ([2007](#)) had also concluded that along with these commonly stated risk factors, 46% of the variance of third-trimester depressive symptoms was due to negative mood states during the first trimester ([Records & Rice, 2007](#)). Anxiety in late pregnancy (T2) has been associated with the

thoughts about labour, birth, and wellbeing of the baby ([Goodman, 2014](#); [Ross, 2006](#)). Once the baby is born, these reasons for anxiety are alleviated in most cases, and long-term effects of late pregnancy anxiety may not persist.

This study characterised several aspects of the role of a history of depression in pregnancy and postpartum depression and anxiety scores. First, the course of depression and anxiety scores were different for mothers with history of depression as compared to mothers without the history of depression. For mothers with history of depression, depression and anxiety scores were highest in early pregnancy (T1) and declined steadily subsequently. However, for the mothers with no history of depression no significant difference was observed from early pregnancy (T1) up to early postpartum (T3) depression scores with scores finally declining before three years after birth (T4).

Second, the effects of history of depression varied at different observation times during the study. Both EPDS depression scores and anxiety scores were significantly higher in early pregnancy (T1) and three years after birth (T4) among mothers with history of depression as compared to mothers with no history of depression, but there was no difference in late pregnancy (T2) or in the early postpartum period (T3).

Third, this study described mediator and moderator effects of history of depression on stress in early pregnancy (T1) and their combined effect on predicting longitudinal anxiety scores. The impact of stress in early pregnancy (T1) on both depression and anxiety during and after pregnancy was greater in women with a history of depression. In the presence of history of depression, stress in early pregnancy (T1) significantly increased both depression and anxiety scores both during and after pregnancy. This finding is supported in part by the finding that the effect of history of depression on anxiety was mediated in part by stress in early pregnancy (T1).

Although, stress in early pregnancy (T1), in the absence of history of depression, was associated with higher overall depression scores over the study period; the impact was much larger in the presence of history of depression.

In our study, along with history of depression and stress in early pregnancy (T1), affective lability scores three years after birth (T4) and stress in the early postpartum period (T3) were associated with significant increases in the longitudinal depression and anxiety scores. In contrast, some post-secondary education in early pregnancy (T1) were associated with lower anxiety scores across the four study periods. Other factors such as availability of emotional support during the study period and having had more than one child were associated with lower average depression scores from early pregnancy through three years postpartum. The only risk factor that did not have a consistent impact on either EPDS scores or anxiety scores over the study period was the previously discussed history of depression.

Similar findings were observed by Martini et al. ([2015](#)) regarding the protective effects of education, support for the mother, partnership satisfaction, and multi-parity on both depression and anxiety scores. Giallo et al. ([2014](#)) in a study in Australia had also concluded that having a history of depression, not completing high school, poor relationship quality, and more stressful life events were some of the strongest predictors of ‘persistently’ high depressive symptoms. Poor socio-economic status, lack of social support, and prior history of maternal mental health problems and complex obstetric history were some of the most commonly reported risk factors for maternal perinatal anxiety ([Leach et al., 2015](#)). Borri et al. ([2008](#)) had similarly concluded that low education level, low socioeconomic status, and single marital status were significant predictors of anxiety disorders in pregnancy among mothers in Italy. Whereas, Aduwuya et al.

([2006](#)) reported that younger age, primigravida and having a medical condition were significant risk factors for anxiety among mothers in late pregnancy from Nigeria.

Family history of perinatal depression was neither a significant predictor nor a confounder in the final longitudinal models for either depression or anxiety scores. Maternal high-risk behaviours (smoking, alcohol and recreational drug abuse) were also not associated with either depression or anxiety during the study period. Similarly, child-rearing (breastfeeding) and child bearing (birth order, type of birth) practices, and child attributes (sex of the child, overall health of the child) were not found to be significantly associated with depression and anxiety scores. This could be due to loss of power associated with the selective attrition of high-risk mothers from this study before the three-year study time point ([T4](#)) ([Dettori, 2011](#)).

The low retention rate for the fourth round of data collection is one of the most important limitations of this study. Efforts were made to retain mothers using incentives, frequent contact with participants, and providing a range of options for providing data. Mothers who were lost to follow-up were significantly younger, had poorer overall health, were more likely to be single or non-Caucasian, and higher depression scores during pregnancy (Chapter 2). Thus, the study results can be best generalized to predominantly Caucasian mothers with above average family income, and who have some post-secondary education. Similarly, there may have been some loss of variability in the EPDS scores by three-year time point ([T4](#)) due to the selective attrition of mothers with higher EPDS scores in the pregnancy (Chapter 2). Finally, there was also the potential for type 1 error due to a large number of predictors considered for analysis. This risk was managed by choosing risk factors for analysis based on the previous literature and screening variables prior to considering them in building the multivariable models.

The time course and risk factors for anxiety disorder in pregnancy have received limited attention to date. Previously, the early postpartum period has been established as the most important time for the screening and prevention of chronic maternal depression and anxiety. This is one study which has empirically established the significance of both pre-pregnancy and early pregnancy period as important periods for targeting prevention and control strategies for prevention of depression and anxiety during the postpartum period and beyond. The need for systematic efforts to screen and develop maternal mental health services for depression and anxiety are recognized. Interventions for prevention and control of long-term maternal and child effects of chronic depression and anxiety should be focused both during and after pregnancy. Relaxation techniques, psychoeducation, and cognitive-behavioural interventions, and interpersonal therapy designed to improve mother-infant-interaction are promising strategies ([Goodman, 2014](#); [Sockol et al., 2011](#); [Stein et al., 2012](#)). Further research is needed with larger study populations and more observation times to differentiate groups of women with specific trajectories for depression and anxiety during and after pregnancy to better inform time sensitive interventions.

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4.6 Appendices

4.6.1 Appendix 4-A: Table of results from the unconditional or bivariate analysis of depression

Table 1: Estimates of the unconditional associations between potential risk factors and depression measured using a 30 point EPDS scale resulting from linear mixed models accounting for repeated measures within individual women at $p<0.2$ ($N=333$).

Covariates in the unconditional analysis of depression		Change in depression scores (β)	95% CI Lower	95% CI Upper	p-value
Time Point*	1 st vs. 4 th	1.5	1.1	2.0	<0.0001
	2 nd vs. 4 th	1.2	0.7	1.7	<0.0001
	3 rd vs. 4 th	0.9	0.4	1.4	<0.0001
Family history of perinatal depression*	Yes vs. No	1.2	0.5	1.9	0.001
	Don't know/ NA	1.1	0.1	2.0	0.03
history of depression*	Yes vs. No	1.9	1.3	2.5	<0.0001
Education level	Some postsecondary vs. Less than postsecondary	-0.2	-1.3	0.8	0.65
Employment status	Yes vs. No	-0.5	-1.3	0.4	0.31
Planned pregnancy	Yes vs. No	-0.4	-1.3	0.5	0.38
Mothers' age	Centered, Linear	0.03	-0.03	0.1	0.32
Mothers' ethnicity	Caucasian vs. Non-Caucasian	-0.4	-1.7	0.9	0.55
Marital status at enrollment	Married/Common Law vs. Single/Divorced	0.6	-0.8	1.9	0.45
PREGNANCY & NATAL FACTORS (T1 & T2)					
Pregnancy physical abuse*	Yes vs. No	1.3	0.6	2.0	<0.0001
Pregnancy overall health of the mother	Poor/Fair/Okay vs. Excellent/Very good/Good*	2.4	-0.1	4.9	0.06
Stress due to any reason at T1 time point*	Yes vs. No	2.9	1.9	3.9	<0.0001
Stress due to any reason at T2 time point*	Yes vs. No	1.7	0.7	2.7	0.001
Pregnancy complications*	No vs. Yes	-0.6	-1.4	0.3	0.20
Type of birth	Assisted vs. Spontaneous	0.1	-0.9	1.00	0.9
	C-section vs. Spontaneous	-0.4	-1.0	0.3	0.32
Gestation period	Centered, Linear	0.1	-0.1	0.3	0.24
Birth complications*	No vs. Yes	-0.5	-1.1	0.1	0.10
One minute apgar scores	≥ 7 vs. <7	-0.6	-1.5	0.3	0.22
Five minute apgar scores	≥ 7 vs. <7	-1.2	-3.4	0.9	0.27
Neonatal complications	No vs. Yes	0.2	-0.4	0.8	0.46
Birth defects	Yes vs. No	0.5	-0.4	1.5	0.27
Sex of child	Female vs. Male	-0.3	-0.9	0.3	0.40
Weight for gestational age (WHO)	SGA vs. AGA	-2.0	-1.3	0.9	0.70
	LGA vs. AGA	-0.5	-1.5	0.4	0.30
Weight for gestational age (PHAC)	SGA vs. AGA	-0.2	-1.3	0.9	0.70
	LGA vs. AGA	-0.5	-1.5	0.4	0.30

Covariates in the unconditional analysis of depression		Change in depression scores (β)	95% CI Lower	95% CI Upper	p-value
T3 TIME POINT MEASURES					
Birth order	Second vs. First	0.1	-0.5	0.8	0.70
	Third or more vs. First	-0.2	-1.2	0.7	0.60
Gravida status	Multigravida - Primigravida	0.1	-0.6	0.7	0.8
Stress due to any reason*	Yes vs. No	1.9	1.3	2.7	<0.0001
Breastfeeding initiated*	Yes vs. No	-0.9	-1.7	-0.0	0.04
T4 TIME POINT MEASURES					
Any subsequent pregnancy*	Yes vs. No	-0.8	-1.4	-0.2	0.006
Emotional support*	Yes vs. No	-4.3	-7.5	-1.1	0.008
Mood disorder scores*	Continuous	0.2	0.2	0.2	0.000
Maternal overall health *	Fair/Good vs. Excellent/ Very good	-1.7	-3.0	-0.5	0.005
Child overall health *	Fair/Good vs. Excellent/ Very good	1.2	-0.2	2.5	0.08
History of diagnosis & treatment of depression during the study time period	Non-pharmacological methods vs. Not diagnosed	0.03	-2.2	2.3	0.98
	Pharmacological methods vs. Not diagnosed	0.5	-0.3	1.3	0.24
Satisfaction with the relationship with father of the child*	Very satisfied vs. No relationship *	-1.0	-2.5	0.4	0.17
	Not very satisfied vs. No relationship	1.7	0.1	3.2	0.03
Employment status	Yes vs. No	-0.1	-0.9	0.6	0.73
Family Income	$\geq \$40,000$ vs. $<\$40,000$ / year	-0.6	-1.6	0.4	0.21
Current education status	Some postsecondary vs. Less than postsecondary	0.02	-1.1	1.1	0.97
Total number of pregnancies at three years*	Multigravida (1) vs. Primigravida	-1.3	-2.2	-0.3	0.01
Current marital status	Married /Common law vs. Single/ Divorced/ Separated	0.7	-0.5	1.8	0.24
Exercise	Yes vs. No	-0.1	-0.6	0.5	0.8
Smoke	Quit vs. Never	0.2	-0.6	0.9	0.7
	Smoke vs. Never	0.5	-0.6	1.6	0.34
Drug abuse*	Quit vs. Never	-0.03	-1.0	0.9	0.96
	Abuse vs. Never	1.8	-0.04	3.6	0.06
Alcohol	Quit vs. Never	-0.2	-0.7	0.3	0.48
	Drink vs. Never	-0.1	-0.5	0.3	0.65

* Unconditionally associated with linear longitudinal maternal depression

4.6.2 Appendix 4-B: Table of results from the unconditional or bivariate analysis of anxiety

Table 2: Estimates of the unconditional associations between potential risk factors and anxiety scores (9-point scale) resulting from linear mixed models accounting for repeated measures within individual women at p<0.2 (N=333).

Covariates in the unconditional analysis of anxiety		Change in anxiety scores	95% CI Lower	95% CI Upper	p-value
Time Point	1 st vs. 4 th	0.9	0.6	1.1	0.01
	2 nd vs. 4 th	0.6	0.3	0.8	<0.0001
	3 rd vs. 4 th	0.3	0.1	0.6	<0.0001
Family history of perinatal depression*	Yes vs. No	0.5	0.2	0.9	0.002
	Don't know/ Not applicable	0.5	0.1	1.0	0.02
history of depression	Yes vs. No	0.9	0.6	1.2	<0.0001
Education level*	Some postsecondary vs. Less than postsecondary	-0.5	-0.9	0.1	0.08
Employment status	Yes vs. No	-0.1	-0.5	0.3	0.71
Planned pregnancy	Yes vs. No	-0.2	-0.6	0.3	0.45
Mothers' age	Centered, Continuous	0.01	-0.2	0.0	0.61
Mothers' ethnicity	Caucasian vs. Non-Caucasian	-0.1	-0.7	0.5	0.72
Marital status at enrollment	Married/Common Law vs. Single/Divorced	0.3	-0.3	1.0	0.32
PREGNANCY & NATAL FACTORS (T1 & T2)					
Pregnancy physical abuse*	Yes vs. No	0.6	0.2	0.9	0.001
Pregnancy overall health of the mother	Poor/Fair/Okay vs. Excellent/ Very good/ Good	0.7	-0.5	2.0	0.25
Stress due to any reason at T1 time point*	Yes vs. No	1.2	0.7	1.7	<0.0001
Stress due to any reason at T2 time point*	Yes vs. No	0.7	0.2	1.2	0.004
Pregnancy complications*	No vs. Yes	-0.3	-0.7	0.1	0.17
Type of birth	Assisted vs. Spontaneous C-section vs. Spontaneous	0.04 -0.01	-0.4 -0.3	0.5 0.3	0.87 0.96
Gestation period	Centered, Continuous	0.1	-0.0	0.1	0.26
Birth complications	No vs. Yes	-0.2	-0.05	0.1	0.30
One minute apgar scores	≥ 7 vs. <7	-0.2	-0.6	0.3	0.43
Five minute apgar scores	≥ 7 vs. <7	-0.5	-1.6	0.5	0.32
Neonatal complications	No vs. Yes	0.2	-0.1	0.5	0.21
Birth defects	Yes vs. No	0.2	-0.3	0.7	0.37
Sex of child*	Female vs. Male	-0.2	-0.5	0.1	0.13
Weight for gestational age (WHO)	SGA vs. AGA LGA vs. AGA	-0.1 -0.2	-0.7 -0.6	0.6 0.2	0.87 0.40
Weight for gestational age (PHAC)	SGA vs. AGA LGA vs. AGA	-0.01 -0.1	-0.6 -0.6	0.6 0.3	0.97 0.54
T3 TIME POINT MEASURES					
Birth order*	Second vs. First	-0.04	-0.4	0.3	0.81

Covariates in the unconditional analysis of anxiety		Change in anxiety scores	95% CI Lower	95% CI Upper	p-value
	3 rd or more vs. First	-0.5	-0.9	0.0	0.06
Gravida status	Multigravida vs. Primigravida	-0.1	-0.4	0.2	0.55
Stress due to any reason*	Yes vs. No	0.8	0.4	1.1	<0.0001
Breastfeeding initiated*	Yes vs. No	-0.3	-0.7	0.1	0.12
T4 TIME POINT MEASURES					
Any subsequent pregnancy*	Yes vs. No	-0.2	-0.5	0.1	0.19
Emotional support*	Yes vs. No	-1.4	-2.9	0.2	0.08
Mood disorder scores*	Continuous	0.1	0.1	0.1	<0.0001
Maternal overall health*	Fair/Good vs. Excellent/Very good	-0.5	-1.1	0.1	0.08
Child overall health	Fair/Good vs. Excellent/Very good	0.3	-0.3	0.9	0.38
History of diagnosis & treatment of depression during the study time period	Non-pharmacological methods vs. Not diagnosed	0.5	-0.6	1.6	0.41
	Pharmacological methods vs. Not diagnosed	0.2	-0.2	0.6	0.25
Satisfaction with the relationship with father of the child*	Very satisfied vs. No relationship	0.04	-0.6	0.7	0.91
	Not very satisfied vs. No relationship	0.6	-0.1		0.09
Employment status	Yes vs. No	-0.1	-0.5	0.3	0.51
Family Income	≥\$40,000/year vs. <\$40,000/year	-0.2	-0.7	0.2	0.34
Current education status	Some postsecondary vs. Less than postsecondary	-0.4	-0.9	0.2	0.16
Total number of pregnancies at three years*	Multigravida vs. Primigravida	-0.5	-0.9	-0.1	0.025
Current marital status	Married /Common law vs. Single/Divorced/ Separated	0.2	-0.4	0.7	0.57
Exercise	Yes vs. No	0.1	-0.1	0.4	0.31
Smoke	Quit vs. Never	-0.1	-0.4	0.3	0.73
	Smoke vs. Never	0.2	-0.3	0.7	0.53
Drug abuse*	Quit vs. Never	-0.1	-0.6	0.4	0.69
	Abuse vs. Never	0.8	-0.1	1.6	0.07
Alcohol	Quit vs. Never	-0.1	-0.3	0.2	0.62
	Drink vs. Never	0.1	-0.1	0.3	0.36

*Unconditionally associated with linear longitudinal maternal depression

**CHAPTER 5: PREDICTORS OF BETTER PHYSICAL, COGNITIVE,
PERSONAL - SOCIAL DEVELOPMENT OF CHILDREN AT THREE
YEARS OF AGE – WHY SOME KIDS FAIR BETTER THAN OTHERS**

5.0 Abstract

In Canada, 25% to 30% of school-age children are reported to have physical, social, emotional, cognitive, or communication delays. This study examines the role of maternal and child factors in enhancing early childhood development. Children of mothers who completed the three-year follow-up of five-year longitudinal Feelings in Pregnancy (FIP) study in Saskatoon, Saskatchewan formed the cohort. The Ages and Stages Questionnaire (ASQ3) was used to measure communication, gross motor, fine motor, problem-solving, and personal-social scores. Scores above the published threshold for normal development were categorized into three equal groups. Ordinal and partial proportional odds regression models were used to test the association between maternal prenatal behaviours, anxiety, depression, and other socio-demographic factors and the odds of achieving the highest vs. low and intermediate scores for normal childhood development. A total of 339 mother-child dyads formed the study sample. Family history of perinatal depression (OR 0.8, 95% CI 0.4 – 1.6) and alcohol consumption (OR 0.4, 95% CI 0.2 – 0.9) during pregnancy were associated with lower odds of high personal-social scores. Breastfeeding initiation in the early postpartum period was associated with the high gross motor (OR 2.1, 95%CI 1.1 – 4.1) and communication (OR 2.0, 95% CI 1.1 – 3.7) scores at three years of age. Term babies as compared to pre-term (OR 2.9, 95% CI 1.2 – 6.9) and post-term (OR 8.4, 95% CI 2.0 – 35.7) babies were more likely to have high problem-solving scores. Girls (OR 3.0, 95% CI 1.8 – 5.2) had three times the odds of having high fine motor scores as compared to boys. Girls (OR 437, 95% CI 14.4 – 13313) with mothers that smoked were also found to be more resilient to the effects of prenatal smoking on personal-social development scores than boys. Our results support previous research identifying social environment factors in addition to biological differences that are important for early childhood development.

5.1 Introduction

The origins of adult health and productivity begin even before pregnancy and patterns of growth and development are determined very early in life ([Victora et al., 2008](#)). For example, brain size increases four-fold during the preschool period, reaching approximately 90% of the adult volume by age six. However, structural changes continue throughout childhood and adolescence ([Stiles & Jernigan, 2010](#)). Thus, most dramatic changes happen in the early years of life.

These changes are guided to a large extent by the child's sensory experiences ([Shonkoff & Phillips, 2000](#)). Healthy physical-social-emotional development entails the ability to form satisfying, trusting relationships with others, play, communicate, learn, face challenges, and experience and handle the full range of emotions ([Braveman & Barclay, 2009](#); [Cohen, 2006](#)). Unfortunately, not all children have the same positive experiences or opportunities, and these differences can lead to disparities ([Grantham-McGregor et al., 2007](#); [Shonkoff & Phillips, 2000](#)). As these gaps extend into the reproductive years and adulthood, they affect subsequent generations, perpetuating a negative cycle of economic and health disparities ([Black & Hurley, 2014](#)).

When compared with 29 OECD (Organization for Economic Co-operation and Development) countries, Canada ranked 27th in childhood obesity and 21st in child well-being including mental health ([Leitch, 2007](#)). Overall, Canada ranked 12th among the 21 industrialised countries of the world in United Nations' assessment of lives and well-being of children and young people ([UNICEF, 2007](#)). In Canada at the time of birth, no more than 5% of children have detectable biological or physical limitation to their development. However, overall between 25% to 30% of children are reported to have physical, social, emotional, language/cognitive, and/or communication delay by the school going age in the provinces of British Columbia, Manitoba,

Prince Edward Island, and Ontario ([Hertzman, 2009](#)). Early developmental problems are often associated with lower school readiness and poor school performance ([Montes et al., 2012](#); [Romano et al., 2010](#)).

Risk factors identified in the literature that compromise children's development and the developing brain include biological risk factors (e.g., stunting, infections, anemia, intrauterine growth retardation, pre-term birth), psychosocial risk factors (e.g., inadequate cognitive stimulation, exposure to violence, household dysfunction), and sociodemographic risk factors (e.g., poverty) ([Aboud & Yousafzai, 2016](#); [Bradley & Corwyn, 2002](#); [Brooks-Gunn & Duncan, 1997](#); [McCormick et al., 2011](#); [Moster et al., 2008](#); [Walker et al., 2011](#)). Similarly, maternal depression and anxiety have been shown to have consequences for child development. Prenatal anxiety was a strong and significant predictor of behavioural, emotional, and cognitive problems ([Correia & Linhares, 2007](#); [O'Connor et al., 2002](#)), as was maternal depression ([Cummings & Davies, 1994](#)). However, sometimes children with depressed or anxious parents do not display behavioural dysfunctions; probably due to the moderating and mediating effects of parental mental health ([Cicchetti et al., 1998](#)).

In Canada, along with prenatal depression, pre-term birth, and low community engagement increased the risk of developmental delay at one year of age. Whereas, relationship happiness, perceived parenting self-efficacy, community engagement, and higher social support decreased the risk developmental delay at one year of age ([McDonald et al., 2016](#)). The building blocks of adult health and productivity begin before conception and take shape very early in life ([Victora et al., 2008](#)). Early intervention in the first three years of a child's life has been shown to be more effective than later remediation. The first 1,000 days (conception through to 24

months of age) provide a good opportunity for interventions that can prevent lifelong negative health outcomes ([Doyle et al., 2009](#)).

Most reports to date have focused on the predictors of poor childhood outcomes; however, understanding predictors of above average physical, cognitive, and personal-social development in early childhood development provides an excellent opportunity to help develop interventions to improve outcomes in vulnerable populations. Hence, this study examines the role of maternal and child factors in attaining high scores for early childhood development in a cohort of mothers and their three-year-old children. We also sought to inform the understanding of potential causal pathways by examining the mediation and moderation effects of important factors identified in the models.

5.2 Methods

The Feelings in Pregnancy and Motherhood' (FIP) study was a longitudinal study of Canadian women who were screened for anxiety, depression, and mood problems in pregnancy and their children were observed for physical, cognitive, and social development ([Bowen et al., 2012](#)). Mothers were recruited during the second trimester of pregnancy. The mean duration of gestation at recruitment and the first data collection point was 17 weeks \pm SD 4.4 weeks labelled as 'early pregnancy' (T1);'. The second measurement, labelled as 'late pregnancy' (T2), was later in the pregnancy at a mean gestation of 30.4 weeks \pm SD 2.4 weeks. The third measurement was at an average four weeks \pm SD 2.0 weeks after birth, and the fourth measurement was completed at an average age of 36.4 months \pm SD 1.6 weeks; these visits were labelled as 'early postpartum'(T3) and 'three years after birth'(T4), respectively. Data were collected on a wide range of health determinants for both the mother and their child. Data were obtained from hospital charts, in-person and telephone interview, and written questionnaire by two research

assistants. Data were compiled using SPSS (v20.0 – 24.0) software and summaries developed after each cycle of data collection. Of the 648 women recruited for the study, 338 (333 singleton pregnancies and five twin pregnancies) completed the fourth phase of data collection when their children were three years old. Data from these 343 children were included in this analysis. The average age of children at the time of data collection was 36.4 ± 1.6 months. The outcomes of interest for this analysis were the physical, cognitive, and personal – social development of the children at three years of age as measured by the Ages and Stages Questionnaire ([Squires et al., 2009](#)). The study was funded by Canadian Institute of Health Research (CIHR) (grant#145179) and Saskatchewan Health Research Foundation (SHRF). The study was approved by University of Saskatchewan Behavioural Research Ethics Board (Beh-REB # 13-284)

5.2.1 Child measures

5.2.1.1 Ages and Stages Questionnaire (ASQ3®)

The ASQ3® is a series of parent-completed questionnaires designed to screen the developmental performance of children aged 1 – 66 months which includes communication skills, gross motor skills, fine motor skills, problem-solving, and personal-social skills ([Squires et al., 2009](#)). The ASQ3® was standardised in a national sample of 12,695 children and cut-offs were computed to differentiate between normal and subnormal development at 36 months of age ([Squires et al., 2009](#)). Each of the five subscales had six questions, and each question was measured on the 3-point Likert scale; ‘Yes’, ‘Sometimes’, or ‘Not Yet’. Score value for ‘Yes’ was ten points, ‘Sometimes’ was five points, and ‘Not Yet’ was zero points. Hence, each child could have a maximum score of sixty (60) for each subscale ([Squires et al., 2009](#)). However, due to the five point increments, they could not be strictly considered continuous.

The cut-off for communication skills was 30.99, for gross motor skills was 36.99, for fine motor skills was 18.07, for problem-solving skills was 30.29, and for personal-social skills was 35.33 ([Squires et al., 2009](#)). Test-retest reliability was found to be 0.91, and inter-rater reliability was found to be 0.92. The ASQ3® was found to have a sensitivity of 86%, specificity of 85%, and validity of 0.82 - 0.88 ([Squires et al., 2009](#)).

ASQ3® was administered at T4. Each ASQ3® subscale was dichotomized based on established cut-offs ([Squires et al., 2009](#)). In total 17/343 (5%) children reported scores below the cut-off for one or more of the subscales. The number of children in each subscale that were below the cut-off ranged from four to six. Only data from the children with scores above each cut-off were included in the relevant analysis.

Table 5-1: Summary of distribution of children in the study population based on the categorization of data above the cut-off point for communication, gross motor, fine motor, problem-solving and personal-social skills used for model building.

Subscale	Categories	Label*	N	Percentage
Children with total ASQ communication scores above 30.99 (n = 339)	ASQ communication scores between 51 – 60	2	241	71.1%
	ASQ communication scores between 41 – 50	1	93	27.4%
	ASQ communication scores between 31 – 40	0	5	1.5%
Children with total ASQ gross motor scores above 36.99 (n = 338)	ASQ gross motor scores between 54 – 60	2	284	84%
	ASQ gross motor scores between 46 – 53	1	31	9.2%
	ASQ gross motor scores between 37 – 45	0	23	6.8%
Children with total ASQ fine motor scores above 18.06 (n = 338)	ASQ fine motor scores between 47 – 60	2	257	72.8%
	ASQ fine motor scores between 32 – 46	1	70	20.7%
	ASQ fine motor scores between 19 – 32	0	11	6.5%
Children with total ASQ problem-solving scores above 30.3 (n = 337)	ASQ problem-solving scores between 51 – 60	2	222	65.9%
	ASQ problem-solving scores between 41 – 50	1	93	27.6%
	ASQ problem-solving scores between 31 – 40	0	22	6.5%
Children with total ASQ personal-social scores above 35.3 (n=338)	ASQ personal-social scores between 52 – 60	2	255	75.4%
	ASQ personal-social scores between 44 – 51	1	78	23.1%
	ASQ personal-social scores between 36 – 43	0	5	1.5%

*2 – High skills, 1 – Intermediate skills, 0 – Low skills

Scores above the cut-off were categorized into three equal groups based on the observed range of the total available scores above the threshold for normal development. The resulting

categories were labeled as ‘high’ (highest scores), ‘intermediate’ (middle scores), and ‘low’ (lowest scores) development (Table 5-2).

5.2.1.2 Other child measures

The child’s birth weight, birth length, one- and five-minute ‘Apgar’ (Appearance, Pulse, Grimace, Activity, and Respiration) scores, type of birth, and any neonatal or birth complications were extracted from hospital discharge records. Apgar scores were dichotomized as seven or above and below seven ([Apgar, 1972](#)). Child birth weights were converted into weight for gestational age categories and were referred to as ‘appropriate weight for gestational age’ (AGA) (weight between 10th and 90th percentile for gestational age), ‘small for gestational age’ (SGA)(weight below 10th percentile for gestational age), and ‘large for gestational age’ (LGA) (weight above 90th percentile for gestational age) ([Kramer et al., 2001](#)). Completed gestation at the time of birth was centred by subtracting the mean gestation. Gestation was also categorized as (when necessary to address failure of the linearity assumption); less than 37 weeks of gestation was labelled ‘pre-term’, 37 – 41 6/7 weeks was labelled ‘term’, and more than 42 weeks of gestation as ‘post-term’ ([Eisfeld, 2014](#); [UN, 2001](#)).

Information about initiation and duration of breastfeeding was collected at T3 and T4. Information about the child’s overall health reported by the mother was dichotomized by summarising ‘Okay’, ‘Fair’, and ‘Poor’ categories as ‘Poor’ and ‘Good’, ‘Very good’, and ‘Excellent’ as ‘Good’.

5.2.1.3 Maternal measures

Questionnaire captured information regarding mood changes, high-risk behaviours (smoking, alcohol, recreational drug use), self and family history of perinatal depression, medical and obstetric history, stressors, relationship with the father of the child, physical or emotional

abuse during or after pregnancy, and supports available to the mother, such as partner, mother, friends and relatives. The Edinburgh Postpartum Depression Scale (EPDS) was used to screen mothers for depression during and after pregnancy and three years after the birth of the baby ([Cox et al., 1987](#); [Murray & Cox, 1990](#)). Mothers with total EPDS (Edinburgh Postpartum Depression Scores) scores of ≥ 12 were categorised as depressed ([Choate & Gintner, 2011](#); [Cox et al., 1987](#)). EPDS has also been validated as a useful measure to screen for anxiety (items 3, 4, & 5) during pregnancy and during the postpartum period ([Matthey et al. \(2013\)](#)). The Affective Lability Scale – Short Form (ALS-SF), the 18-item scale was used to measure self-reported mood changes in the mothers at T4 time point only ([Harvey et al., 1989](#); [Oliver & Simons, 2004](#)). Total EPDS anxiety subscale (item 3, 4, & 5) and ALS-SF scores were evaluated as linear predictors in the model.

Annual family income, employment history, and education status of the mother were obtained at each time point and were considered as time-varying covariates in the model. Similarly, information about high-risk behaviours, relationship with the father of the child, and life stressors were also obtained at each study time point to be considered as time-varying covariates in the model.

Maternal age at the time of enrollment was categorised into less than 25 years, 25 – 34 years, and greater than or equal to 35 years. Mother's education was dichotomized as 'some post-secondary education' and 'less than post-secondary education'. Mother's employment status was dichotomized as 'Yes' vs. 'No'. Annual family income was dichotomized using the annual income of \$40,000 as a cut-off (based on the estimates of low-income cut-off for a family of four in Canada) ([Statcan, 2015](#)).

Maternal overall health was measured by asking ‘how would you rate your overall health today’ and dichotomized by summarising ‘Fair’ and ‘Poor’ categories as ‘Poor’ and then ‘Good’, ‘Very good’, and ‘Excellent’ as ‘Good’. Any family history of perinatal depression or treatment of depression in the mother or any of her siblings was combined into one binary variable. History of exposure to smoking, alcohol, and recreational drug use at time point T1, T2, T3, & T4 were included as a nominal variable, ‘0’ indicating never exposed, ‘1’ quit and ‘2’ continued exposure.

Maternal relationship status was a nominal variable with options including ‘no relationship’, ‘not satisfied’, ‘somewhat satisfied/neutral’, and ‘very satisfied’. However, due to relatively few observations in the ‘not satisfied’ and ‘somewhat satisfied/neutral’ categories; the variable was re-categorised as ‘very satisfied’, ‘not very satisfied’, and ‘no relationship’. Information regarding any subsequent pregnancy, miscarriage, or birth was also obtained from the mother.

5.2.1.4 Model building strategy

Potential determinants of more advanced early childhood development measured as higher category scores for the five subscales of communication skills, gross motor skills, fine motor skills, problem-solving skills, and personal-social skills in children at three years of age were evaluated using ordinal regression by STATA 12.0 ([StataCorp, 2009](#)). Independent variables selected for analysis were based on extensive literature review. Before building the multivariable model, independent variables were further screened by examining the unadjusted associations between each risk factor and outcome at p-value <0.2. The multivariable models were built using ‘ologit’ programs in STATA 12.0 for ordinal regression ([Long & Freese, 2006](#)).

The significance of the independent variables was assessed using Wald's Chi-square test at 5% level of significance ([Dohoo et al., 2012](#)).

Variables with unadjusted p-value <0.2 based on the type 3 Wald test were retained for consideration in building the final multivariable model ([Dohoo et al., 2012](#)). Manual stepwise backward selection was used to develop the main effects model, retaining only variables where p-value <0.05 ([Dohoo et al., 2012](#)). Potential confounders were assessed based on a >20% change in regression coefficients for variables of interest ([Kleinbaum, 1982](#)). Significant predictors and confounders in the final model were checked for potential mediation effects based on *a priori* hypotheses ([Kenny, 2013](#); [MacKinnon et al., 2000](#)). Biologically relevant two-way interactions were considered and retained in the final model if p <0.05. Variable significance was checked by type 3 Wald test ([Dohoo et al., 2012](#)).

Continuous predictors were checked for linearity (linear association with the logit of the outcome) ([Dohoo et al., 2012](#)). All ranked categorical and continuous risk factor variables were checked for collinearity using Pearson's or Spearman's correlation coefficients, as appropriate. Where variables were highly correlated ($p \geq 0.9$), the variable with fewer missing values or that was most biologically relevant was retained ([Dohoo et al., 2012](#)).

Covariates associated in the unadjusted analysis were further checked for the proportional odds assumption using 'brant' test at 5% level of significance ([Long & Freese, 2006](#)). However, if the 'brant' test failed to compute the p-values, 'gologit2' with 'autofit' subcommand was used to identify the predictor which failed the assumption ([Vincent, 1999](#); [Williams, 2005](#)). The 'gologit2' user written program fits generalised ordered logit model as well as less restrictive models including the partial proportional odds model ([Williams, 2005](#)). If the proportional odds

assumption was violated due to an empty cell or cells in a contingency table for the outcome variable and a covariate, transformation into binary independent variables was considered.

If the proportional odds assumption was otherwise violated, the variable was conditionally retained in the model, and the assumption for proportional odds was checked again for the final multivariable model using ‘brant’ test or ‘gologit2’ command with ‘autofit’ ([Williams, 2005](#)). If the assumption was violated in the final model, a partial proportional odds model was built using the ‘npl’ command to allow individual variables to fail the parallel odds assumption using ‘gologit2’ ([Williams, 2005](#)) and separate effect estimates were reported for each level of increase in the outcome for the affected variables.

Since standardized residuals could not be computed directly after ordinal regression, binary models were built and standardized residuals computed to check for the extreme outliers ([Berry, 1993](#)). The ‘potential influence’ of an extreme outlier was investigated by building the model with and without them and comparing the estimates ([Fox, 1991](#)). Changes in the predictor estimates with and without the outlying data points were examined to evaluate the significance of these outliers in the model ([Fox, 1991](#)). Individual values that resulted in substantial changes (>10%) in the model effect estimates were considered influential and were removed during the model building process ([Dohoo et al., 2012](#)). This was done to minimise the chance of a variable being included or excluded based on a very small proportion of data. However, after the model structure was finalized, the influential observations were included for the calculation of the final effect estimates ([Dohoo et al., 2012; Fox, 1991](#)).

Mediation effects of the confounding variables and significant variables were checked using ‘sgmediation’ and bootstrapping procedure (Sobel-Goodman tests) ([Preacher & Hayes, 2004](#)). When there was more than one mediator, the ‘khb’ command was used to estimate the

proportion of indirect effect contributed by each of the mediators ([Breen et al., 2013](#)). The Goodness of fit (GOF) for the ordinal model was evaluated by comparing the likelihood value obtained by fitting the multinomial model. A large value of likelihood ratio chi-square ($p < 0.05$) indicates a poor fit to the data ([Long & Freese, 2006](#); [Long & Freese, 2014](#)).

Odds ratios (ORs) with 95% confidence intervals (CIs) using robust standard errors were reported for the final regression models. Computed ORs represent the odds of attaining high versus intermediate/low scores as well as the odds of high/intermediate versus low scores for physical and cognitive development as measured by the ASQ3® from the ordinal or proportional odds models. Variables that failed the proportional odds assumption that were examined using a partial model were presented with specific odds ratios for each comparison. Predicted probabilities for individual score categories were computed, which were used to graphically represent the effects of the individual predictors on the probability that an outcome would fall into a particular category ([Dohoo et al., 2012](#); [Long & Freese, 2006](#); [Long & Freese, 2014](#)).

5.3 Results

Data were available for 343 mother-child dyads where the mean age of the children was $36.4 \text{ months} \pm 1.6 \text{ months}$ and the mean age of the mothers was $29.9 \pm 4.4 \text{ years}$. The number of mothers screened positive for depression (i.e., EPDS ≥ 12) were 33 (9.6%) at T1, 21 (6.2%) at T2, 23 (6.7%) at T3, and 20 (5.8%) at T4. Average anxiety score $\pm \text{S.D}$ at T1 was 3.0 ± 1.9 , at T2 was 2.8 ± 1.8 , at T3 was 2.5 ± 1.9 , and at T4 was 2.2 ± 1.8 . The average ALS-SF scores at T4 was 28.4 ± 8.7 .

Only 20 (5.8%) mothers reported having smoked during late pregnancy which increased to 21 (6.0%) at T3 and to 33 (9.6%) at T4. Most 230 (67%) reported ‘quitting’ alcohol; however, 18 (5.3%) continued to ‘drink’ at T1, which increased to a total of 22 (6.5%) at T2, and 128

(37.5%) at T3, and 312 (91%) at T4. About, 44 (12.8%) mothers reported ‘quitting’ recreational drug use, but 5 (1.5%) continued to use drugs at T1. Four out of the five women who used drugs at T1 quit at T2 (late pregnancy) and did not report drug use for the remainder of the study.

Little more than half 175 (51%) of the children were born with a spontaneous normal vaginal birth; 113 (33%) were born by caesarean section, 45 (13%) were born by assisted vaginal birth. For the remaining 10 (3%) children information about the type of birth was missing. Of 343 births, 52.5% (180/343) were girls, and 41.1% (141/343) were the first child. Most of the children 309 (90.1%) were born at term, 20 (5.8%) were pre-term, and the remaining 8 (2.3%) were post-term. One minute Apgar scores were available for 320 (93.3%) children, most 276 (86.3%) had scores of seven or more. Most 269 (78.4%) children had appropriate birth weight for gestational age, 32 (9.3%) were small for gestational age, and 38 (11.1%) were large for gestational age. Breastfeeding was initiated at T3 for most, 285 (83%) of the children, and almost all 283 (99.3%) were reported to have been breastfed at T4.

Very few 10.5% (36) of the children were reported to have birth defects including the neural tube defect, cleft lip/palate, heart defect, multiple defects. Approximately 61% (209) of the children were reported to have neonatal complications within four weeks of birth including meconium aspiration, infection, jaundice, drug withdrawal, Rh incompatibility, Group B streptococcal infection, or admitted to neonatal intensive care unit (NICU). Most of the children were rated as excellent or very good health by their mothers (324/339, 94.5%).

Based on the ASQ data, the proportion of children reported as having high communication skill scores were 71%, high gross motor skill scores were 84%, high fine motor skill scores were 76%, high problem-solving skill scores were 66%, and high personal-social skill scores were 75%.

5.3.1 Communication skills

History of maternal depression, history of drug use at T1, prenatal physical abuse at T1 and/or T2, overall good health of the mother at T1 & T4, stressors at T1 & T2, anxiety scores at T1 & T4, one minute Apgar scores, presence of birth defects, weight for gestational age, initiation of breastfeeding, and overall good health of the child at three years of age (T4) were associated with higher communication skill scores based on the unadjusted analysis ($p<0.2$) (Appendix 5-A – Table 1).

In the final multivariable model, factors significantly associated with the higher communication skill scores included one minute Apgar scores, weight for gestational age, and initiation of breastfeeding (Table 5-3). For a child born LGA, the odds of high compared to intermediate or low communication scores decreased by 30% as compared to babies born AGA (Table 5-3). However, there was no significant difference in communication skill scores between AGA babies and SGA babies. Children who were breastfed in the early postpartum period had twice the odds of having high communication skill scores than those who were not (Table 5-3).

Table 5-3: Estimated odds ratio, p-value, and 95% confidence intervals for significant predictors of high communication skills (top third of normal ASQ3® scores) in the final multivariable model based on ordinal regression (n=313).

Variable	Odds Ratio	95% CI Lower	Upper	p-value
Weight for gestational age	SGA vs. AGA	1.7	0.6	5.0
	LGA vs. AGA	0.3	0.2	0.6
1 minute Apgar score (binary)	≥ 7 vs. <7	2.4	1.2	4.6
Breastfeeding initiated	Yes vs. No	2.0	1.1	3.7

AGA – Appropriate for gestational age, SGA – Small for gestational age, LGA – Large for gestational age

Wald test of parallel lines assumption for the final model: $\chi^2(4) = 0.56$, p-value = 0.9

Likelihood ratio test of goodness of fit: LR $\chi^2(4) = 1.12$, p-value = 0.9 (Good fit)

5.3.2 Gross motor skills

Family history of anxiety or depression, education status of the mother at T1 & T4, exercise at T2, smoking at T2, T3, & T4, overall good health at T1, depression at T2, initiation of

breastfeeding at T3, anxiety at T3, and satisfied with relationship at T4, education level and employment status at T4 were associated with higher gross motor skill scores based on the unadjusted analysis ($p<0.2$) (Appendix 5-A – Table 2).

Initiation of breastfeeding was the only significant predictor in the final model. Children who were breastfed in early postpartum period (T3) were twice likely to have higher gross motor skill scores as compared to those who were not breastfed (Table 5-4).

Table 5-4: Estimated odds ratio, p-value, and 95% CI of significant predictors of high gross motor skills (top third of normal ASQ3® scores) in the final multivariable model based on ordinal regression (n=333).

Variable		Odds ratios	95% CI		p-value
			Lower	Upper	
Breastfeeding initiated	Yes vs. No	2.1	1.1	4.1	0.03
Family history of perinatal depression M	Yes vs. No Don't know/NA vs. No	0.7 0.5	0.4 0.2	1.5 1.1	0.23 0.03

M – Mediator

Wald test of parallel lines assumption for the final model: $\chi^2(3) = 5.4$, p-value = 0.15

Likelihood ratio test of goodness of fit: LR $\chi^2(3) = 5.8$, p-value = 0.12

Family history of perinatal depression was a mediator to the effects of initiation of breastfeeding. Family history of perinatal depression mediated approximately 20% of the total effects of breastfeeding in predicting gross motor skills.

5.3.3 Fine motor skills

History of depression, planned pregnancy, marital status at T1 & T4, satisfaction of relationship with partner at T2 & T3, prenatal exposure to alcohol, anxiety at T1 & T3, early pregnancy depression, sex of the child, birth order of the index child, smoking at T3, and ALS scores at T4 were associated ($p<0.20$) with fine motor skill scores based in the unadjusted analysis ($p<0.2$) (Appendix 5-A – Table 3).

In the final multivariable model, depression at T3, sex of the child, and status of relationship with the partner at T3 were significant predictors of higher fine motor skill scores.

Anxiety at T3 was a confounder with respect to the effects of early postpartum (T3) depression in predicting the fine motor skill scores at three years of age (Table 5-5:).

Table 5-5: Estimated odds ratio, p-value, and 95% CI of significant predictors and confounders of high fine motor skills (top third of normal ASQ3® scores) in the final multivariable model based on ordinal regression (n=338).

Variable	Description of categories	Odds ratios	95% CI		p-value
			Lower	Upper	
Early postpartum depression (T3)	Yes vs. No	0.4	0.2	0.9	0.05
Sex of the child	Female vs. Male	3.0	1.8	5.2	<0.0001
Relationship satisfaction (T3)	Not very satisfied vs. No relationship	14.1	2.7	73.5	0.002
	Very satisfied vs. No relationship	11.9	2.8	50.8	0.001
	Continuous	0.95	0.81	1.11	0.5
C – Confounder in the model, T3 – Early postpartum					
Brant test of parallel regression assumption: $\chi^2 (5) = 3.2$, p = 0.67					
Likelihood ration test of goodness of fit: LR $\chi^2 (5) = 3.1$, p = 0.69 (good fit)					

The odds of having high as compared to intermediate/low fine motor skill scores in children of the mothers who screened positive for depression (EPDS ≥ 12) at T3 were 0.4 times that of mothers who did not have depression at T3. Children of the mothers in a relationship regardless of the quality of the relationship were more likely to have high fine motor skill scores as compared to mothers not in a relationship (Table 5-5). Female children had three times greater odds of having high fine motor skill scores as compared to male children (Table 5-5).

5.3.4 Problem-solving skills

Prenatal overall health, anxiety and depression at T1, smoking at T2 & T3, and recreational drug use at T2, pregnancy complications, type of birth, gestation period, neonatal complications, birth defects, birth order, initiation of breastfeeding, exercise at T3 & T4, and late postpartum mood disorder were associated with problem-solving skill scores in the unadjusted analysis (p<0.2) (Appendix 5-A – Table 4).

In the final multivariable model, smoking and drug use at T2, gestation period, birth order, neonatal complications, and birth defects were significantly associated with higher

problem-solving skill scores. Type of birth was a mediator with respect to birth order. There were total of 11 outliers (standardized residuals >2.0 or <-2.0) detected. All of these 11 outliers were influential ($>10\%$ change in the estimates) (Appendix 5-B – Table1). Hence, a new model was built without these influential data points to avoid the inclusion of biased results.

In the final multivariable model built without the influential data points, gestation period and birth order were predictors of higher problem-solving skills at age three (Table 5-6). Both pre-term and post-term babies had lower odds of high problem-solving skill scores compared to the term babies (Table 5-6). As compared to first-born children, a second-born child had lower odds of high problem-solving skill scores. Anxiety scores at T1, smoking at T2, and drug use at T2 were confounders with respect to both gestation period and birth order (Table 5-6).

Table 5-6: Estimated odds ratio, p-value, and 95% CI of significant predictors of high problem-solving skills (top third of normal ASQ3® scores) in the final multivariable model based on ordinal regression (n=322).

Variable		Odds ratios	95% CI	p-value
			Lower	Upper
Gestation period	Term vs. Pre-term	2.9	1.2	6.9
	Term vs. Post-term	8.4	2.0	35.7
Birth order	First vs. Second	2.1	1.2	3.6
	Third vs. Second	2.1	1.1	4.0
Anxiety at T1 C	Continuous	0.89	0.79	1.02
Smoking at T2 C	Smoke/Quit vs. Never	0.5	0.2	1.1
Drug use at T2 C	Abuse/Quit vs. Never	8.2	0.9	75.1
Neonatal complications M	Yes vs. No	1.7	1.0	3.0
Type of birth M	Assisted vs. Spontaneous	1.4	0.7	3.0
	C-Section vs. Spontaneous	0.6	0.4	1.1

C – Confounder in the model, M – Mediator in the model, T1 – Early pregnancy, T2 – Late pregnancy

Wald test of parallel lines assumption $\chi^2(10) = 5.4$, p-value = 0.9

Likelihood ratio test for goodness of fit: LR $\chi^2(10) = 20.0$, p = 0.03 (Not a good fit to the data)

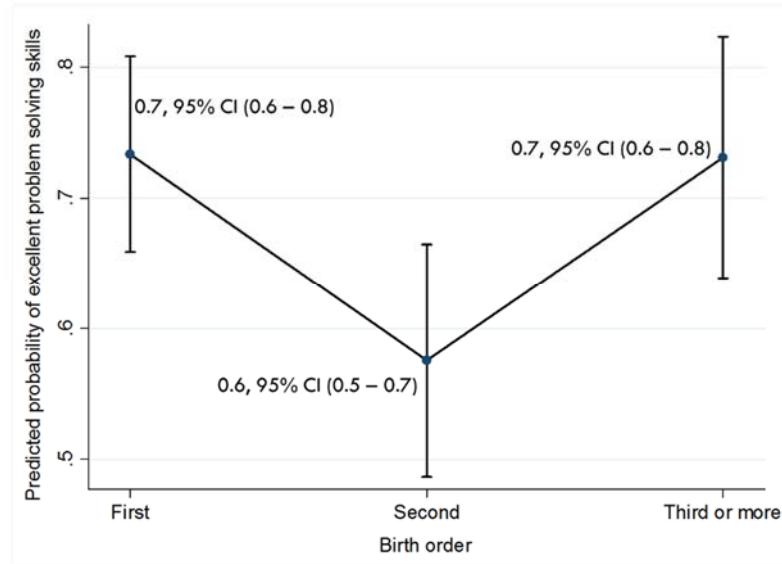


Figure 5-1: Margins plot of predicted probability of high problem-solving skills (top third of normal ASQ3® scores) based on the period of birth order of the baby (n=322).

Having a neonatal complication was a mediator with respect to gestation. Gestation was a significant predictor of having a neonatal complication ($p = 0.01$). Ninety-eight percent of the effect of gestation was explained by having a neonatal complication.

Similarly, type of birth was a mediator with respect to birth order. Birth order was a significant predictor of type of birth ($p = 0.015$). The proportion of the total effect of birth order that was mediated through type of birth was 117%.

5.3.5 Personal-social skills

Family history of diagnosis or treatment of depression, maternal age at the time of enrollment, whether in a relationship in T2, maternal smoking at T1, T2, T3, and T4, maternal alcohol use at T1 and recreational drug use at T1, T3, and T4, maternal exercise at T2 and T4, and family income at T1 and T4, sex of the child, maternal anxiety at T3 and T4, ALS-SF score at T4 and overall health of the child at three years of age were associated with personal-social skill scores in the unadjusted analysis ($p < 0.2$) (Appendix 5-A – Table 5). Smoking status of the

mother at T3 and T4 was converted into a binary variable, ‘Yes’ indicating smoke/quit and ‘No’ indicating never smoked due to empty cells in the matrix.

The multivariable model included overall excellent/good health of the child at T4, being a female child, annual family income greater than \$40,000, and smoking at T1 as positive predictors of high personal-social skill scores. Alcohol use at T1 and smoking at T2 were negative predictors of high personal-social skill scores. Family history of perinatal depression and drug use at T1 were confounders with respect to smoking at T1 and age of the mother was a confounder with respect to annual family income at T4. There were total 16 outliers (standardized residuals >2.0 or <-2.0) detected. Eight were extreme outliers (standardized residuals >3.0 or <-3.0) and 11 of them were found to be influential ($>10\%$ change in the estimates) (Appendix 5-B – Table 2). Hence, new model was built without these influential data points to avoid the inclusion of biased results.

Table 5-7: Estimated odds ratio, p-value, and 95% CI of significant predictors of high personal-social skills (top third of normal ASQ3® scores) in the final multivariable model based on ordinal regression (n=322).

Variable		Odds ratios	95% CI Lower	Upper	p-value
Child overall health at T4	Excellent/Good versus Fair/Poor	5.5	1.8	16.6	0.002
Alcohol consumption at T1	Quit vs. Never	0.4	0.2	0.9	0.04
	Drink vs. Never	0.1	0.0	0.2	<0.0001
Annual income at T4	$\geq \$40,000$ vs. $<\$40,000$	2.7	1.1	6.5	0.03
Family history of perinatal depression	Yes vs. No	0.8	0.4	1.6	0.5
	Don't know/N/A vs. No	0.3	0.1	0.8	0.01
Drug use at T1 M	Quit vs. Never	0.9	0.4	2.1	0.73
	Use vs. Never	0.2	0.01	2.7	0.23
Interaction effects of smoking at T1 and sex of the child					0.03
M – Mediator with respect to family history of perinatal depression, T1 – Early pregnancy, T4 – Three years after birth.					
Wald test of parallel lines assumption (χ^2 (13) = 0.22, p = 0.99)					

The final multivariable model built without the influential data points had history of postpartum depression, alcohol use at T1, smoking at T2, sex of the child, annual family income

and overall health of the child at T4 as significant predictors of high personal-social skill scores (Table 5-6). There was a significant interaction between the sex of the child and the smoking status at T1 (Table 5-8, Figure 5-2).

Girls were more likely to have higher personal-social skill scores than boys regardless of the smoking status of the mother, but the difference was greatest for mothers who smoked at T1 (Table 5-8, Figure 5-2). There were no significant differences in social skill scores among girls associated with their mother's smoking status. However, boys with mothers who smoked or quit smoking prior to or during pregnancy were less likely to have higher personal-social skill scores as compared to those who never smoked (Table 5-8, Figure 5-2).

Table 5-8: Estimated odds ratio, p-value, and 95% CI of two-way comparison of the interaction effects of early pregnancy (T1) smoking and sex of the child in the model for high personal-social skills (top third of normal ASQ3® scores).

Variable	Odds ratios	95% CI		p-value
		Lower	Upper	
Interaction effects of smoking at T1 and sex of the child				0.03
Pairwise comparisons among different smoking histories for mothers of male children				
Mothers with male child who quit smoking vs.	Mothers with male child who never smoked	0.2	0.1	0.7
Mothers with male child who smoke vs.	Mothers with male child who never smoked	0.01	0.0	0.1
Mothers with male child who smoke vs.	Mothers with male child who quit smoking	0.04	0.0	0.7
Pairwise comparisons among different smoking histories for mothers of female children				
Mothers with female child who quit smoking vs.	Mothers with female child who never smoke	3.2	0.3	34.4
Mothers with female child who smoke vs.	Mothers with female child who never smoke	1.4	0.2	12.5
Mothers with female child who smoke vs.	Mothers with female child who quit smoking	0.5	0.02	10.2
Pairwise comparisons between sex of child for mothers with specific smoking history				
Mothers with female child who never smoked vs.	Mothers with male child who never smoked	2.4	1.2	4.7
Mothers with female child who quit smoking vs.	Mothers with male child who quit smoking	36.8	2.8	484
Mothers with female child who smoke vs.	Mothers with male child who smoke	437	14.4	13,313
Wald test of parallel lines assumption (χ^2 (13) = 0.22, p = 0.99				

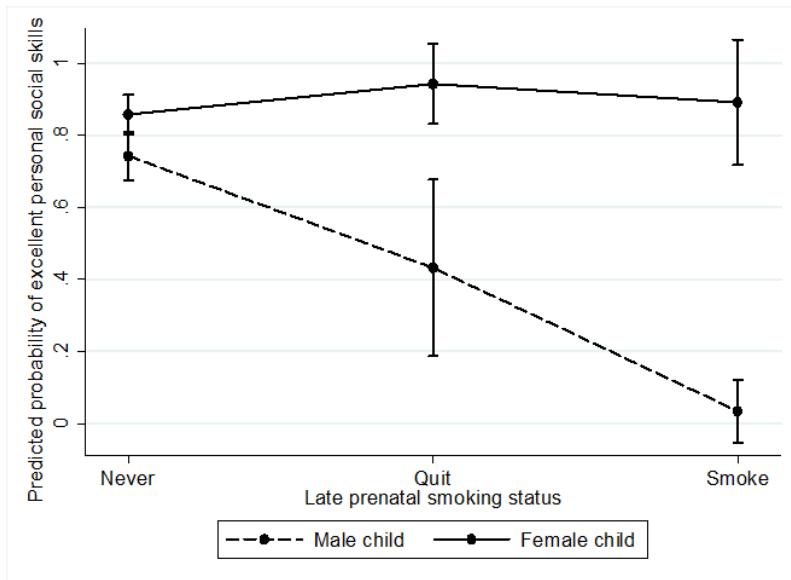


Figure 5-2: Predicted probability of high personal-social skills (top third of normal ASQ3® scores) based on the interaction effects of sex of the child and early pregnancy smoking based on the final multivariable ordinal regression (n=322).

Recreational drug use at T1 was a partial mediator with family history of perinatal depression and it was a significant predictor of early pregnancy recreational drug use (OR 1.1, 95% CI 1.0 – 1.2). Approximately 17% of the effects of family history of perinatal depression were mediated through the recreational drug use at T1.

5.3.6 Summary

Along with risk factors identified during pregnancy and the postpartum period, the pre-pregnancy period was associated with the physical and personal-social development at three years of age. However, for cognitive development (communication and problem-solving skill scores) the post pregnancy period was the most sensitive time period. In our study, maternal prenatal high-risk behaviours (smoking, alcohol, drug use), negative pregnancy outcomes (weight for gestational age, Apgar scores, gestation period), and maternal early postpartum

depression were associated with lower odds of high physical, cognitive, and personal-social skill development.

Table 5-9: Summary of the significant predictors, interactions, confounders and mediators of high ASQ scores from the final multivariable models

ASQ Subscale	Significant variables	Confounding variables
Communication skills	Weight for gestational age One minute Apgar score Breastfeeding initiation	
Gross motor skills	Breastfeeding initiation	Family history of perinatal depression M
Fine motor skills	Sex of the child Satisfaction with partner at T4 Depression at T3	Early postpartum anxiety scores
Problem-solving skills	Gestation period Birth order	Having neonatal complication M Anxiety at T1 Smoking at T2 Drug use at T2 Type of birth M
Personal-social skills	Family history of perinatal depression Alcohol at T1 Sex of the child# Smoking at T1# Overall health of the child at T4 Annual family income at T4	Drug use at T1 M

Variables interacting with each other

M - Variables which were mediators in the model with respect to the significant predictor, T1 – Early pregnancy, T2 – Late pregnancy, T3 – Early postpartum, T4 – Three years after birth

5.4 Discussion

Our results support previous research describing the powerful interaction of biology and the social environment on the development of physical, cognitive, and personal-social skills of children at age three. Results suggest that the key factors that promote higher physical, cognitive, and social development include: 1) avoidance of high-risk exposures like perinatal smoking, alcohol, and drug use; 2) natal factors including term pregnancy, appropriate weight for gestational age, female gender, being the first child, and high one minute Apgar scores; 3)

postpartum factors including maternal depression, breastfeeding, mother in a relationship and having above average annual family income.

The effects of maternal smoking on child cognitive and behavioural development have been studied since the 1980s ([Abel, 1980](#)). In our study, late pregnancy smoking significantly lowered the odds for high personal-social skill scores in male children and early postpartum (T3) smoking was a confounder with respect to the birth defects in predicting higher problem-solving skill scores in children. Existing literature suggests causal effects between pregnancy nicotine exposure and externalizing problems in the children ([Tiesler & Heinrich, 2014](#)); however, results are mixed for the internalizing symptoms of depression and anxiety in children ([Tiesler & Heinrich, 2014](#)). It is well known that smoking in pregnancy is a risk factor for pre-term birth ([Andres & Day, 2000](#); [Polanska & Hanke, 2005](#); [Wisborg et al., 1996](#)). However, research on effects of pregnancy smoking on physical, cognitive, and personal-social behaviour is less consistent.

Research also shows that new mothers are at higher risk for alcohol and illicit drug use in the postpartum period and mothers with a history of substance use have a higher probability of postpartum depression and other mental health comorbidities ([Chapman & Wu, 2013](#); [Hans, 1999](#)). Consistent with previous research ([Johnson & Leff, 1999](#)), our study showed that exposure to alcohol, smoke, and recreational drug in early pregnancy affects the personal-social development of the child. The observed mediating effects of prenatal drug use on the family history of perinatal depression in predicting the personal-social skill scores are well grounded in previous research; however, this is the first time that linkages have been reported using empirical data.

Child bearing and rearing practices influence every aspect of child development. Pre-term birth is a known risk factor for delayed child development ([McDonald et al., 2016](#); [Poulsen et al., 2013](#)); however, our study highlighted the impact of both pre- and post-term birth on problem-solving skill scores in young children. We provided empirical evidence of confounding effects of prenatal smoking and drug use on birth defects and detailed the mediation effects of neonatal complications on gestation in achieving higher problem-solving skill scores at three years of age. Thirty-five percent of the brain growth and approximately 50% of the increase in cortical volume occurs between 34 and 40 weeks gestation ([Adams-Chapman, 2006](#); [Kinney, 2006](#)). Therefore, pre-term birth is more likely to influence the cognitive development in early childhood. The graded relationship between gestation and cognitive ability comes from two Scandinavian studies ([Eide et al., 2007](#); [Ekeus et al., 2010](#)) concluded that mean intelligence scores increased with gestational age of up to 41 weeks and birth weight of 4500 gm, beyond which a decline in intellectual performance was observed ([Eide et al., 2007](#)).

In our study, first-born children had higher problem-solving skills compared to second-born. The literature supports this finding as the first child receives relatively more attention in terms of feeding intervals, interaction time, stimulation, and play from both the mother and father ([Keller & Zach, 2002](#)).

Systematic reviews and meta-analysis have tried to quantify the sex differences in personality. Female children in our study were more likely to have high fine motor and personal-social skill scores, which is consistent with meta-analyses which have concluded that girls perform better on tasks involving flexibility and fine motor coordination, have a larger vocabulary, show a higher level of language complexity, and have a prosocial behaviour or emotions in early childhood ([Cook & Cook, 2009](#); [Feingold, 1994](#)). Feingold ([1994](#)) also

concluded that males were more assertive and have slightly higher self-esteem than females and females were better in extraversion (sociability), anxiety, trust, and nurturance than males and that these differences were generally constant across ages, educational levels, and nationalities ([Feingold, 1994](#); [Weisberg et al., 2011](#)).

In our study higher one-minute Apgar scores (>7) were associated with higher communication skills at three years of age, which confirms a study from Sweden that found one-minute low Apgar scores were associated with lower logical, technical, and IQ (Intelligent Quotient) scores ([Odd et al. \(2008\)](#)). Marschik et al. ([2007](#)) concluded that lower Apgar scores were associated with delayed word production and minor neurological dysfunctions.

Maternal depression and anxiety have been known to exert powerful effects on both cognitive and behavioural development in children. In our study, early postpartum (T3) depression was negatively associated with the fine motor skill scores at three years of age. Maternal prenatal (T1 & T2) and postpartum (T3 & T4) anxiety were not the significant predictors of childhood development, but they acted as confounders for the problem-solving and fine motor skill scores of the children at three years of age. Consistent with our research, Ibanez et al., ([2015](#)) and Ali et al., ([2013](#)) reported that postpartum depression was significantly associated with lower fine motor skill scores.

In our study, family history of perinatal depression significantly lowered the odds of attaining high gross motor and personal-social skill scores at three years of age (T4) and early pregnancy (T1) drug use mediated the effects of family history of perinatal depression in predicting personal-social skill scores at three years of age. Literature confirms that family history of perinatal depression or psychosis is a risk factor for maternal prenatal and postpartum

depression ([Forty et al., 2006](#); [Kimmel et al., 2015](#); [Murphy-Eberenz et al., 2006](#); [Payne et al., 2008](#)).

Breastfed infants were found to have a cognitive advantage over formula-fed infants in a meta-analysis of observational studies ([Anderson et al., 2003](#)). Breastfed infants in our study had higher communication and gross motor skill scores as compared to non-breastfed infants.

Consistent with our results, a study from Australia using ASQ® reported that infants breastfed up to four months of age or longer had significantly higher mean fine motor and communication scores at age one and three years ([Oddy et al., 2011](#)). Breastfeeding has also been associated with educational attainment later in life. Children who were breastfed in the early weeks of life had significantly higher IQ at 7 ½ - 8 years of age compared to those who were not breastfed ([Lucas et al., 1992](#)). Similarly, a study from Brazil reported a 50% to 80% increase in grades by 18 years of age which translated into 10% – 15% increase in the income levels among breastfed children ([Walker et al., 2011](#)).

Family history of perinatal depression was a mediator with respect to breastfeeding initiation in predicting gross motor skills. Family history of perinatal depression has been associated with higher risk of maternal postpartum depression ([Forty et al., 2006](#); [Kimmel et al., 2015](#); [Murphy-Eberenz et al., 2006](#); [Payne et al., 2008](#)) and shorter breastfeeding duration ([McCarter-Spaulding & Horowitz, 2007](#)). Our study shows that above \$40,000 annual income at T4 or three years after birth significantly increased the odds of high personal-social skill scores. The effect of income and child development has been well studied and have guided the tax benefits and direct transfer programs across Canada ([Aughinbaugh & Gittleman, 2003](#); [Blau, 1999](#)). Pathways in which income affects child development are complex and non-linear. Larger negative health effects are seen in the low-income group as compared to the middle and higher

income groups, and other family background variables like maternal education and marital status have higher effects as compared to income on early child development ([Aughinbaugh & Gittleman, 2003](#); [Blau, 1999](#)). Parental interaction seems to have more impact on the child development as compared to income once the basic needs are taken care of ([Duncan et al., 2014](#)).

5.5 Limitations

To our knowledge, this is the one study to examine the mediating effects of type of birth, prenatal drug use, and neonatal complications on birth order, family history of perinatal depression, and gestation period respectively in the attainment of higher problem-solving and personal-social skill scores. However, limited variability in both development outcomes and risk factor status was one of the major limitations of our study. Most of the children in our study belonged to the highest ASQ® score category labelled as ‘high’. This might have resulted in a lack of power to identify associations. There was also limited variability in the risk factors as the highest risk women were most likely to drop out before the three-year postpartum visit. There was potential for type 1 error due to a large number of predictors considered for analysis. This risk was managed by choosing risk factors for analysis based on the literature and screening variables prior to considering them in building the multivariable models.

5.6 Conclusions

It is well known that early life-course and experiences impact the development of later life health, social, and economic outcomes ([McDonald et al., 2016](#)). To date, research has mainly focused on determining the risk factors of poor development. To our knowledge, this is one study that has focused on the study of children with normal ASQ® scores and predictors of high ASQ scores at age three years. Although, children born in the industrialised world, regardless of socio-economic level, are remarkably similar ([Hertzman, 2009](#)), developmental delays continue

to impact many children, while others perform above and beyond their contemporaries.

Identifying key factors and recognising the associations that help some children become high achievers can inform policy development and program initiatives at local, provincial, and national levels. Breastfeeding initiation and support to prolong the duration of breastfeeding could help promote higher gross motor and communication skills at three years of age. Maternal smoking, alcohol, and drug abuse cessation before, during, and after pregnancy could improve personal-social and problem-solving skills at three years of age. Finally, higher average annual family income and relationship support to postpartum mothers could enhance personal-social and fine motor skill scores, respectively. Another contribution of this study was the quantitative approach used to explore mediating factors on causal pathways for higher physical, cognitive, and social development beyond individual predictors of high ASQ® skills so as to bridge the science-policy gap and optimise early child development.

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5.8 Appendices

5.8.1 Appendix 5-A: Table 1 of unadjusted analysis for communication skills

Table 1: Odds ratios, 95% CI, and p-values of the unadjusted analysis of potential covariates of high communication skills (top third of normal ASQ3® scores) resulting from ordinal regression model $p<0.2$ ($N= 339$)

Covariates for unadjusted analysis of communication skills	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Family history of perinatal depression	Yes vs. No	0.9	0.5	1.6	0.72
	Don't know vs. No	0.8	0.4	1.7	0.54
Previous history of depression*	Yes vs. No	0.7	0.4	1.1	0.11
Education level	Some postsecondary vs. Less than postsecondary	0.8	0.3	1.9	0.61
Employment status	Yes vs. No	0.7	0.3	1.5	0.36
Planned pregnancy	Yes vs. No	1.2	0.6	2.4	0.54
Mothers' age	Centered, Continuous	1.0	0.9	1.1	0.90
Mothers' age cat	25-34 vs. <25	1.0	0.5	2.2	0.95
	≥35 vs. <25	1.2	0.5	3.2	0.72
Mothers' ethnicity	Caucasian vs. Non-Caucasian	0.6	0.2	2.0	0.43
Marital status at enrollment	Married/Common Law vs. Single/Divorced	0.7	0.3	1.8	0.47
Satisfied with the father of the child (early pregnancy)	Very satisfied vs. No relationship	0.6	0.1	4.0	0.61
	Not very satisfied vs. No relationship	1.3	0.2	7.0	0.78
Satisfaction with the father of the child (late pregnancy)	Very satisfied vs. No relationship	0.6	0.1	3.2	0.52
	Not very satisfied vs. No relationship	0.9	0.2	4.3	0.85
Exercise at T1	Yes vs. No	1.1	0.5	2.3	0.75
Exercise at T2	Yes vs. No	1.1	0.5	2.3	0.74
Smoking at T1	Quit vs. Never	1.1	0.6	1.9	0.80
	Smoke vs. Never	0.8	0.3	2.1	0.62
Smoking at T2	Quit vs. Never	0.8	0.3	1.8	0.56
	Smoke vs. Never	0.5	0.2	1.4	0.20
Drug use at T1*	Quit vs. Never	1.8	0.8	4.1	0.14
	Drug use vs. Never	0.3	0.1	1.7	0.19
Drug use at T2	Quit vs. Never	1.2	0.2	6.1	0.81
	Drug use vs. Never	0.1	0.0	3.5	0.19
Alcohol at T1	Quit vs. Never	1.2	0.7	2.0	0.54
	Drink vs. Never	0.8	0.3	2.5	0.77
Alcohol at T2	Quit vs. Never	1.2	0.6	2.3	0.54
	Drink vs. Never	1.1	0.4	2.8	0.59
Family Income at T1	≥\$40,000 vs. <\$40,000/ year	1.4	0.8	2.4	0.25
Prenatal physical abuse*	Yes vs. No	1.5	0.8	2.7	0.18

Covariates for unadjusted analysis of communication skills	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Prenatal overall health of the mother*	Poor/Fair/Okay vs. Excellent/Very good/Good	0.2	0.0	1.2	0.08
Cambridge worry scores at T1*	Continuous	1.0	0.9	1.0	0.15
Cambridge worry scores at T2*	Continuous	1.0	0.9	1.0	0.15
Anxiety scores at T1*	Continuous	0.9	0.8	1.0	0.19
Anxiety scores at T2	Continuous	0.9	0.8	1.1	0.42
Depression at T1	Yes vs. No	1.1	0.5	2.5	0.79
Depression at T2	Yes vs. No	1.0	0.4	2.6	0.94
Pregnancy complications	No vs. Yes	1.0	0.5	1.9	0.94
Type of birth	Assisted vs. Spontaneous	1.1	0.5	2.2	0.88
	C-section vs. Spontaneous	0.7	0.4	1.2	0.19
Gestation period	Centered, Continuous	1.0	0.9	1.1	0.87
Birth complications	No vs. Yes	0.8	0.5	1.2	0.24
One minute Apgar scores*	≥ 7 vs. <7	2.3	1.2	4.4	0.01
Five minute Apgar scores	≥ 7 vs. <7	1.5	0.4	6.2	0.59
Neonatal complications	No vs. Yes	1.3	0.8	2.2	0.26
Birth defects*	Yes vs. No	0.5	0.2	0.9	0.03
Sex of child	Female vs. Male	1.3	0.8	2.1	0.22
Weight for gestational age (WHO)*	SGA vs. AGA	1.3	0.5	3.2	0.64
	LGA vs. AGA	0.3	0.2	0.7	0.01
Weight for gestational age (PHAC)*	SGA vs. AGA	1.1	0.5	2.6	0.78
	LGA vs. AGA	0.4	0.2	0.8	0.01
EARLY POSTPARTUM PERIOD (T3)					
Birth order ordinal	Second vs. First	0.8	0.5	1.4	0.45
	Third or more vs. First	0.8	0.4	1.4	0.37
Gravida status	Multigravida vs. Primigravida	0.8	0.5	1.3	0.33
Stress due to any reason*	Yes vs. No	0.9	0.9	1.0	0.002
Breastfeeding initiated*	Yes vs. No	1.9	1.1	3.5	0.03
Satisfaction with the father of the child	Very satisfied vs. No relationship	3.9	0.7	22.7	0.13
	Not very satisfied vs. No relationship	2.2	0.5	10.7	0.32
Exercise	Yes vs. No	1.0	0.6	1.7	0.99
Smoking	Quit vs. Never	1.6	0.3	7.8	0.54
	Smoke vs. Never	0.7	0.3	1.9	0.49
Drug abuse	Quit vs. Never			Not estimated	
	Drug use vs. Never	0.9	0.1	9.3	0.90
Alcohol	Quit vs. Never	0.7	0.2	2.2	0.55
	Drink vs. Never	1.1	0.7	1.9	0.59
Anxiety scores	Continuous	0.9	0.8	1.1	0.25
Depression	Yes vs. No	0.8	0.3	1.9	0.56
THREE YEAR AFTER BIRTH (T4)					
Any subsequent pregnancy	Yes vs. No	1.1	0.7	1.8	0.61
Emotional support	Yes vs. No			Not estimated	
Mood disorder scores	Continuous	1.0	1.0	1.0	0.54

Covariates for unadjusted analysis of communication skills	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Maternal overall health*	Excellent/Very good vs. Poor/ Fair/ Okay	0.4	0.1	1.3	0.14
Child overall health*	Fair/Good vs. Excellent/Very good	2.3	0.6	8.0	0.20
History of diagnosis & treatment of depression during the study time period	Non-pharmacological methods vs. Not diagnosed	2.1	0.2	18.4	0.49
	Pharmacological methods vs. Not diagnosed	1.2	0.6	2.3	0.53
Satisfaction with the father of the child (late postpartum)	Very satisfied vs. No relationship	2.0	0.6	6.5	0.23
	Not very satisfied vs. No relationship	1.9	0.7	5.1	0.22
Employment status	Yes vs. No	1.1	0.6	2.0	0.74
Family Income	$\geq \$40,000$ vs. $<\$40,000$ / year	1.2	0.6	2.5	0.59
Current education status	Some postsecondary vs. Less than postsecondary	0.9	0.4	2.3	0.88
Current marital status	Common law/ Married vs. Single/ Divorced/ Separated	0.8	0.4	1.8	0.62
Gravida status	Multigravida vs. Primigravida	0.9	0.4	1.7	0.68
Exercise	Yes vs. No	0.8	0.4	1.7	0.60
Smoking	Quit vs. Never			Not estimated	
	Smoke vs. Never	0.9	0.4	1.9	0.75
Drug abuse	Quit vs. Never			Not estimated	
	Drug use vs. Never	0.4	0.1	2.1	0.29
Alcohol use	Yes vs. No	0.9	0.4	2.0	0.74
Anxiety scores*	Continuous	0.9	0.8	1.0	0.08
Depression	Yes vs. No	1.0	0.4	2.6	0.95

*Unadjusted association at p<0.2

T1 – Early pregnancy, T2 – Late pregnancy, T3 – Early postpartum, T4 – Three years after birth

5.8.2 Appendix 5-A: Table 2 of unadjusted analysis for gross motor skills

Table 2: Odds ratios, 95% CI, and p-values of the unadjusted analysis of potential covariates of high gross motor skills (top third of normal ASQ3® scores) resulting from ordinal regression model $p<0.2$ ($N= 338$)

Covariates considered in unadjusted analysis of gross motor skills using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Family history of perinatal depression*	Yes vs. No	0.6	0.3	1.3	0.20
	Don't know vs. No	0.4	0.2	0.8	0.02
Previous history of depression	Yes vs. No	0.8	0.4	1.4	0.40
Education level	Some postsecondary vs. Less than postsecondary	1.8	0.8	4.6	0.18
Employment status	Yes vs. No	0.9	0.4	2.2	0.87
Planned pregnancy	Yes vs. No	1.5	0.7	3.2	0.30
Mothers' age	Centered, Linear	1.0	0.9	1.1	0.72
Mothers' age cat	25-34 vs. <25	0.7	0.2	2.0	0.49
	≥35 vs. <25	1.5	0.3	6.4	0.61
Mothers' ethnicity	Caucasian vs. Non-Caucasian	0.5	0.1	2.4	0.42
Marital status at enrollment	Married/Common Law vs. Single/Divorced	0.8	0.3	2.4	0.67
Satisfaction with the father of the child at T1	Very satisfied vs. No relationship	2.4	0.3	17.1	0.40
	Not very satisfied	2.8	0.5	15.1	0.24
	No relationship				
Satisfaction with the father of the child at T2*	Very satisfied vs. No relationship	3.1	0.6	16.4	0.19
	Not very satisfied vs.	3.1	0.7	12.6	0.12
	No relationship				
Exercise at T1	Yes vs. No	0.8	0.3	2.0	0.61
Exercise at T2*	Yes vs. No	1.8	0.8	4.0	0.16
Smoking at T1	Quit vs. Never	1.0	0.5	2.0	0.89
	Smoke vs. Never	0.4	0.1	1.3	0.14
Smoking at T2*	Quit vs. Never	4.5	0.6	34.3	0.14
	Smoke vs. Never	0.4	0.1	0.9	0.03
Drug use at T1	Quit vs. Never	0.8	0.4	1.9	0.63
	Drug use vs. Never	0.6	0.1	5.9	0.69
Drug use at T2	Drug use/Quit vs. Never	0.5	0.1	2.7	0.46
Alcohol at T1	Quite vs. Never	1.2	0.7	2.3	0.51
	Drink vs. Never	1.7	0.3	7.9	0.53
Alcohol at T2	Quit vs. Never	0.9	0.4	2.0	74
	Drink vs. Never	1.1	0.3	4.0	0.85
Family Income at T1	≥\$40,000/year vs. <\$40,00/year	1.3	0.6	2.6	0.47
Prenatal physical abuse	Yes vs. No	0.8	0.4	1.5	0.46
Prenatal overall health of the mother	Poor/Fair/Okay vs. Excellent/Very good/Good	0.2	0.0	1.2	0.08

Covariates considered in unadjusted analysis of gross motor skills using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Cambridge worry scores at T1	Continuous	1.0	1.0	1.0	0.75
Cambridge worry scores at T2	Continuous	1.0	1.0	1.1	0.75
Anxiety scores at T1	Continuous	1.0	0.8	1.1	0.76
Anxiety scores at T2	Continuous	1.0	0.8	1.2	0.88
Depression at T1	Yes vs. No	0.7	0.3	1.6	0.39
Depression at T2*	Yes vs. No	3.9	0.5	29.5	0.19
Gravida status at T1	Multigravida – Primigravida	0.9	0.5	1.8	0.95
Pregnancy complications	No vs. Yes	1.1	0.5	2.6	0.83
Type of birth	Assisted vs. spontaneous	0.9	0.4	2.3	0.88
	C-section vs. spontaneous	1.0	0.5	1.9	0.93
Gestation period*	Pre-term vs. Term	0.6	0.1	2.7	0.53
	Post-term vs. Term	0.1	0.02	1.2	0.07
Birth complications	No vs. Yes	1.0	0.6	1.8	0.99
One minute Apgar scores	≥ 7 vs. <7	1.0	0.4	2.5	0.95
Five minute Apgar scores	≥ 7 vs. <7		Not estimated		
Neonatal complications	No vs. Yes	0.9	0.5	1.7	0.78
Birth defects	Yes vs. No	2.1	0.6	7.1	0.23
Sex of child	Female vs. Male	1.0	0.5	1.7	0.92
Weight for gestational age (WHO)	SGA vs. AGA	0.8	0.3	2.2	0.63
	LGA vs. AGA	1.1	0.5	2.7	0.79
Weight for gestational age (PHAC)	SGA vs. AGA	0.7	0.3	1.6	0.36
	LGA vs. AGA	1.5	0.5	4.6	0.43
EARLY POSTPARTUM PERIOD (T3)					
Birth order ordinal	2 nd vs. 1 st	1.0	0.5	1.9	0.97
	3 rd or more vs. 1 st	0.9	0.4	1.9	0.84
Breastfeeding initiated*	Yes vs. No	2.1	1.1	4.1	0.03
Satisfaction with the partner*	Very satisfied vs. No relationship	3.7	0.7	20.5	0.13
	Not very satisfied vs. No relationship	3.6	0.9	15.5	0.08
Exercise	Yes vs. No	0.8	0.4	1.6	0.59
Smoking*	Smoke/Quit vs. Never	0.5	0.2	1.1	0.09
Drug abuse	Drug use vs. Never	0.3	0.0	1.6	0.15
	Quit vs. Never	0.3	0.0	3.3	0.31
Alcohol	Quit vs. Never	1.0	0.2	4.8	0.99
	Drink vs. Never	0.9	0.5	1.7	0.82
Anxiety scores*	Continuous	0.9	0.8	1.0	0.15
Depression	Yes vs. No	1.9	0.4	8.2	0.41
THREE YEARS AFTER BIRTH (T4)					
Any subsequent pregnancy	Yes vs. No	0.7	0.4	1.3	0.30
Emotional support	Yes vs. No		Not estimated		
Mood disorder scores	Continuous	1.0	1.0	1.1	0.26

Covariates considered in unadjusted analysis of gross motor skills using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Maternal overall health	Excellent/Very good vs. Poor/ Fair/ Okay	0.7	0.2	2.5	0.62
Child overall health	Excellent/Very good vs. Fair/Good	3.7	0.5	28.0	0.21
History of diagnosis & treatment of depression during the study time period	Non-pharmacological methods vs. Not diagnosed Pharmacological methods vs. Not diagnosed	0.3 1.4	0.1 0.6	1.7 3.3	0.17 0.44
Satisfaction with the father of the child*	Very satisfied vs. <u>No relationship</u>	3.2	0.6	17.4	0.19
	Not very satisfied vs. <u>No relationship</u>	1.0	0.3	3.5	0.98
Employment status*	Yes vs. No	0.5	0.2	1.3	0.15
Family Income	$\geq \$40,000/\text{year}$ vs. $<\$40,000/\text{year}$	1.0	0.4	2.6	0.94
Education status*	Some postsecondary vs. Less than postsecondary	2.3	1.0	5.6	0.06
Marital status	Common law/ Married vs. Single/ Divorced/ Separated	1.3	0.4	3.9	0.64
Gravida status	Multigravida vs. Primigravida	1.3	0.6	2.9	0.52
Exercise	Yes vs. No	0.7	0.3	1.9	0.52
Smoking*	Smoke/Quit vs. Never	0.5	0.2	0.9	0.05
Drug abuse	Drug use/Quit vs. Never	1.0	0.1	8.8	0.98
Alcohol use	Yes vs. No	1.1	0.4	2.9	0.92
Anxiety scores	Continuous	1.0	0.8	1.1	0.61
Depression	Yes vs. No	1.0	0.3	3.4	0.96

*Unadjusted association ($p<0.2$)

T1 – Early pregnancy, T2 – Late pregnancy, T3 – Early postpartum, T4 – Three years after birth

5.8.3 Appendix 5-A: Table 3 of unadjusted analysis for fine motor skills

Table 3: Odds ratios, 95% CI, and p-values of the unadjusted analysis of potential covariates of high fine motor skills (top third of normal ASQ3® scores) resulting from ordinal regression model at p<0.2 (N=338)

Covariates considered for the unadjusted analysis of fine motor skills	Variable category	Odds ratio	95% CI Lower	95% CI Upper	p-value
Family history of perinatal depression	Yes vs. No Don't know vs. No	1.2 1.6	0.7 0.6	2.1 4.0	0.59 0.33
Previous history of depression*	Yes vs. No	0.6	0.3	0.9	0.02
Education level	Some postsecondary vs. Less than postsecondary	1.1	0.5	2.7	0.80
Employment status	Yes vs. No	0.7	0.3	1.5	0.35
Planned pregnancy*	Yes vs. No	1.6	0.8	3.1	0.18
Mothers' age	Centered, Continuous	1.0	0.9	1.0	0.56
Mothers' age cat	25-34 vs. <25 ≥35 vs. <25	1.4 0.9	0.6 0.3	3.1 2.3	0.47 0.80
Mothers' ethnicity	Caucasian vs. Non-Caucasian	0.6	0.2	2.0	0.37
Marital status at enrollment*	Married/Common Law vs. Single/Divorced	0.5	0.2	1.4	0.18
Satisfaction with partner at T1	Very satisfied vs. No relationship Not very satisfied vs. No relationship	2.6 2.0	0.3 0.3	20.2 11.3	0.35 0.45
Satisfaction with partner at T2*	Very satisfied vs. No relationship Not very satisfied vs. No relationship	2.8 3.6	0.6 0.9	13.4 14.2	0.19 0.07
Exercise at T1	Yes vs. No	0.7	0.3	1.6	0.36
Exercise at T2	Yes vs. No	1.2	0.6	2.6	0.59
Smoking at T1	Quit vs. Never Smoke vs. Never	0.9 0.5	0.5 0.2	1.6 1.4	0.67 0.18
Smoking at T2	Quit vs. Never Smoke vs. Never	0.7 0.6	0.3 0.2	1.7 1.7	0.42 0.37
Drug use at T1	Quit vs. Never Drug use vs. Never	1.5 0.7	0.7 0.1	3.3 7.5	0.34 0.77
Drug use at T2	Quit vs. Never Drug use vs. Never	2.3	0.3	18.5 Not estimated	0.45
Alcohol at T1*	Quit vs. Never Drink vs. Never	0.5 0.4	0.3 0.1	1.0 1.3	0.05 0.12
Alcohol at T2	Quit vs. Never Drink vs. Never	0.8 0.7	0.4 0.3	1.6 1.7	0.55 0.39
Family Income at T1	≥\$40,000 vs. <\$40,000/ year	1.1	0.6	2.1	0.69
Prenatal physical abuse	Yes vs. No	1.4	0.7	2.6	0.30
Prenatal overall health of the mother	Poor/Fair/Okay vs. Excellent/Very good/Good	0.9	0.2	3.4	0.89
Cambridge worry scores at T1*	Continuous	1.0	0.9	1.0	0.04

Covariates considered for the unadjusted analysis of fine motor skills	Variable category	Odds ratio	95% CI	p-value
			Lower	Upper
Cambridge worry scores at T2	Continuous	0.9	0.8	1.0
Anxiety scores at T1*	Continuous	0.9	0.8	1.0
Anxiety scores at T2*	Continuous	0.9	0.8	1.0
Depression at T1*	Yes vs. No	0.6	0.3	1.3
Depression at T2	Yes vs. No	0.6	0.2	1.5
Pregnancy complications	No vs. Yes	1.1	0.5	2.2
Type of birth	Assisted vs. Spontaneous	0.7	0.3	1.4
	C-section vs. Spontaneous	0.8	0.5	1.4
Gestation period	Centered, Continuous	1.0	0.9	1.1
Birth complications	No vs. Yes	0.9	0.6	1.5
One minute Apgar scores	≥ 7 vs. <7	1.3	0.6	2.6
Five minute Apgar scores	≥ 7 vs. <7	0.4	0.1	3.6
Neonatal complications	No vs. Yes	0.9	0.5	1.5
Birth defects	Yes vs. No	1.0	0.4	2.2
Sex of child*	Female vs. Male	2.8	1.6	<0.0001
Weight for gestational age (WHO)	SGA vs. AGA	0.7	0.3	1.8
	LGA vs. AGA	0.6	0.3	1.1
Weight for gestational age (PHAC)	SGA vs. AGA	0.7	0.3	1.6
	LGA vs. AGA	0.7	0.3	1.4
EARLY POSTPARTUM PERIOD (T3)				
Birth order ordinal*	2nd vs. 1st	0.6	0.3	1.0
	3rd or more vs. 1st	1.4	0.7	2.9
Gravida status	Multigravida vs. Primigravida	0.8	0.5	1.4
Breastfeeding initiated	Yes vs. No	1.4	0.8	2.7
Satisfaction with partner*	Very satisfied vs. No relationship	7.6	1.5	37.2
	Not very satisfied vs. No relationship	7.2	1.8	29.6
Exercise	Yes vs. No	1.2	0.7	2.2
Smoking	Smoke vs. Never	0.7	0.1	7.2
	Quit vs. Never	1.1	0.5	2.6
Drug abuse	Quit vs. Never		Not estimated	
	Drug use vs. Never	0.7	0.1	3.6
Alcohol	Quit vs. Never	1.7	0.4	7.8
	Drink vs. Never	0.8	0.5	1.4
Anxiety scores*	Continuous	0.9	0.8	1.0
Depression*	Yes vs. No	0.4	0.2	1.0
THREE YEARS AFTER BIRTH (T4)				
Any subsequent pregnancy	Yes vs. No	1.3	0.8	2.1
Emotional support	Yes vs. No		Not estimated	
Mood disorder scores*	Continuous	1.0	1.0	1.0
Maternal overall health	Excellent/Very good vs. Poor/ Fair/ Okay	1.0	0.4	2.5
				0.93

Covariates considered for the unadjusted analysis of fine motor skills	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Child overall health	Fair/Good vs. Excellent/Very good	0.6	0.2	1.7	0.33
History of diagnosis & treatment of depression during the study time period	Non-pharmacological methods vs. Not diagnosed	1.6	0.2	13.6	0.68
	Pharmacological methods vs. Not diagnosed	0.8	0.4	1.5	0.52
Satisfaction with the partner	Very satisfied vs. No relationship		Not estimated		
	Not very satisfied vs. No relationship		Not estimated		
	Yes vs. No	1.0	0.5	1.9	0.97
	$\geq \$40,000$ vs. $<\$40,000$ / year	0.9	0.4	2.0	0.79
Education status	Some postsecondary vs. Less than postsecondary	1.4	0.6	3.4	0.41
Marital status*	Common law/ Married vs. Single/ Divorced/ Separated	0.6	0.3	1.3	0.19
Gravida status	Multigravida vs. Primigravida	1.2	0.6	2.3	0.69
Exercise	Yes vs. no	1.3	0.6	2.7	0.44
Smoking	Quit vs. Never	0.7	0.1	7.3	0.75
	Smoke vs. Never	1.1	0.5	2.6	0.86
Drug abuse	Quit vs. Never		Not estimated		
	Drug use vs. Never		Not estimated		
Alcohol use	Yes vs. No	1.0	0.4	2.5	0.98
Anxiety scores	Continuous	0.9	0.8	1.1	0.46
Depression	Yes vs. No	0.8	0.3	2.0	0.60

*Unadjusted association ($p<0.2$)

T1 – Early pregnancy, T2 – Late pregnancy, T3 – Early postpartum, T4 – Three years after birth

5.8.4 Appendix 5-A: Table 4 of unadjusted analysis for problem-solving skills

Table5: Odds ratios, 95% CI, and p-values of the unadjusted analysis of potential covariates of high problem-solving skills (top third of normal ASQ3® scores) from ordinal regression model at p<0.2 (N=337).

Covariates considered in unadjusted analysis of problem-solving skills	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Family history of perinatal depression	Yes vs. No	0.9	0.6	1.6	0.77
	Don't know vs. No	0.7	0.4	1.5	0.36
Previous history of depression	Yes vs. No	0.8	0.5	1.4	0.48
Education level	Some postsecondary vs. Less than postsecondary	1.2	0.5	2.6	0.67
Employment status	Yes vs. No	1.4	0.8	2.7	0.24
Planned pregnancy	Yes vs. No	0.9	0.5	1.7	0.75
Mothers' age	Centered, Linear	1.0	0.9	1.0	0.44
Mothers' age cat	25-34 vs. <25	0.7	0.3	1.6	0.44
	≥35 vs. <25	0.9	0.3	2.3	0.79
Mothers' ethnicity	Caucasian vs. Non-Caucasian	1.0	0.4	2.6	0.98
Marital status at enrollment	Married/Common Law vs. Single/Divorced	1.2	0.5	3.3	0.68
Satisfaction with the partner at T1	Very satisfied vs. No relationship	1.6	0.2	11.2	0.62
	Not very satisfied vs. No relationship	0.8	0.2	4.5	0.84
Satisfaction with the partner at T2	Very satisfied vs. No relationship	0.8	0.1	4.3	0.75
	Not very satisfied vs. No relationship	0.6	0.1	3.1	0.57
Exercise at T1	Yes vs. No	0.7	0.3	1.4	0.29
Exercise at T2	Yes vs. No	0.7	0.3	1.4	0.30
Smoking at T1	Quit vs. Never	1.0	0.6	1.8	0.89
	Smoke vs. Never	0.8	0.3	2.2	0.67
Smoking at T2*	Quit vs. Never	0.7	0.3	1.5	0.33
	Smoke vs. Never	0.4	0.2	1.1	0.07
Drug use at T1	Quit vs. Never	1.7	0.8	3.7	0.15
	Drug use vs. Never	0.7	0.1	4.2	0.67
Drug use at T2*	Drug use/Quit vs. Never	4.2	0.5	33.5	0.18
Alcohol at T1	Quite vs. Never	1.0	0.6	1.6	0.84
	Drink vs. Never	1.0	0.4	2.9	0.98
Alcohol at T2	Quite vs. Never	0.7	0.4	1.3	0.27
	Drink vs. Never	0.5	0.2	1.3	0.17
Family Income	≥\$40,000/year vs. <\$40,00/year	1.1	0.7	2.0	0.63
Prenatal physical abuse	Yes vs. No	1.2	0.7	2.0	0.55
Prenatal overall health of the mother*	Poor/Fair/Okay vs. Excellent/Very good/Good	0.2	0.0	1.2	0.07
Cambridge worry scores at T1	Continuous	1.0	1.0	1.0	0.32

Covariates considered in unadjusted analysis of problem-solving skills	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Cambridge worry scores at T2	Continuous	1.0	1.0	1.0	0.76
Anxiety scores at T1*	Continuous	0.9	0.8	1.0	0.11
Anxiety scores at T2	Continuous	1.0	0.9	1.1	0.89
Depression at T1*	Yes vs. No	0.6	0.3	1.3	0.20
Depression at T2	Yes vs. No	0.6	0.3	1.5	0.31
Gravida status at t1	Multigravida– Primigravida	0.9	0.6	1.4	0.64
Pregnancy complications*	No vs. Yes	1.9	0.9	3.8	0.08
Type of birth*	Assisted vs. Spontaneous	1.2	0.6	2.4	0.62
	C-section vs. Spontaneous	0.6	0.4	0.9	0.03
Gestation period*	Term vs. Pre-term	3.1	1.3	6.9	0.01
	Post-term vs. Pre-term	0.5	0.1	2.5	0.40
Birth complications	No vs. Yes	1.1	0.7	1.8	0.56
One minute Apgar scores	≥ 7 vs. <7	0.9	0.5	1.8	0.88
Five minute Apgar scores	≥ 7 vs. <7	1.6	0.4	5.8	0.50
Neonatal complications*	No vs. Yes	1.8	1.1	2.9	0.01
Birth defects*	Yes vs. No	0.4	0.2	0.8	0.01
Sex of child	Female vs. Male	1.3	0.8	2.0	0.29
Weight for gestational age (WHO)	SGA vs. AGA	1.0	0.4	2.3	0.96
	LGA vs. AGA	0.8	0.4	1.5	0.45
Weight for gestational age (PHAC)	SGA vs. AGA	0.8	0.4	1.7	0.62
	LGA vs. AGA	0.8	0.4	1.7	0.57
EARLY POSTPARTUM PERIOD (T3)					
Birth order ordinal*	2nd vs. 1st	0.7	0.4	1.2	0.20
	3rd or more vs. 1st	1.2	0.7	2.2	0.47
Breastfeeding initiated*	Yes vs. No	1.8	1.0	3.2	0.03
Satisfaction with the partner	Very satisfied vs. No relationship	1.6	0.3	9.8	0.63
	Not very satisfied vs. No relationship	0.8	0.2	4.4	0.83
Exercise	Yes vs. no	1.6	1.0	2.7	0.06
Smoking*	Smoke/Quit vs. Never	0.5	0.3	1.1	0.09
Drug abuse	Drug use/Quit vs. Never	0.6	0.1	2.8	0.54
Alcohol	Quit vs. Never	1.0	0.3	3.4	0.99
	Drink vs. Never	1.0	0.6	1.6	0.95
Anxiety scores*	Continuous	0.9	0.8	1.1	0.37
Depression*	Yes vs. No	0.7	0.3	1.6	0.37
THREE YEAR AFTER BIRTH (T4)					
Any subsequent pregnancy	Yes vs. No	1.0	0.6	1.6	0.98
Emotional support	Yes vs. No	2.6	0.4	18.6	0.35
Mood disorder scores*	Continuous	1.0	1.0	1.0	0.07
Maternal overall health	Excellent/Very good vs. Poor/ Fair/ Okay	0.6	0.2	1.4	0.22
Child overall health	Fair/Good vs. Excellent/Very good	1.1	0.4	3.0	0.79

Covariates considered in unadjusted analysis of problem-solving skills	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
History of diagnosis & treatment of depression during the study time period	Non-pharmacological methods vs. Not diagnosed	1.5	Empty cell		
	Pharmacological methods vs. Not diagnosed		0.8	2.8	0.19
	Not diagnosed				
Satisfaction with the partner	Very satisfied vs. No relationship	0.9	0.3	3.0	0.92
	Not very satisfied vs. No relationship		1.3	0.5	0.57
	Yes vs. No	1.2	0.7	2.1	0.53
Family Income	$\geq \$40,000/\text{year}$ vs. $<\$40,000/\text{year}$	1.3	0.7	2.7	0.42
Current education status	Some postsecondary vs. Less than postsecondary	1.7	0.8	3.6	0.21
Current marital status	Common law/ Married vs. Single/ Divorced/ Separated	1.1	0.5	2.6	0.75
Gravida status	Multigravida vs. Primigravida	1.1	0.6	2.0	0.84
Exercise*	Yes vs. no	1.6	0.8	3.1	0.16
Smoking	Smoke vs. Quit/Never	0.6	0.3	1.3	0.23
Drug abuse	Drug use/Quit vs. Never	0.5	0.1	1.9	0.32
Alcohol use	Yes vs. No	1.4	0.7	2.9	0.38
Anxiety scores	Continuous	0.9	0.8	1.1	0.39
Depression	Yes vs. No	0.7	0.3	1.8	0.52

*Unadjusted association ($p<0.2$)

T1 – Early pregnancy, T2 – Late pregnancy, T3 – Early postpartum, T4 – Three years after birth

5.8.5 Appendix 5-A: Table 5 of unadjusted analysis for personal-social skills

Table 4: Odds ratios, 95% CI, and p-values of the unadjusted analysis of potential covariates of high personal-social skills (top third of normal ASQ3® scores) from ordinal regression model at p<0.2 (N=338)

Covariates considered in unadjusted analysis of personal-social skills	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Family history of perinatal depression*	Yes vs. No	0.7	0.4	1.2	0.17
	Don't know vs. No	0.4	0.2	0.8	0.01
Previous history of depression	Yes vs. No	0.7	0.4	1.2	0.25
Education level	Some postsecondary vs. Less than postsecondary	0.8	0.3	2.1	0.66
Employment status	Yes vs. No	0.9	0.4	1.8	0.72
Planned pregnancy	Yes vs. No	0.7	0.3	1.6	0.42
Mothers' age*	Centered, Continuous	1.0	0.9	1.0	0.12
Mothers' age cat	25-34 vs. <25	1.2	0.5	2.6	0.70
	≥35 vs. <25	0.8	0.3	2.0	0.61
Mothers' ethnicity	Caucasian vs. Non-Caucasian	0.6	0.2	1.9	0.36
Marital status at enrollment	Married/Common Law vs. Single/Divorced	1.8	0.5	6.3	0.36
Satisfaction with the partner at T1	Very satisfied vs. No relationship		Not estimated		
	Not very satisfied vs. No relationship		Not estimated		
Satisfaction with the partner at T2*	Very satisfied vs. No relationship	0.2	0.0	2.0	0.17
	Not very satisfied vs. No relationship	0.5	0.1	4.0	0.50
Exercise at T1	Yes vs. No	1.4	0.7	2.9	0.38
Exercise at T2*	Yes vs. No	1.9	0.9	3.7	0.09
Smoking at T1*	Quit vs. Never	0.6	0.3	1.1	0.09
	Smoke vs. Never	0.5	0.2	1.4	0.17
Smoking at T2*	Quit vs. Never	0.7	0.3	1.6	0.40
	Smoke vs. Never	0.3	0.1	0.8	0.01
Drug use at T1*	Quit vs. Never	0.5	0.3	1.1	0.08
	Drug use vs. Never	0.1	0.0	0.4	0.004
Drug use at T2	Quit vs. Never		Not estimated		
	Drug use vs. Never		Not estimated		
Alcohol at T1*	Quit vs. Never	0.6	0.3	1.2	0.13
	Drink vs. Never	0.2	0.1	0.5	0.001
Alcohol at T2	Quit vs. Never	1.0	0.5	1.9	0.90
	Drink vs. Never	1.0	0.3	2.7	0.94
Family Income*	≥\$40,000 vs. - <\$40,000/year	1.6	0.9	2.9	0.10
Prenatal physical abuse	Yes vs. No	1.0	0.5	1.7	0.87
Prenatal overall health of the mother	Poor/Fair/Okay vs. Excellent/Very good/Good	0.3	0.1	2.3	0.28

Covariates considered in unadjusted analysis of personal-social skills	Variable category	Odds ratio	95% CI Lower	95% CI Upper	p-value
Cambridge worry scores at T1	Continuous				
Cambridge worry scores at T2	Continuous	1.0	0.9	1.0	0.30
Anxiety scores at T1	Continuous	1.0	0.9	1.1	0.98
Anxiety scores at T2	Continuous	1.0	0.8	1.1	0.56
Depression at T1	Yes vs. No	1.0	0.5	2.4	0.93
Depression at T2	Yes vs. No	1.3	0.4	4.0	0.64
Gravida status at enrollment	Multigravida vs. Primigravida	1.1	0.7	1.8	0.73
Pregnancy complications	No vs. Yes	0.8	0.4	1.5	0.42
Type of birth	Assisted vs. Spontaneous	0.9	0.4	1.8	0.67
	C-section vs. Spontaneous	1.0	0.6	1.7	0.90
Gestation period	Centered, Continuous	1.1	0.9	1.2	0.38
Birth complications	No vs. Yes	1.3	0.8	2.1	0.36
One minute Apgar scores	≥ 7 vs. <7	1.2	0.6	2.6	0.55
Five minute Apgar scores	≥ 7 vs. <7	0.4	0.1	3.7	0.45
Neonatal complications	No vs. Yes	1.3	0.8	2.2	0.29
Birth defects	Yes vs. No	1.4	0.6	3.4	0.43
Sex of child*	Female vs. Male	2.7	1.6	4.5	<0.0001
Weight for gestational age (WHO)	SGA vs. AGA	1.4	0.5	3.9	0.50
	LGA vs. AGA	1.0	0.5	2.0	0.91
Weight for gestational age (PHAC)	SGA vs. AGA	1.2	0.5	2.9	0.70
	LGA vs. AGA	1.4	0.6	3.3	0.46
EARLY POSTPARTUM PERIOD (T3)					
Birth order ordinal*	2 nd vs. 1 st	1.2	0.7	2.2	0.46
	3 rd or more vs. 1 st	0.9	0.5	1.7	0.81
Breastfeeding initiated	Yes vs. No	1.4	0.7	2.6	0.31
Satisfaction with the partner*	Very satisfied vs. No relationship	1.1	0.2	7.0	0.90
	Not very satisfied vs. No relationship	1.6	0.3	8.5	0.61
Exercise	Yes vs. No	1.2	0.7	2.1	0.47
Smoking*	Smoke/Quit vs. Never	0.3	0.1	0.7	0.01
Drug abuse*	Quit vs. Never	1.0	0.1	9.4	0.98
	Drug use vs. Never	0.1	0.0	0.9	0.04
Alcohol	Quit vs. Never	0.7	0.2	2.4	0.61
	Drink vs. Never	1.0	0.6	1.6	0.88
Anxiety scores*	Continuous	0.9	0.8	1.0	0.15
Depression	Yes vs. No	0.6	0.3	1.5	0.27
THREE YEAR AFTER BIRTH (T4)					
Any subsequent pregnancy	Yes vs. No	1.2	0.8	2.0	0.40
Emotional support	Yes vs. No	Empty cell			
Mood disorder scores*	Continuous	1.0	1.0	1.0	0.10
Maternal overall health	Excellent/Very good vs. Poor/ Fair/ Okay	1.2	0.5	2.9	0.72

Covariates considered in unadjusted analysis of personal-social skills	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Child overall health*	Fair/Good vs. Excellent/Very good	0.4	0.1	0.9	0.03
History of diagnosis & treatment of depression during the study time period	Non-pharmacological methods vs. Not diagnosed	0.7	0.1	3.8	0.68
	Pharmacological methods vs. Not diagnosed	1.3	0.7	2.6	0.43
Satisfaction with the partner	Very satisfied vs. No relationship	1.2	0.4	4.1	0.75
	Not very satisfied vs. No relationship	1.4	0.5	4.2	0.53
Employment status	Yes vs. No	1.1	0.6	2.1	0.68
Family Income*	$\geq \$40,000/\text{year}$ vs. $<\$40,000/\text{year}$	2.2	1.1	4.5	0.03
Current education status	Some postsecondary vs. Less than postsecondary	1.2	0.5	2.9	0.72
Current marital status	Common law/ married vs. Single/ Divorced/ Separated	0.8	0.3	1.7	0.51
Gravida status	Multigravida vs. Primigravida	1.3	0.6	2.5	0.52
Exercise*	Yes vs. no	1.6	0.8	3.3	0.16
Smoking*	Quit vs. Never	0.5	0.2	1.0	0.12
Drug abuse*	Drug use/Quit vs. Never	0.3	0.1	1.6	0.18
Alcohol use	Yes vs. No	1.0	0.4	2.3	0.92
Anxiety scores*	Continuous	0.9	0.8	1.0	0.16
Depression	Yes vs. No	0.8	0.3	2.1	0.60

*Unadjusted association ($p<0.2$)

T1 – Early pregnancy, T2 – Late pregnancy, T3 – Early postpartum, T4 – Three years after birth

5.8.6 Appendix 5-B – Table 1: Descriptive summary of the influential data points that were removed from the multivariable analysis of problem-solving skills

Table 1: Descriptive summary of the influential data points that were removed from the multivariable analysis of problem-solving skills

Data #	Gestation	Birth order	Type of birth	Neonatal complication	Smoking at T2	Drug use at T2	Anxiety scores at T1
543	Term	1 st	C-section	Yes	Never	Never	5
558	Term	1 st	C-section	Yes	Never	Never	3
587	Term	1 st	Spontaneous	Yes	Never	Never	1
740	Term	1 st	Spontaneous	Yes	Never	Never	0
782	Term	1 st	Assisted	Yes	Never	Never	0
834	Term	1 st	C-section	Yes	Never	Never	3
922	Term	1 st	Spontaneous	Yes	Never	Never	2
1007	Pre-term	3 rd or more	C-section	Yes	Yes/quit	Never	3
1139	Pre-term	3 rd or more	C-section	Yes	Yes/quit	Never	3
1200	Term	1 st	C-section	Yes	Never	Never	3
1215	Term	1 st	Assisted	Yes	Never	Never	4

T1 – Early pregnancy, **T2** – Late pregnancy,

5.8.7 Appendix 5-B - Table 2: Descriptive summary of the influential data points that were removed from the multivariable analysis of personal-social skills

Table 1: Descriptive summary of the influential data points that were removed from the multivariable analysis of personal-social skills

Data Points	Gestation category	Birth order	Sex of the child	Neonatal complication	Birth defect	Type of birth	Breastfeeding	One minute Apgar scores	Overall health of the child
522	Term	1 st	Female	Yes	No	Assisted	Yes	≥7	Good
542	Term	2 nd	Male	Yes	No	Spontaneous	Yes	≥7	Good
631	Term	≥3 rd	Male	Yes	No	C-section	Yes	≥7	Good
752	Term	1 st	Male	No	No	C-section	Yes	≥7	Good
1007	Pre-term	≥3 rd	Female	Yes	No	C-section	No	<7	Good
1021	Term	2 nd	Female	No	No	C-section	No	≥7	Good
1022	Term	1 st	Male	Yes	No	Assisted	Yes	≥7	Good
1103	Term	≥3 rd	Female	No	No	Spontaneous	No	<7	Poor
1120	Term	2 nd	Male	No	No	Spontaneous	Yes	.	Poor
1123	Term	1 st	Female	No	No	Spontaneous	Yes	≥7	Good
1201	Term	1 st	Female	Yes	No	C-section	Yes	≥7	Good

CHAPTER 6: UNDERSTANDING THE EFFECTS OF MATERNAL HIGH-RISK BEHAVIOURS AND MATERNAL MENTAL HEALTH ON EARLY CHILDHOOD EMOTIONAL AND BEHAVIOURAL DEVELOPMENT – IS THERE A TIME SENSITIVE OR A MEDIATING EFFECT

6.0 Abstract

Emotional and behavioural development are complex processes that begin in infancy and continue into adulthood. The study was designed to understand the long-term effects of prenatal and postnatal high-risk behaviour and socio-demographic factors on emotional and behavioural development of three-year-old children. Children of mothers who completed the three-year follow-up assessment from a five-year longitudinal Feelings in Pregnancy (FIP) study in Saskatoon, Saskatchewan formed the cohort. A re-specified Child Behaviour Checklist 1.5–5 (CBCL) (Chapter 3) provided information used to assess anxiety/depression, sleep problems, withdrawn behaviours, aggressive behaviours and attention problems in children at three years of age. Individual syndrome scores were examined as ordinal variables with all values above 93rd percentile categorized as a single value consistent with borderline/clinical problem scores. Data were analysed using proportional odds and partial proportional odds regression. The mean age of the 343 children was 36.4 months + 1.6 months. Maternal anxiety at three years after birth increased the odds of borderline/clinical anxiety/depression (OR 1.2, 95% CI 1.1 – 1.4) and withdrawn behaviours (OR 1.1, 95% CI 1.0 – 1.3) scores in children. Early postpartum maternal depression (OR 2.7, 95% CI 1.1 – 6.8), higher maternal affective lability scores (OR 1.1, 95% CI 1.0 – 1.1), and maternal smoking (OR 2.2, 95% CI 1.1 – 4.7) three years after birth increased the odds of high aggression scores. Maternal depression during early postpartum (OR 4.0, 95% CI 1.7 – 9.8) and at three years after birth (OR 2.6, 95% CI 1.0 – 6.7) increased the odds of sleep problems in the children as did family history of perinatal depression (OR 2.7, 95% CI 1.4 – 5.2). Maternal alcohol consumption during the early postpartum period moderated the effects of family history of perinatal depression in predicting higher anxiety/depression scores at three

years ($p<0.0001$). Our research shows that along with maternal mental health, perinatal experiences are crucial for the healthy emotional and behavioural development in children.

6.1 Introduction

The early childhood period is characterized by rapid social, cognitive, physical development, and learning ([GOC, 2011](#)). Emotional and behavioural development are complex processes that begin in infancy and continue into adulthood ([KidsMatter, 2012](#)). Children learn to express emotions from parents, caregivers, and teachers ([KidsMatter, 2012](#)). Emotional development in children is influenced by many factors including values and beliefs about how children should express emotions ([KidsMatter, 2012](#)). Emotional development is also influenced by the child's temperament, how effectively the child's emotional needs are met, and the child's observations and experiences ([KidsMatter, 2012](#)).

Many behavioural theories of child development, described by proponents such as John B. Watson, Ivan Pavlov and B. F. Skinner, focus on how environmental interaction influences behaviour ([Cuny, 1964](#); [Pavlov & Kaplan, 1966](#); [Skinner, 1974](#); [Watson, 1925](#)). However, Jean Piaget's cognitive child development theory suggests that children think differently than adults and have an active role in gaining knowledge ([Piaget & Inhelder, 2008](#)). In addition to behavioural and cognitive child theories of child development, social theories from Albert Bandura and Lev Vygotsky focus on the role of parents, caregivers, peers and how other social influences impact development ([Bandura, 1977](#); [Vygotsky, 1980](#)). Some other theories focus on how early attachment influences development, while others are centred on how children learn by observing people around them ([Armstrong et al., 2014](#); [Baldwin, 1980](#)).

Perinatal environmental determinants of development, behaviour, and health have been studied since the 1940s for humans and even earlier, for animals ([Van den Bergh et al., 2005](#)). Across cultures and throughout history, the idea that the emotions of a pregnant woman could influence the development of her unborn child were common; these ideas are now being supported by research ([Byrne & Phillips, 2000](#)). The fetal programming hypothesis states that

adverse exposures during sensitive periods in pregnancy have permanent effect on the phenotype ([Barker, 2004](#)). This window during pregnancy provides an opportunity to impact developmental skills and competencies ([Fox & Rutter, 2010](#)).

Developmental psychopathology has examined risk factors for emotional and behavioural problems in childhood ([Harland et al., 2002](#)). Externalizing problems include symptoms of conflicts with others, aggression and attention problems ([Achenbach & Rescorla, 2000](#); [Carneiro et al., 2016](#)). Internalizing problems include syndromes concerning symptoms of anxiety, depression, somatic problems, and withdrawal.

This study was designed to identify risk factors for behavioural syndromes of aggression, attention deficit, anxiety, sleep problems, and withdrawn behaviour that contribute towards externalizing and internalizing behavioural domains among a sample of healthy three-year-old children. To date, few studies have undertaken such an inclusive and comprehensive approach to studying factors associated with symptoms of emotional and behavioural problems in three-year-old children.

We hypothesized that children of mothers with a history of prenatal and postpartum mental health issues, such as anxiety, depression, or mood disorders, would have higher emotional and behavioural problem scores as compared to children from mothers having no history of depression and anxiety. Further, we hypothesize that each of these exposures is time sensitive, that is, exposure during the prenatal and postpartum period might differentially affect the emotional and behavioural development of children at three years of age. Since maternal high-risk behaviours during pregnancy and postpartum period are correlated with the maternal mental health ([Gyllstrom et al., 2012](#)), we also hypothesized that the children of mothers who are exposed to high-risk behaviours, such as smoking, drug abuse, and alcohol consumption, during

and after pregnancy would also have a higher risk of developing emotional and behavioural problems. In contrast, children of mothers who had a supportive environment during and after pregnancy should have a lower risk of developing higher emotional and behavioural problems scores.

6.2 Methods

Children of mothers who completed the three-year follow-up for the longitudinal ‘Feelings in Pregnancy & Motherhood’ (FIP) study in Saskatoon, Saskatchewan formed the cohort considered in this analysis ([Bowen et al., 2012b](#)). Of the 648 women recruited for the study, 338 (333 singleton pregnancies and five twin pregnancies) completed the fourth phase of data collection when their children were three years old. The 343 children born to this group of 338 mothers formed the cohort for analysis.

Information was collected from mothers during and after pregnancy. Mothers were recruited during the second trimester of pregnancy. The mean duration and standard deviation of gestation at recruitment and the first data collection point was 17 weeks \pm 4.4 weeks labelled as ‘early pregnancy/T1’. The second measurement was late in pregnancy with a mean gestation and standard deviation of 30.4 weeks \pm 2.4 weeks, labelled as ‘late pregnancy/T2’. The third measurement was completed at an average of 4 weeks \pm 2.0 weeks after birth, and the fourth measurement was done at an average age of 36.4 months \pm 1.6 weeks, labelled as ‘early postpartum/T3’ and ‘three years after birth/T4’ respectively. Data were obtained by in-person interview, written questionnaire, and telephonic interview by two research assistants. The study was funded by Canadian Institute of Health Research (CIHR #145179) and Saskatchewan Health Research Foundation (SHRF). The study was approved by University of Saskatchewan Behavioural Research Ethics Board (Beh-REB # 13-284).

6.2.1 Dependent variables

The Child Behaviour Checklist (CBCL) – Preschool (1.5 – 5 years) is a mother/ caregiver administered tool and has been used to predict psychopathology in preschool children ([Achenbach & Rescorla, 2000](#)). Five syndrome scales of the Child Behaviour Checklist (CBCL) (1.5–5 years) developed through Item Factor Analysis were used to measure aggression, attention problems, anxiety/depression, sleep problems, and withdrawn behaviour at the fourth time point of the study. CBCL obtains caregivers ratings of problem items which in this case was the mother for all of the children. Each indicator was scored as (0, 1, or 2) where ‘0’ is ‘Not true (as far as you know)’, ‘1’ is ‘somewhat or sometimes true’, and ‘2’ is ‘very true or often true’. Cumulative scores were developed by adding the scores of items of each of the syndrome scale together developed during Item Factor Analysis (Chapter 3).

Several data transformation options, including log, inverse, square, cube, and inverse distributions, were attempted to normalize the results and fit linear models. However, as none of the attempted transformations resulted in a normal distribution, the outcome variables were considered ordinal. To avoid the issue of too few observations in each ordinal category for the analysis, all the categories above the 93rd percentile (recommended cut-off for borderline/clinical cases) of scores were collapsed to form the highest category representing previously reported cut-off values for borderline/clinical cases ([Achenbach & Rescorla, 2000](#)) (Table 6-2). All observed categories below the 93rd percentile were retained for analysis in all but one measure (Table 6-2). For the aggression variable, because the number of categories below the 93rd percentile was too large (n=13) for ordinal analysis, the scores below the 93rd percentile were divided into two categories using the median value of six (Table 6-2).

6.2.2 Independent variables

Questionnaires were completed to capture information about maternal mental health (depression, anxiety, mood changes), high-risk behaviour (smoking, alcohol, recreational drug abuse), family history of perinatal depression, medical and obstetric history, socio-economic status, stressors, relationship with the father of the child, and supports available to the mother. These questionnaires were originally developed based on extensive literature review and their use in this cohort previously reported by two of the authors (AB and NM) ([Bowen et al., 2012b](#); [Bowen et al., 2009](#)).

6.2.3 Maternal mental health factors

Edinburgh Postpartum Depression Scale (EPDS) was used to screen mothers during pregnancy, the early postpartum period, and three years after birth for depression and anxiety ([Cox et al., 1987](#); [Murray & Cox, 1990](#)). The EPDS scale has ten items, and each item has four responses scored from 0 to 3 with total maximum score of 30. A cut-off score of 12 or more was used to dichotomize the variable for depression ([Bergink et al., 2011](#)). EPDS has also been validated as a useful measure to screen for anxiety (items 3, 4, & 5) (EPDS – 3A) in pregnancy and postpartum period among women by Matthey et al. ([2013](#)). Total anxiety scores were used for model building and scores could range from 0 to 9.

Affective lability refers to rapid shifts in outward emotional expressions between normal to angry, depressed/elated, or depressed/anxious ([Look et al., 2010](#)). Affective Lability Scale – Short Form (ALS-SF), an 18-item scale was used to measure self-reported mood changes in the mothers in the late postpartum period ([Harvey et al., 1989](#); [Oliver & Simons, 2004](#)). No cut-offs have been recommended for the scale or the total scores; hence, for the purpose of this analysis, total scores were used for model building. Any family history of perinatal depression, anxiety, or

treatment of depression in the mother or any of her siblings was combined into one binary variable.

6.2.4 Maternal high-risk behavioural factors

History of exposure to smoking, alcohol, and recreational drug abuse at each time point were included as a nominal variable, ‘0’ indicating never exposed, ‘1’ quit, and ‘2’ continued exposure. However, if there were too few observations in one of the categories, binary variable, ‘0’ indicating never, and ‘1’ indication exposed/quit was used for the analysis.

6.2.5 Maternal socio-demographic factors

Maternal age at the time of enrollment (T1) was categorised into less than 25, 25 – 34, and greater than or equal to 35 years. Maternal overall health at each time point was dichotomized by summarizing ‘Okay’, ‘Fair’, and ‘Poor’ were labelled as ‘Poor’ and then ‘Good’, ‘Very good’, and ‘Excellent’ as ‘Good’.

Information about the maternal marital status was obtained at T1 and T4 time points. Mothers who were in a stable relationship (common law or married) were labelled as ‘married’, and those who were either single or separated were labelled as ‘single’. Maternal relationship satisfaction was a nominal variable with options including ‘no relationship’, ‘not satisfied’, ‘somewhat satisfied’ and ‘very satisfied’. However due to relatively few observations in the ‘not satisfied’ and ‘somewhat satisfied’ categories; the variable was re-categorised as ‘very satisfied’, ‘not very satisfied’, and ‘no relationship’. History of physical abuse and emotional support were included as binary variables for each time point.

Annual family income, employment history, and education status of the mother were obtained at T1 and T4 time points. Mother’s education was dichotomized as ‘some post-secondary education’ and ‘less than post-secondary education’. Mother’s employment status was

dichotomized as ‘Yes’ vs. ‘No’. Annual family income was dichotomized using annual income of \$40,000 as a cut-off (based on the estimates of low-income cut-off for a family of four in Canada in 2007 ([Statcan, 2015](#))).

6.2.6 Natal and child-related factors

The child’s birth weight, birth length, one- and five-minute ‘Apgar’ (Appearance, Pulse, Grimace, Activity, and Respiration) scores, type of birth, any neonatal or birth complications were extracted from hospital discharge records. Apgar scores were dichotomized as seven or above and below seven ([Apgar, 1972](#)). Child birth weights were converted into weight for gestational age categories and were referred to as ‘appropriate weight for gestation age’ (AGA) (weight between 10th and 90th percentile at the gestation age), ‘small for gestation age’ (SGA) (weight below 10th percentile for gestation age), and ‘large for gestation age’ (LGA) (weight above 90th percentile for gestation age) ([Kramer et al., 2001](#)). Completed gestation period at the time of birth was centered by subtracting the mean gestation period. Completed gestation period was also categorized when necessary to address failure of the linearity assumption; less than 37 weeks of gestation was labelled ‘pre-term’, 37 – 41 6/7 weeks was labelled ‘term’, and more than 42 weeks of gestation as ‘post-term’ ([Eisfeld, 2014](#); [UN, 2001](#)).

Information about initiation of breastfeeding was collected during the early postpartum period (T3), and duration of breastfeeding was collected from the mother at T4. Information about the child’s overall health and reported by mother was dichotomized by summarizing ‘Okay’, ‘Fair’ and ‘Poor’ categories as ‘Poor’ and then ‘Good’, ‘Very good’ and ‘Excellent’ as ‘Good’. Information regarding any subsequent pregnancy, miscarriage, or birth was also obtained from the mother.

6.2.7 Statistical model building strategy

Potential determinants for increasing scores on the five syndrome scales for aggressive behaviour, anxious/depressed, attention problems, sleep problems, and withdrawn behaviour in children at three years of age was evaluated using ordinal regression by STATA 12.0 ([StataCorp, 2009](#)). Independent variables selected for analysis were initially based on a literature review, including those identified in the study objectives, potential modifiers and potential confounders. Independent variables were then individually screened prior to building each multivariable model by examining the unconditional associations between each risk factor and outcome. The models were built using ‘ologit’ programs in STATA 12.0 for ordinal regression ([Long & Freese, 2006](#)). Significance of the independent variables was assessed using Wald’s Chi-square test at 5% level of significance ([Dohoo et al., 2012](#)).

Variables with a bivariate or unadjusted p-value <0.20 based on the type 3 Wald test were retained for consideration in building the final multivariable model ([Dohoo et al., 2012](#)). Manual stepwise backward selection was used to develop main effects model, retaining variables where p-value <0.05 ([Dohoo et al., 2012](#)). Variables that were not significant were included in the model as confounders if their inclusion in the model resulted in a $>20\%$ change in regression coefficients of the significant main effects in the model and they were not on the same causal pathway as the variables of interest (i.e., not antecedent or mediator variables) ([Kleinbaum, 1982](#)). Biologically relevant two-way interactions were considered and retained in the final model if p <0.05 ([Dohoo et al., 2012](#)).

Continuous predictors were checked for linearity, and if the assumption was violated, the variables were categorized by using pre-determined cut points wherever possible ([Dohoo et al., 2012](#)). All ranked categorical and continuous risk factor variables were checked for collinearity using Pearson’s or Spearman’s correlation coefficients, as appropriate. Where variables were

highly correlated ($p \geq 0.9$), the variable with fewer missing values or that was most biologically relevant was retained ([Dohoo et al., 2012](#)).

Covariates that were identified in the bivariate or unadjusted analysis were further checked for the proportional odds assumption using ‘brant’ test at the 5% level of significance ([Long & Freese, 2006](#)). However, if the ‘brant’ test failed to compute the p-values, generalized linear regression command ‘gologit2’ with ‘autofit’ subcommand were used to identify the predictor which failed the assumption ([Vincent, 1999](#); [Williams, 2005](#)). The ‘gologit2’ user written program fits generalized ordered logit model as well as less restrictive models including the partial proportional odds model. Hence, it can be used to evaluate the proportional odds assumption for individual variables in the multivariable regression as well as to provide an overall test of proportional odds for the final model ([Williams, 2005](#)). If the proportional odds assumption was violated due to an empty cell or cells in a contingency table for the outcome variable and a covariate, transformation into binary independent variables was considered.

If the proportional odds assumption was otherwise violated, the variable was conditionally retained in the model, and the assumption for proportional odds was checked again for the final multivariable model using ‘brant’ test or ‘gologit2’ command with ‘autofit’ and ‘gamma’ ([Williams, 2005](#)). If the assumption was violated in the final model, a partial proportional odds model was built using the ‘npl’ command to allow the variables to fail the parallel odds assumption using ‘gologit2’ ([Williams, 2005](#)) and compute separate effect estimates for each level of increase in the outcome. Partial proportional odds model computes a series of logistic regression equations. The first panel has estimates for dependent variable category 1 = 0 versus categories $>1 = 1$. The second panel has estimates for the model with category 1 & 2 = 0 versus categories $>2 = 1$ and with similarly evolving estimates for subsequent

levels of the outcome. If the assumption of the ordered logit model is met, the estimates are same in all the panels ([Williams, 2005](#)). Partial proportional models are restricted in their computation of marginal effects and model fit estimates. However, they are more parsimonious than the alternative multinomial models ([Williams, 2005](#)).

Since standardized residuals could not be computed directly after ordinal regression, binary models were built by dichotomizing the outcome as highest category versus all the lower categories. Standardized residuals were then computed to check for the extreme outliers by plotting standardized residuals vs. the linear predictor ([Berry, 1993](#)). The potential for influence by individual data points was investigated by building the model with and without the extreme outliers ([Fox, 1991](#)). Changes in the predictor estimates with and without the outlying data points were examined to evaluate the importance of these outliers in the model ([Fox, 1991](#)). Individual values that resulted in substantial changes (>10%) in the model effect estimates were considered influential and were removed during the final steps in the model building process ([Dohoo et al., 2012](#)). This was done to minimize the chance of a variable being included or excluded based on very small proportion of data. However, after the model structure was developed, the influential observations were included for the calculation of the final effect estimates ([Dohoo et al., 2012](#); [Fox, 1991](#)).

Odds ratios (ORs) with 95% CI using robust standard errors were reported for the final regression models. For models where the proportional odds assumption was met, the odds ratios reflect the odds of reporting scores in all higher categories to the lowest category, the odds of reporting scores in all higher categories to the two lowest categories, and all possible subsequent increasing comparisons. Included in this is the odds of reporting scores above the highest category ($\geq 93^{\text{rd}}$ percentile or recommended cut-off for borderline/clinical cases) as compared to

all lower scores. This interpretation is emphasized in the results as most clinically relevant. Predicted probabilities for individual score categories were computed. These estimates were used in the case of significant interactions to graphically represent the effects of the individual predictors on the probability an outcome would be in the highest category ([Dohoo et al., 2012](#)).

6.3 Results

Data were available for 343 mother-child dyads where the mean age of the children was 36.4 months \pm 1.6 months and the mean age of the mothers was 29.9 \pm 4.4 years. The number of mothers screened positive for depression (i.e., EPDS \geq 12) was 33 (9.6%) at T1, 21 (6.2%) at T2, 23 (6.7%) at T3, and 20 (5.8%) at T4. Average anxiety score \pm S.D at T1 was 3.0 \pm 1.9, at T2 was 2.8 \pm 1.8, at T3 was 2.5 \pm 1.9, and at T4 was 2.2 \pm 1.8. The average ALS-SF scores at T4 was 28.4 \pm 8.7.

In early pregnancy (T1), 17 (5.0%) mothers reported smoking in last one month which increased to 20 (5.9%) in late pregnancy (T2), 21 (6.1%) in early postpartum, and 33 (9.7%) at three years of age. In early pregnancy (T1), 18 (5.3%) mothers reported alcohol consumption in the last one month, which increased to 22 (6.5%) in late pregnancy (T2), 128 (37.5%) in early postpartum (T3) and 312 (91%) at three years of age. In early pregnancy, five (1.5%) reported drug use in the last one month, which decreased to one (0.3%) in late pregnancy. However, in early postpartum (T3) period three (0.9%) mothers reported drug use and at three-year visit seven (2.0%) mothers reported drug use.

Most 294 (85.7%) children were born at term between 37 – 41 6/7 weeks of gestation, 36 (10.5%) were pre-term deliveries, and nine (2.6%) were post-term pregnancies. Half, 175 (53.4%), were born by spontaneous birth and 109 (33.2%) by Caesarean section. Breastfeeding was initiated immediately after birth for 83.1% (285) of the babies, and 64.0% (220) were breast-

fed for more than six months. The median duration of breastfeeding was nine months with interquartile range of ten months.

The observed range of individual syndrome scores in the participating children at three years of age was: 0 – 21 for aggression, 0 – 8 for attention deficit, 0 – 8 for anxiety/depression, 0 – 7 for sleep problems, and 0 – 4 for withdrawn behaviour (Table 6-1).

Table 6-1: Mean (standard deviation), median (interquartile range), and range of the re-specified transformed CBCL (1.5 – 5 year) in the study population (N=343).

Variables	Mean (SD)	Median (IQR)	Range (observed)	Range (possible)
Aggression	5.4 (4.0)	5 (0.0, 1.0)	0 – 21	0 – 26
Attention problems	1.7 (1.6)	1 (0.0, 3.0)	0 – 8	0 – 8
Anxiety/ Depression	1.4 (1.4)	1 (0.0, 2.0)	0 – 7	0 – 10
Sleep problems	1.4 (1.5)	1 (0.0, 2.0)	0 – 7	0 – 8
Withdrawn behaviour	0.8 (0.9)	1 (0.0, 1.0)	0 – 4	0 – 6
Externalizing behaviour	7.1 (5.1)	7 (3.0, 10.0)	0 – 28	0 – 34
Internalizing behaviour	3.6 (2.8)	3 (2.0, 5.0)	0 – 15	0 – 24

Based on the previously reported cut point at the 93rd percentile, the frequency of children with: borderline/clinical aggression was 14 (4.1%), attention deficit was 19 (5.5%), anxiety was 27 (7.9%), sleep problems was 38 (11.1%), and withdrawn behaviour was 68 (19.8%) (Table 6-2).

Table 6-2: Distribution of re-specified transformed CBCL (1.5 – 5 year) in the study population for regression analysis (N=343).

Categories	Label	Frequency	Percentage
Aggression (Range 0 – 21) 93rd percentile – 13			
Scores 0 – 5	0	194	56.6
Scores 6 – 12	1	135	39.4
Scores ≥ 13	2	14	4.1
Attention problems (Range 0 – 8) 93rd percentile – 5			
Scores 0	0	87	25.5
Scores 1	1	102	29.7
Scores 2	2	50	14.6
Scores 3	3	52	15.2
Scores 4	4	33	9.6
Scores ≥ 5	5	19	5.5
Anxiety/Depression (Range 0 – 7) 93rd percentile – 4			
Scores 0	0	112	32.6
Scores 1	1	102	29.7
Scores 2	2	69	20.1
Scores 3	3	33	9.6
Scores ≥ 4	4	27	7.9
Sleep problems (Range 0 – 7) 93rd percentile – 4			
Scores 0	0	115	33.5
Scores 1	1	99	28.9
Scores 2	2	49	14.3
Scores 3	3	42	12.2
Scores ≥ 4	4	38	11.1
Withdrawn behaviour (Range 0 – 4) 93rd percentile – 3			
Scores 0	0	163	47.5
Scores 1	1	112	32.6
Scores ≥ 2	2	68	19.8

6.3.1 Aggressive behaviour at three years

Maternal mental health and behavioural factors of family history of perinatal depression, anxiety scores at T3 and T4, depression scores at T3 and T4, mood disorder (ALS) at T4, stress at T3, maternal smoking at T2 and T4, recreational drug use at T2 and exercise at T3 and T4 were associated ($p < 0.20$) with high aggressive behaviour scores ($\geq 93^{\text{rd}} \text{ percentile}$ or $\geq 13/21$) in children at three years of age based on unadjusted analysis. The other maternal factor retained for consideration in building the final model ($p < 0.20$) was physical abuse at T2. Child factors including birth defects, neonatal complications, overall health at T3 and T4, and maternal socio-

cultural factors of ethnicity, gravida status, and employment history at T1 were also associated ($p<0.20$) with high aggressive behaviour scores in children at three years of age (Appendix 6-A – Table 1).

In the final multivariable model, the factors associated with high aggressive behaviour scores (≥ 93 rd percentile or $\geq 13/21$) included depression at T3, maternal mood disorders at T4 measured by affective lability scores, and maternal smoking at T4. Other variables retained in the final model included physical abuse at T2, increasing gravida status, and less than very good maternal overall health, lack of neonatal complications, and the presence of birth defects in the child (Table 6-3).

Children of mothers screened positive for early postpartum (T3) depression had 2.7 times the odds of high aggression scores as compared to children of the mothers who were not screened positive for early postpartum (T3) depression (Table 6-3). Similarly, one-unit increase in the affective lability scores significantly increased the odds of high aggression scores at three years of age (Table 6-3). Children of the mothers who smoked/quit at T4 had 2.2 times higher odds of having high aggression scores as compared to children of the mothers who did not smoke (Table 6-3).

Table 6-3: Odds ratios, 95% confidence limits and p-values for the significant predictors of high aggressive behaviour scores ($\geq 93^{\text{rd}}$ percentile or $\geq 13/21$) among children at three years of age (N=336).

Variables		Odds ratio	95% CI		p-value
			Lower	Upper	
Depression at T3	Yes vs. No	2.7	1.1	6.8	0.03
Affective lability scores at T4	Per unit increase in score	1.1	1.0	1.1	<0.0001
Maternal smoking at T4	Smoke/quit vs. Never	2.2	1.1	4.7	0.03
Physical abuse at T2	Yes vs. No	5.2	1.2	22.5	0.02
Gravida status at T4	Multigravida vs. Primigravida	2.2	1.1	4.6	0.04
Maternal overall health at T3	Poor/Fair/Good vs. Excellent/Very good	3.2	1.1	9.3	0.03
Neonatal Complications	No vs. Yes	1.9	1.2	3.1	0.008
Birth defects	Yes vs. No	2.2	1.1	4.4	0.03
Wald test of parallel lines assumption for the final model with constraints for parallel lines not imposed for maternal smoking at T4 – $\chi^2(df = 9) = 3.8$, p=0.92					
Likelihood ratio test for goodness of fit – LR $\chi^2(df = 10) = 7.69$, p=0.65 indicates a good fit					
McFadden's Adj R ² : 5.8%					
T2 – Late pregnancy, T3 – Early postpartum, T4 – Three years after birth					

6.3.2 Attention problems at three years

Maternal anxiety scores at T2, T3, and T4 and depression at T3 were associated with high scores for attention problems ($\geq 93^{\text{rd}}$ percentile or $\geq 5/8$) in children at three years of age based on the unadjusted analysis at (p<0.20) (Appendix 6-A – Table 2). Other maternal factors (p<0.20) that were retained for consideration in building the final model included: physical abuse at T2, satisfaction with their partner at T1 and T4, education level at T1 and T4, and family income at T1 (Appendix 6-A – Table 2). Natal factors associated (p<0.20) with attention problems of children at three years of age based on unadjusted analysis were completed gestation period, type of birth, and sex of the child (Appendix 6-A – Table 2).

In the final multivariable model, an increase in the affective lability scores increased the odds of high scores for attention problems ($\geq 93^{\text{rd}}$ percentile or $\geq 5/8$) in children at three years of age (T4) (Table 6-4). Having less than post-secondary education as compared to some post-

secondary education was also retained in the final model. One unit increase in the maternal mood disorder scores measured by affective lability scores increased the odds of high attention problem scores in children at three years of age by 5% (Table 6-4). The four detected extreme outliers (standardized residual ≥ 3.0) were not influential and were thus retained in the model.

Table 6-4: Odds ratios, 95% confidence limits, and p-values for the significant predictors of high scores for attention problems ($\geq 93^{\text{rd}}$ percentile or $\geq 5/8$) among children at three years of age (n=342).

Variables		Odds ratio	95% CI		p-value
			Lower	Upper	
Affective Lability Scores at T4	Per unit increase in score	1.1	1.0	1.1	<0.0001
Education status at T1	Less than post-secondary vs. Some post-secondary	1.9	1.0	3.6	0.04
Brant test of parallel regression assumption – $\chi^2(12) = 7.31$, p-value 0.84					
Likelihood ratio test of goodness of fit indicates a good fit (LR $\chi^2(12) = 8.5$, p=0.75)					
McFadden adjusted R ² = 0.4%					
T1 – Early pregnancy, T4 – Three years after birth					

6.3.3 Anxiety/depression at three years

Maternal mental health and high-risk behavioural factors including: the previous history of depression, anxiety scores at T1, T2, T3, and T4, screened positive for depression (EPDS ≥ 12) at T1, T3, and T4, Cambridge worry scores at T2, family history of perinatal depression, alcohol intake at T2 and T3, exercise at T3, availability of emotional support and history of diagnosis and treatment of anxiety or depression after birth up to three years were associated (p<0.20) with anxiety/depression scores at or above the 93rd percentile ($\geq 4/7$) for children at three years of age based on unadjusted analysis (Appendix 6-A – Table 3). Maternal marital status at T1, satisfaction with partner at T4, education level at T1 and T4, overall health of the mother at T1 and T3, and natal factors of gestation period at birth, type of birth, birth order of the child, overall health of the child were also associated (p<0.20) with anxiety/depression scores at or

above the 93rd percentile in children at three years of age based on unadjusted analysis (Appendix 6-A – Table 3).

In the final multivariable model, maternal mental health and behavioural factors associated with having high anxiety/depression scores at or above the 93rd percentile ($\geq 4/7$ or the cut-off for borderline/clinical problems) included anxiety scores at T4, family history of perinatal depression, and alcohol consumption at T3. A one-unit increase in the maternal anxiety scores at T4 increased the odds of having high anxiety/depression scores by 20% (Table 6-5). Less than post-secondary maternal education at T1, having a pre-term or post-term birth and poor overall health of the child at T4 also increased the odds of having high anxiety/depression scores at three years of age (Table 6-5).

Table 6-5: Odds ratios, 95% confidence limits, and p-values for the significant predictors of high anxious/depressed scores ($\geq 93^{\text{rd}}$ percentile or $\geq 4/7$) among children at three years of age (n=337).

Variables		Odds ratio	95% CI		p-value
			Lower	Upper	
Anxiety scores at T4	Per unit increase in score	1.22	1.08	1.37	0.001
<i>Interaction effects of alcohol at T3 and family history of perinatal depression</i>					
Maternal education at T1	Less than postsecondary vs. Some postsecondary	2.0	1.0	3.9	0.05
Gestation at birth	Pre-term vs. Term	3.1	1.3	7.7	0.01
	Post-term vs. Term	3.8	0.8	17.0	0.08
Child overall health at T4	Poor/Fair vs. Good/Excellent	5.3	2.2	14.5	<0.0001
Birth order ^C	2 nd vs. 1 st	1.2	0.7	1.9	0.52
	3 rd vs. 1 st	0.7	0.4	1.2	0.22

C – confounder with respect to alcohol consumption at T3

Wald test of parallel lines assumption – $\chi^2(df = 51) = 42.2$, p=0.80

Likelihood ratio test for goodness of fit – LR $\chi^2(df = 51) = 60.3$, p=0.17 indicates a good fit

McFadden's Adj R2: 3.8%

T1 – Early pregnancy, T4 – Three years after birth

Significant interaction effects (p=0.007) were observed between the family history of perinatal depression and alcohol consumption at T3 (Table 6-6, Figure 6-1).



Figure 6-1: Predicted probability of high anxiety/depression scores ($\geq 4/7$ or at or above the 93rd percentile) based on the interaction effects of alcohol consumption in early postpartum (T3) period and family history of perinatal depression (n=337).

In the absence of family history of perinatal depression, children of mothers who quit drinking had increased odds of high scores for anxious/depressed behaviour at three-years-age as compared to children of mothers who never consumed alcohol ($p=0.007$) or who consumed alcohol ($p=0.05$) (Table 6-6). For mothers with a family history of perinatal depression, children of mothers who never consumed alcohol had increased odds of high scores for anxious/depressed behaviour at three-years as compared to children of mothers who drank alcohol ($p=0.004$) (Table 6-6).

For the children of mothers who never consumed alcohol, the presence of family history of perinatal depression increased the odds of high scores for anxious/depressed behaviour by 2.7 times as compared to those with no family history of perinatal depression ($p=0.001$) (Table 6-6).

Table 6-6: Odds ratios, 95% confidence limits, and p-values for the pairwise comparisons of interaction effects of early postpartum (T3) alcohol consumption and family history of perinatal depression in predicting high anxious/depressed scores ($\geq 93^{\text{rd}}$ percentile or $\geq 4/7$) among children at three years of age (n=337).

Variables		Odds ratio	95% CI Lower Upper	p-value
Interaction effects of status of alcohol consumption at T3 with no family history of perinatal depression				
Quit alcohol and no family history vs.	Drink alcohol and no family history	3.3	1.0 12.5	0.05
Drink alcohol and no family history vs.	Never drink alcohol and no family history	1.6	0.9 2.7	0.09
Quit alcohol and no family history vs.	Never drink alcohol and no family history	5.3	1.6 17.7	0.007
Interaction effects of status of alcohol consumption at T3 with family history of perinatal depression				
Quit alcohol and family history vs.	Drink alcohol and family history	4.9	0.8 33.3	0.09
Never drink alcohol and family history vs.	Drink alcohol and family history	3.3	0 7.4	0.004
Quit alcohol and family history vs.	Never drink alcohol and family history	1.5	0.3 9.0	0.66
Interaction effects of family history of perinatal depression with each level of alcohol consumption				
Never consumed alcohol and family history vs.	Never consumed alcohol and no family history	2.7	1.5 5.0	0.001
Quit alcohol and family history vs.	Quit alcohol and no family history	0.8	0.1 6.1	0.80
Drink alcohol and family history	Drink alcohol and no family history	0.8	0.4 1.7	0.60

6.3.4 Sleep problems at three years

Maternal mental health and behavioural factors of family history perinatal depression, depression at T1, T2, T3, and T4, anxiety scores at T3 and T4, history of diagnosis and treatment of depression between T3 and T4, drug use at T3, exercise at T1 and T4, Cambridge worry scores at T2 were associated ($p < 0.20$) with increased odds of high scores for sleep problems ($\geq 93^{\text{rd}}$ percentile or $\geq 4/7$) in children at three years of age based on unadjusted analysis at $p < 0.2$ (Appendix 6-A – Table 4). Maternal overall health at T1 and T4, marital status at T4, relationship with a partner at T4, physical abuse at T1, availability of emotional support at T4,

and natal factors of gestation period at birth, type of birth, breastfeeding initiated at T3, and overall health of the child at T4 were also retained ($p<0.20$) for consideration in building the final multivariable model based on unadjusted analysis (Appendix 6-A – Table 5).

In the final multivariable generalized ordinal regression model, family history of perinatal depression and maternal depression (EPDS ≥ 12) at T3 and T4 were significant predictors of increased odds of high scores for sleep problems ($\geq 93^{\text{rd}}$ percentile or $\geq 4/7$) at three years of age (T4). Other factors included in the final model included: physical abuse at T1, maternal marital status at T4, type of birth, initiation of breastfeeding at birth, and overall health of the child at T4. However, the proportional odds assumption was not satisfied for this model, and the model as compared to the multinomial model (Likelihood $\chi^2(39) = 58.3$, p-value=0.02) was a poor fit to the data. A partial proportional odds model had the best fit (as compared to multinomial model and ordinal model) with constraints of parallel lines not imposed for family history of perinatal depression, type of birth category, breastfeeding initiated, physical abuse at T1, and overall health of the child at T4 (Table 6-7).

Children of mothers who screened positive for depression at T3 and T4 had increased odds of high scores for sleep problems ($\geq 93^{\text{rd}}$ percentile or $\geq 4/7$) at three years of age as compared to children of the mothers who did not screen positive for depression at T3 and T4 respectively (Table 6-7). Overall, children of single or separated mothers had 2.8 times increased odds of high scores for sleep problems at three years of age as compared to children of the married or mothers living with a common-law partner (Table 6-7). Affective lability scores and relationship satisfaction at T4 were confounders with respect to depression at T4 and marital status at T4 respectively.

Table 6-7: Odds ratios, p-values and 95% confidence limits for the predictors (proportional odds assumption true) and confounders of high scores for sleep problems ($\geq 93^{\text{rd}}$ percentile or $\geq 4/7$) among children at three years of age (n=333).

Variables		Odds ratio	95% CI		p-value
			Lower	Upper	
Estimates for predictors for whom the parallel lines assumption was true					
Depression at T3	EPDS ≥ 12 vs. EPDS<12	4.0	1.7	9.8	0.002
Depression at T4	EPDS ≥ 12 vs. EPDS<12	2.6	1.0	6.7	0.05
Affective Lability Scores ^c	Per unit increase in score	1.01	0.98	1.04	0.40
Marital status at T4	No vs. Yes	2.8	1.3	5.8	0.008
Very Satisfied at T4 ^c	No relationship vs. Very satisfied	1.2	0.3	5.3	0.85
	Not very satisfied vs. No relationship	1.7	0.4	7.4	0.49

Likelihood ratio test for goodness of fit – LR χ^2 (df = 18) = 5.32, p=0.99 indicates a good fit as compared to multinomial model.

McFadden adjusted R² for the ordinal model – 12.8%

C – Confounder, T3 – Early postpartum, T4 – Three years after birth

Wald test of parallel lines assumption for the final model was true for the partial proportional odds model (χ^2 (df=15) = 11.30, p=0.73). Since the ordinal sleep variable had five categories; four panels of estimates were computed for the variables that were not constrained by the proportional odds assumption (Appendix 6-A Table 5, Table 6-8).

Table 6-8: Odds ratios, p-values and 95% confidence limits for the predictors (where the proportional odds assumption did not apply) of children above the 93rd percentile for sleep problem scores ($\geq 4/7$) as compared to children below the 93rd percentile (n=333).

Variables		Odds ratio	95% CI		p-value
			Lower	Upper	
Estimates for sleep category 4 vs. categories 0, 1, 2, & 3					
Family history of perinatal depression	Yes vs. No	2.7	1.4	5.2	0.002
	Don't know vs. No	1.6	0.7	3.8	0.23
Physical abuse at T1	Yes vs. No	1.7	0.9	3.2	0.09
Type of birth	Assisted vs. Spontaneous	2.6	1.1	5.9	0.02
	C-section vs. Spontaneous	1.8	1.0	3.1	0.04
Breastfeeding initiated	Yes vs. No	2.5	1.2	4.8	0.009
Child's overall health at three years of age	Excellent/good vs. Poor/Fair	3.94e-07	0	0	0.97

Mothers with family history of perinatal depression had significantly higher odds of being in highest sleep problem category as compared to mothers with no family history of perinatal depression (Table 6-8). Children of mother who were physically abused at T1, had assisted birth or caesarean section as compared to normal spontaneous birth, and who were breastfed also had significantly increased odds of being in the highest category (above 93rd percentile) as compared being in all the lower categories at three years of age (Table 6-8).

6.3.5 Withdrawn behaviour at three years

Maternal mental health and socio-behavioural factors including: anxiety scores at T1, T2, T3, and T4, Cambridge worry scores at T2, stress due to any reason at T2 and T3, affective lability scores and maternal drug use at T4 were associated with high withdrawn behaviour scores ($\geq 93^{\text{rd}}$ percentile or $\geq 3/4$) in children at three years of age (Appendix 6-A – Table 6). Other factors including overall health of the mother at T1, birth order of the child, and gravida status of the mother at T1 and T4 were also considered in building the final multivariable model. Gravida status at T1 was highly correlated ($\rho = 0.91$) with gravida status at T4; gravida status at T1 was retained for building the model due to the smaller p-value.

Table 6-9: Odds ratios, 95% confidence limits, and p-values for the significant predictors and confounders of high scores for withdrawn behaviour ($\geq 93^{\text{rd}}$ percentile or $\geq 3/4$) at three years of age (n=343).

Variables		Odds ratio	95% CI		p-value
			Lower	Upper	
Anxiety scores at T4	Per unit increase in score	1.1	1.0	1.3	0.04
Birth order	1st vs. 2nd	0.5	0.3	0.8	0.004
	3rd vs. 2nd	0.5	0.3	0.8	0.009
Affective lability scores at T4 C	Per unit increase in score	1.0	0.9	1.1	0.55
Likelihood ratio test for goodness of fit – LR $\chi^2(df = 5) = 5.86$, p=0.32 indicates a good fit					
McFadden Adjusted R ² = 0.7%					
C – Confounder in the model, T4 – Three years after birth					

In the final multivariable model for high scores for withdrawn behaviour ($\geq 93^{\text{rd}}$ percentile or $\geq 3/4$), anxiety scores at T4 and birth order of the child were the only significant predictors; affective lability scores at T4 was a confounder ($>20\%$ change in the estimates) with respect to anxiety scores at T4 (Table 6-9). One unit increase in the maternal anxiety scores at three years of age increased the odds of high withdrawn behaviour scores ($\geq 93^{\text{rd}}$ percentile or $\geq 3/4$) (Table 6-9).

6.3.6 Summary

In our study, maternal mental health (family history of perinatal depression, depression, anxiety, mood disorder) were independent predictors of the emotional and behavioural development of the child at three years of age (Table 6-10). Socio-behavioural (maternal smoking, maternal alcohol consumption, maternal education level, maternal physical abuse during pregnancy) and, cultural factors (ethnicity, marital status, breastfeeding) were also independent predictors of the emotional and behavioural development of the child at three years of age (Table 6-10). Similarly, biological factors including type of birth, birth defects, neonatal complications, gravida status, overall maternal prenatal health and child's overall perceived health at three years of age were associated with emotional and behavioural development at three years of age (Table 6-10).

Table 6-10: Significant predictors, confounders, and moderators of emotional and behavioural development of children at three years of age measured by high scores ($\geq 93^{\text{rd}}$ percentile) from a re-specified Child Behaviour Checklist 1.5–5 (CBCL).

Behavioural syndromes	Significant predictors # significant interactions	Confounding variables
Aggression	Depression at T3 Affective lability scores at T4 Maternal smoking at T4 Physical abuse at T2 Overall health at T3 Gravida status at T4 Neonatal complications Birth defects	
Attention	Affective lability scores at T4 Education at T1	
Anxiety	Anxiety scores at T4 Alcohol at T3# Family history of perinatal depression# Education at T1 Gestation at birth Child overall health at T4	Birth order
Sleep	Depression at T3 Depression at T4 Family history of perinatal depression Marital status at T4 Physical abuse at T1 Type of birth Breastfeeding initiated Child overall health at T4	Affective lability scores at T4 Relationship satisfaction at T4
Withdrawn	Anxiety scores at T4 Birth order	Affective lability scores at T4

T1 – Early pregnancy, T2 – Late pregnancy, T3 – Early postpartum, T4 – Three years after birth

6.4 Discussion

This study supported our hypothesis that maternal mental health factors including anxiety, affective lability, and depression increase the odds of high scores for specific externalizing and internalizing behaviours such as aggression, attention problems, anxiety/depression, sleep problems, and withdrawal among children at three years of age. Also,

as hypothesized, these associations appeared to be time sensitive with only maternal health measured at T3 or T4 significantly associated with the outcomes of interest in the final models. Similarly, there was also evidence of children of mothers who were exposed to high-risk behaviours, such as smoking and alcohol consumption, after pregnancy had an increased risk for high emotional and behavioural problems. Family history of perinatal depression was also associated with the emotional and behavioural development of the child at three years of age.

In Canada, approximately 12.5% of children in the age group of two to five years and 6.4% of children in the age group of two to three years display signs of physical aggression ([GOC, 2011](#)). If unchecked, aggressive behaviours in early childhood can be stable and predict aggressive behaviour risk of delinquency and substance abuse in adolescence and among adults ([Olweus, 1979](#); [Tremblay et al., 2004](#)). In our study, early postpartum (T3) depression and maternal affective disability at three years after birth (T4), measured with high lability scores, significantly increased the odds of aggressive behaviour in three-year-old children. Effects of maternal mental health problems, including depression, on aggressive behaviour in children have been linked to mother's emotional unavailability, low attentiveness and responsiveness, and her inability to teach self-regulation ([Beardslee et al., 1983](#); [Smith, 2004](#); [Webster-Stratton & Hammond, 1988](#)). Consistent with our results, maternal depression and anxiety have previously been associated with aggressive behaviours in children ([Beardslee et al., 1983](#); [Becker & Ginsburg, 2011](#)).

In the present study, maternal smoking at T4 increased the odds of higher aggressive behaviour scores at three years of age (T4). Negative effects of prenatal smoking on the emotional and behavioural and cognitive development in infants, toddlers, and along the life course has been well documented ([Ball et al., 2010](#); [Carter et al., 2008](#); [Cornelius et al., 2012](#);

[Liu et al., 2013](#); [Stene-Larsen et al., 2009](#)). Smoking during pregnancy has been specifically linked to aggressive behaviour of children in early infancy and the preschool period ([Paterson et al., 2013](#); [Reebye, 2005](#)). Similarly, exposure to second-hand smoke in infancy has also been linked to externalizing behaviours in primary school children in France ([Chastang et al., 2015](#)).

A history of physical abuse in the late pregnancy (T2) also increased the odds of higher aggression scores at three years of age. Consistent with our results, literature supports the fact that exposure to physical abuse and violence in pregnancy leads to higher risk of aggressive behaviour in children through changes in the maternal fetal axis ([Campbell et al., 2007](#); [Reebye, 2005](#); [Susman et al., 1999](#)).

The relationship between parity and pregnancy outcomes has been of concern for decades ([Solomons, 1934](#)). However, little research is available on the longitudinal effects of parity on emotional and behavioural development in children. Women with higher parity tend to be older, more likely to be in lower socioeconomic classes, and more likely to be smokers with higher risk of neonatal morbidity, characterized by low birth weight and preterm deliveries, as compared to women having their first baby ([Cnattingius et al., 1993](#); [Finlay et al., 2011](#); [Kenny et al., 2013](#)). Thus, high parity tends to be associated with socioeconomic disadvantage ([Bai et al., 2002](#); [Cnattingius et al., 1993](#)). This could very well explain the observed higher risk of having higher aggressive behaviour scores among children of multiparous women in our study.

In Canada, approximately 6.2% of age two to five year children exhibit behaviours associated with hyperactivity and inattention ([GOC, 2011](#)). In our study, affective lability scores linked to maternal mood disorders were associated with high attention problem scores. Affective lability or frequent mood changes are commonly reported during pregnancy and postpartum period ([Bowen et al., 2012a](#)). Affective lability or affective dysregulation refers to the

maladaptive patterns of emotional regulation that impair daily-life functioning and have been linked with disruptive child behaviour and impaired mother-infant interactions ([Elgar et al., 2004](#)).

In our study, some post-secondary maternal education was protective against development of attention problems in children at three years of age. Consistent with our research, low maternal education has been previously associated with inattention and hyperactivity symptoms at three years of age ([Foulon et al., 2015](#)). The reported pathways of protective effects of maternal education were associated with higher socio-economic status, longer duration of breastfeeding, and better neurodevelopmental leading to lower levels of inattention and hyperactivity at three years of age ([Foulon et al., 2015](#)).

In Canada, approximately 14.3% of two to five-year-old children exhibit the signs of anxiety ([GOC, 2011](#)). Consistent with our research prenatal and postpartum maternal anxiety has also been associated with emotional and behavioural problems at four years of age ([Connor et al., 2002; Kertz et al., 2008](#)).

Similar to attention problems, some postsecondary education lowered the odds of high anxiety/depression scores at three years of age. There is no doubt that maternal education has a positive influence on child rearing practices ([Ross & Van Willigen, 1997](#)). The link between increasing socio-economic status (SES) and increasing academic achievement in children is well established ([Davis-Kean, 2005; Dubow et al., 2009](#)). Parental education especially maternal education is an important index of socioeconomic status ([Dubow et al., 2009](#)). Family process models have proposed that family structural variables such as parental education and income affect the level of actual interactions within the family and in turn, child behaviour ([Mistry et al., 2002](#)).

In our study, the effects of consuming alcohol on anxious/depressed behaviour were modified by a family history of perinatal depression. The presence of family history of perinatal depression increased the odds of higher scores for anxious/depressed behaviour as compared to those with no family history of perinatal depression, but only for the children of mothers who never consumed alcohol. Quitting alcohol in the absence of family history of perinatal depression as compared to children of mothers who never consumed alcohol or who consumed alcohol, increased the odds of higher anxiety scores among children at three years of age. For those with a family history of perinatal depression, children of mothers who never consumed alcohol had increased odds of higher scores for anxious/depressed behaviour at three years as compared to children of mothers who drank alcohol.

Research indicates that family history of perinatal depression is associated with higher risk of depression and anxiety, alcohol and drug dependence ([Milne et al., 2009](#); [Weissman et al., 1987](#)). However, being married and having satisfied relationship with partner decreases the risk of maternal postpartum alcohol consumption ([McNamara et al., 2006](#); [Røsand et al., 2011](#)). While the results are not exactly as expected, we were able to empirically measure the direction and magnitude of the effects of family history of perinatal depression and maternal postpartum alcohol consumption as it effects the long-term emotional and behavioural development of children at three years of age.

In our study, pre-term and post-term births as compared to term births were associated with higher anxiety scores at three years of age. Pre-term and post-term births have been associated with learning difficulties and significant excess of behavioural problems including depression and anxiety ([Bhutta et al., 2002](#); [Burnett et al., 2011](#); [El Marroun et al., 2012](#); [MacKay et al., 2010](#)). In our study, mother-reported good health of the child lowered the odds of

having high anxiety/depression scores at three years of age. Very little research is available on the direct effects of a mother's perception of their child's health and behaviours like anxiety and sleep problems. Mothers who report their children healthy are less likely to report emotional and behavioural development issues in their children and are better adjusted in parenting roles ([Grusec & Danyliuk, 2014](#)). At the same time, a mother's capacity to accurately identify their children's thoughts and feelings have been linked to children's secure attachment with a positive mother-child attachment ([Bernier & Dozier, 2003](#); [McMahon & Meins, 2012](#)).

Sleep problems and lack of sleep in infancy and early childhood have been associated with delays in physical, cognitive, and social development and higher risk of mental health issues throughout their lifetime ([Ford & Cooper-Patrick, 2001](#); [Touchette et al., 2007](#); [Touchette et al., 2009](#)). In our study, children of mothers having family history of perinatal depression or who screened positive for depression in the early postpartum (T3) visit or at the three-year (T4) visit had increased odds of high sleep problem scores at three years of age. Maternal mental and physical health are known correlates of sleep problems in infancy and early childhood ([Bayer et al., 2007](#); [Martin et al., 2007](#)). Consistent with our research, marital problems, and history of abuse of the mother were also known risk factor of sleep problems in early childhood ([Mannering et al., 2011](#); [Shang et al., 2006](#)).

In our study, children reported to have good health, and who were born through normal birth as compared to assisted or Caesarean section had lower odds of high sleep problem scores; whereas, children who were breastfed were more likely to have high scores. The literature supports the association between type of birth (Caesarean section) and sleep problems in infancy ([Verdult, 2009](#)). Babies given formula milk instead of breast milk were more likely to have behavioural problems by five years of age ([Quigley et al., 2012](#)). However, the negative aspect

of long-term breastfeeding is the weaning from the breast, especially at night time. Higher odds of reported sleep problems were probably due to issues related to breast weaning of the toddler. As reported earlier, in our study, the median duration of breastfeeding was nine months with an interquartile range of ten months. Night weaning of older babies and toddlers can be more difficult as compared to infants. Some studies have reported correlation between breastfeeding and sleep problems at night ([Eaton-Evans & Dugdale, 1988](#); [Elias et al., 1986](#)), and others have refuted this claim ([Kahn et al., 1989](#)). However, the benefits of breastfeeding on the child's health outweigh any sleep problems they might have in the early infancy ([Blair, 2011](#); [Mennella et al., 2007](#)).

Withdrawn behaviour in early childhood is linked to psychological maladaptive behaviour and is considered a representation of social anxiety or depression in children ([Essau, 2006](#)). Similar to our results of anxiety/depression scores, maternal anxiety scores at three years of age (T4) also increased the odds of high scores for withdrawn behaviour at three years of age. Maternal affective lability scores at three years after birth confounded the effects of maternal anxiety. Maternal anxiety has been associated with host of internalizing problems in infancy and early childhood and co-morbidity of anxious and withdrawn behaviours are also well known ([Rubin et al., 2009](#)). The pathways of effects of maternal anxiety have been explained through high level of parental control, low level of autonomy in decision making and tendency to catastrophize the environmental dangers which in turn increases the risk of development of anxious and withdrawn behaviours in children ([Becker et al., 2010](#))

In our study, being a second child as compared to first or third or more order child increased the odds of withdrawn behaviour at three years of age. Researchers working in this area have long speculated that birth order might be related to child outcomes through parental

investments in their offspring and role of peer relationships. Here we need to consider two type of investments - parental time investments and financial investments. First born or elder children get undivided parental attention and time; whereas, younger siblings or later born get more financial investment ([Argys et al., 2006](#); [Behrman & Taubman, 1986](#)). Older siblings might also act as caregivers or authority figures. In addition, having an older sibling may provide more opportunities to interact with, and perhaps copy the behaviour of a different set of friends ([Argys et al., 2006](#); [Rodgers et al., 1992](#)). At the same time, a child's fear of peer rejection may increase the risk of developing withdrawn behaviour ([Rubin et al., 2009](#)).

To our knowledge, this is the first study to comprehensively examine the impact of maternal behavioural-mental health factors on individual emotional and behavioural syndromes of aggression, attention problems, anxiety/depression, sleep problems, and withdrawn behaviours in three-year-old children. One of the strengths of the study was that all the risk factors were measured longitudinally from early pregnancy up to three years after birth. By following this cohort longitudinally, it was possible to establish the time sequence for many of the associations examined. The risk of recall and measurement biases were also minimised by the repeated use of measures throughout the study period.

6.5 Limitations

One of the challenges in analysing the data from this study was the non-normal score distribution for the individual syndromes scores. However, an effort was made to retain the original dependent variable structure in the ordinal regression analysis. For all but one of the outcomes, only the score categories above the 93rd percentile were collapsed for analysis; the choice of the 93rd percentile as a cut-point to identify borderline/clinical problems was based on a previous report ([Achenbach & Rescorla, 2000](#)). Thus, the estimates from the ordinal regression

analysis included the odds of having borderline/clinical behavioural scores as compared to a lower score. Finally, there was a potential for type 1 error due to a large number of predictors considered in the analysis. This risk was managed by choosing risk factors for analysis based on the literature and screening variables prior to considering them in building the multivariable models.

6.6 Conclusions

Development of emotional and behavioural skills in early childhood provides a necessary foundation for reducing health and social inequities across the life course. Investment in the early years in the form of quality education, development, and parenting programs has shown greater economic returns as compared to post-kindergarten investments ([Hertzman, 2009](#)).

Approximately 25% to 30% of Canadian children enter school with some form of physical, socio-emotional, or cognitive delay ([Hertzman, 1998](#)). Canadian trends reveal an increase in developmental vulnerability across several provinces over the past decade ([Hertzman, 1998](#)).

Preschool years due to availability of greater attention from parents and teachers are considered an important window of opportunity for limiting negative child outcomes ([Tichovolsky et al., 2013](#)). Understanding the determinants of higher scores for emotional and behavioural traits in preschoolers will help us develop targeted interventions to reduce the burden of childhood behavioural disorders and mental illnesses in society.

6.7 References

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6.8 Appendices

6.8.1 Appendix 6-A – Table1: Unadjusted analysis of high scores for aggression behaviours ($\geq 93^{\text{rd}}$ percentile).

Covariates considered in unadjusted analysis aggression behaviour using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Family history of perinatal depression*	Yes vs. No	1.3	0.8	2.1	0.28
	Don't know vs. No	1.9	1.0	3.8	0.06
Previous history of depression	Yes vs. No	1.2	0.8	1.9	0.45
Education level	Some postsecondary vs. Less than postsecondary	1.1	0.5	2.4	0.80
Employment status	Yes vs. No	0.6	0.4	1.1	0.13
Planned pregnancy	Yes vs. No	0.9	0.5	1.6	0.73
Mothers' age cat	25-34 vs. <25	1.5	0.7	3.3	0.28
	≥ 35 vs. <25	1.5	0.6	3.7	0.39
Mothers' ethnicity	Caucasian vs. Non-Caucasian	2.7	1.0	7.4	0.06
Marital status at enrollment	Married/Common Law vs. Single/Divorced	0.7	0.3	1.8	0.52
EARLY AND LATE PREGNANCY MEASURES (T1 & T2)					
Satisfaction with the father of the child at T1	Very satisfied vs. No relationship	0.6	3.6		0.12
	Not very satisfied vs. No relationship	0.5	0.1	2.1	0.33
Satisfaction with the father of the child at T2*	Very satisfied vs. No relationship	1.1	0.3	4.9	0.89
	Not very satisfied vs. No relationship	0.8	0.2	3.1	0.77
Exercise at T1	Yes vs. No	1.0	0.5	2.0	0.95
Exercise at T2*	Yes vs. No	0.8	0.4	1.6	0.60
Smoking at T1	Quit vs. Never	1.2	0.7	2.0	0.53
	Smoke vs. Never	1.4	0.5	3.8	0.51
Smoking at T2*	Quit vs. Never	0.7	0.3	1.5	0.32
	Smoke vs. Never	2.2	0.9	5.7	0.10
Drug use at T1	Quit vs. Never	0.8	0.4	1.6	0.59
	Drug use vs. Never	5.6	0.9	34.2	0.06
Drug use at T2	Quit vs. Never	0.7	0.2	3.0	0.67
	Drug use vs. Never	5.5	0.2	189.7	0.35
Alcohol at T1	Quite vs. Never	0.9	0.6	1.4	0.61
	Drink vs. Never	1.2	0.5	3.3	0.69
Alcohol at T2	Quite vs. Never	1.0	0.6	1.8	0.89
	Drink vs. Never	1.1	0.5	2.6	0.85
Family Income at T1	$\geq \$40,000/\text{year}$ vs. $<\$40,00/\text{year}$	0.8	0.5	1.4	0.45
Physical abuse at T1	Yes vs. No	1.0	0.6	1.7	0.99
Physical abuse at T2	Yes vs. No	3.8	0.9	15.4	0.06

Covariates considered in unadjusted analysis aggression behaviour using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Overall health of the mother at T1	Poor/Fair/Okay vs. Excellent/Very good/Good	0.6	0.2	1.9	0.40
Overall health of the mother at T2	Poor/Fair/Okay vs. Excellent/Very good/Good	1.0	0.4	2.2	0.98
Cambridge worry scores at T1	Continuous	1.0	1.0	1.0	0.74
Cambridge worry scores at T2	Continuous	1.0	1.0	1.0	0.88
Stress at T1	Yes vs. No	1.4	0.7	2.9	0.39
Stress at T2	Yes vs. No	1.3	0.6	2.6	0.48
Anxiety scores at T1	Continuous	1.0	0.9	1.1	0.92
Anxiety scores at T2	Continuous	1.0	0.9	1.1	0.96
Depression at T1	Yes vs. No	1.3	0.6	2.7	0.50
Depression at T2*	Yes vs. No	1.6	0.7	3.8	0.31
Pregnancy complications	No vs. Yes	1.0	0.5	1.8	0.93
Type of birth	Assisted vs. Spontaneous	1.2	0.6	2.2	0.66
	C-section vs. Spontaneous	1.0	0.6	1.6	1.00
Gestation period*	Pre-term vs. Term	1.4	0.6	3.6	0.47
	Post-term vs. Term	2.5	0.5	12.2	0.26
Birth complications	No vs. Yes	1.0	0.7	1.5	0.97
One minute Apgar scores	≥ 7 vs. <7	1.0	0.5	1.9	0.99
Five minute Apgar scores	≥ 7 vs. <7	2.0	0.4	10.4	0.40
Neonatal complications	No vs. Yes	0.6	0.4	0.9	0.03
Birth defects	Yes vs. No	2.3	1.1	4.5	0.02
Sex of child	Female vs. Male	0.8	0.5	1.2	0.23
Weight for gestational age (WHO)	SGA vs. AGA	0.7	0.3	1.7	0.47
	LGA vs. AGA	1.5	0.8	2.7	0.18
Weight for gestational age (PHAC)	SGA vs. AGA	0.8	0.4	1.7	0.61
	LGA vs. AGA	1.2	0.6	2.4	0.55
EARLY POSTPARTUM MEASURES (T3)					
Birth order ordinal	2 nd vs. 1 st	1.4	0.8	2.2	0.21
	3 rd or more vs. 1 st	1.0	0.6	1.7	0.96
Gravida status at T1	Multigravida vs. Primigravida	1.2	0.8	1.8	0.40
Breastfeeding initiated*	Yes vs. No	1.0	0.5	1.7	0.90
Satisfaction with the partner*	Very satisfied vs. No relationship	1.2	0.3	6.0	0.80
	Not very satisfied vs. No relationship	1.1	0.2	4.7	0.92
Exercise	Yes vs. No	0.7	0.4	1.1	0.13
Smoking*	Smoke/Quit vs. Never	2.1	1.0	4.5	0.05
Drug abuse	Drug use vs. Never	0.4	0.0	4.1	0.46
	Quit vs. Never	5.8	0.5	74.7	0.18
Alcohol	Quit vs. Never	1.3	0.4	3.8	0.63
	Drink vs. Never	0.9	0.6	1.4	0.53
Anxiety scores*	Continuous	1.1	1.0	1.2	0.06
Depression	Yes vs. No	2.6	1.1	5.9	0.03

Covariates considered in unadjusted analysis aggression behaviour using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Stress	Yes vs. No	1.4	0.8	2.5	0.18
Overall health of the mother	Poor/Fair/Okay vs. Excellent/Very good/Good	2.2	0.8	5.7	0.11
THREE YEARS AFTER BIRTH (T4)					
Any subsequent pregnancy	Yes vs. No	1.0	0.6	1.5	0.96
Emotional support	Yes vs. No	0.8	0.1	12.1	0.90
Mood disorder scores	Continuous	1.1	1.0	1.1	<0.0001
Maternal overall health	Excellent/Very good vs. Poor/ Fair/ Okay	1.2	0.5	2.8	0.61
Child overall health	Excellent/Very good vs. Fair/Good	0.4	0.2	1.0	0.05
History of diagnosis & treatment of depression during the study time period	Non-pharmacological methods vs. Not diagnosed	1.2	0.3	5.8	0.80
	Pharmacological methods vs. Not diagnosed	1.1	0.7	2.0	0.63
Satisfaction with the father of the child*	Very satisfied vs. No relationship	1.8	0.6	5.4	0.27
	Not very satisfied vs. No relationship	1.1	0.4	2.9	0.88
	Yes vs. No	0.9	0.5	1.5	0.70
Family Income	≥\$40,000/year vs. <\$40,000/ year	1.2	0.6	2.4	0.57
Education status*	Some postsecondary vs. Less than postsecondary	1.0	0.5	2.0	0.91
Marital status	Common law/ Married vs. Single/Divorced/Separated	0.7	0.3	1.4	0.28
Gravida status	Multigravida vs. Primigravida	1.7	0.9	3.3	0.11
Exercise	Yes vs. No	0.5	0.3	0.9	0.03
Smoking*	Smoke/Quit vs. Never	1.6	0.8	3.3	0.16
Drug abuse	Drug use/Quit vs. Never	0.5	0.1	2.6	0.41
Alcohol use	Yes vs. No	0.7	0.3	1.4	0.30
Anxiety scores	Continuous	1.1	1.0	1.3	0.04
Depression	Yes vs. No	1.5	0.6	3.6	0.41
Unadjusted association (p<0.2)					
T1 – Early pregnancy, T2 – Late pregnancy, T3 – Early postpartum, T4 – Three year after birth					

6.8.2 Appendix 6-A – Table 2: Unadjusted analysis of high scores for attention problems (\geq 93rd percentile).

Covariates considered in unadjusted analysis of attention problems using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Family history of perinatal depression*	Yes vs. No	1.0	0.7	1.5	1.00
	Don't know vs. No	1.1	0.6	2.1	0.78
Previous history of depression	Yes vs. No	0.9	0.6	1.4	0.72
Education level	Some postsecondary vs. Less than postsecondary	0.5	0.3	1.0	0.04
	Employment status	0.9	0.5	1.5	0.67
Planned pregnancy	Yes vs. No	0.8	0.5	1.4	0.40
Mothers' age cat	25-34 vs. <25	0.7	0.3	1.3	0.21
	≥ 35 vs. <25	0.7	0.3	1.5	0.38
Mothers' ethnicity	Caucasian vs. Non-Caucasian	1.6	0.7	3.6	0.28
	Marital status at enrollment	Married/Common Law vs. Single/Divorced	1.2	0.6	2.6
EARLY AND LATE PREGNANCY (T1 & T2)					
Satisfaction with the father of the child at T1	Very satisfied vs. No relationship	0.9	0.2	3.9	0.88
	Not very satisfied vs. No relationship	0.4	0.1	1.6	0.22
Satisfaction with the father of the child at T2*	Very satisfied vs. No relationship	1.2	0.3	4.7	0.80
	Not very satisfied vs. No relationship	0.9	0.3	3.1	0.87
Exercise at T1	Yes vs. No	0.9	0.5	1.6	0.76
Exercise at T2*	Yes vs. No	1.2	0.6	2.1	0.65
Smoking at T1	Quit vs. Never	1.4	0.9	2.1	0.19
	Smoke vs. Never	0.9	0.4	2.2	0.83
Smoking at T2*	Quit vs. Never	1.1	0.5	2.1	0.87
	Smoke vs. Never	1.4	0.6	3.1	0.48
Drug use at T1	Quit vs. Never	0.9	0.5	1.6	0.80
	Drug use vs. Never	1.5	0.3	6.8	0.62
Drug use at T2	Quit vs. Never	0.8	0.2	2.8	0.78
	Drug use vs. Never	3.6	0.2	61.4	0.38
Alcohol at T1	Quite vs. Never	0.7	0.5	1.1	0.15
	Drink vs. Never	0.9	0.4	2.3	0.83
Alcohol at T2	Quite vs. Never	0.9	0.5	1.5	0.72
	Drink vs. Never	1.0	0.5	2.3	0.98
Family Income at T1	$\geq \$40,000/\text{year}$ vs. < $\$40,000/\text{year}$	0.7	0.4	1.1	0.14
	Physical abuse at T1	Yes vs. No	1.2	0.8	1.9
Physical abuse at T2	Yes vs. No	2.5	0.7	8.3	0.14
Overall health of the mother at T1	Poor/Fair/Okay vs. Excellent/Very good/Good	0.7	0.3	1.7	0.40

Covariates considered in unadjusted analysis of attention problems using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Overall health of the mother at T2	Poor/Fair/Okay vs. Excellent/Very good/Good	0.9	0.5	1.9	0.85
Cambridge worry scores at T1	Continuous	1.0	1.0	1.0	0.44
Cambridge worry scores at T2	Continuous	1.0	1.0	1.0	0.71
Stress at T1	Yes vs. No	1.0	0.5	1.8	0.98
Stress at T2	Yes vs. No	1.1	0.6	2.0	0.68
Anxiety scores at T1	Continuous	1.0	0.9	1.1	0.56
Anxiety scores at T2	Continuous	1.1	1.0	1.2	0.12
Depression at T1	Yes vs. No	1.0	0.6	1.9	0.89
Depression at T2*	Yes vs. No	1.3	0.6	3.1	0.47
Pregnancy complications	No vs. Yes	1.0	0.5	1.8	0.96
Type of birth	Assisted vs. Spontaneous	1.6	0.9	2.8	0.12
	C-section vs. Spontaneous	0.8	0.5	1.3	0.39
Gestation period*	Pre-term vs. Term	1.5	0.7	3.6	0.31
	Post-term vs. Term	3.8	1.0	15.5	0.06
Birth complications	No vs. Yes	1.0	0.7	1.4	0.94
One minute Apgar scores	≥ 7 vs. <7	0.9	0.5	1.6	0.68
Five minute Apgar scores	≥ 7 vs. <7	2.7	0.8	9.1	0.10
Neonatal complications	No vs. Yes	0.8	0.6	1.2	0.39
Birth defects	Yes vs. No	1.4	0.8	2.6	0.23
Sex of child	Female vs. Male	0.7	0.5	1.1	0.12
Weight for gestational age (WHO)	SGA vs. AGA	1.0	0.5	1.9	0.94
	LGA vs. AGA	1.4	0.8	2.3	0.27
Weight for gestational age (PHAC)	SGA vs. AGA	1.1	0.6	2.0	0.87
	LGA vs. AGA	1.2	0.7	2.2	0.56
EARLY POSTPARTUM (T3)					
Birth order ordinal	2 nd vs. 1 st	1.1	0.7	1.7	0.72
	3 rd or more vs. 1 st	1.1	0.7	1.8	0.77
Gravida status at T1	Multigravida vs. Primigravida	1.1	0.7	1.6	0.69
Breastfeeding initiated*	Yes vs. No	0.8	0.5	1.4	0.50
	Very satisfied vs. No relationship	1.3	0.3	6.0	0.73
Satisfaction with the partner*	Not very satisfied vs. No relationship	0.9	0.2	3.8	0.90
Exercise	Yes vs. No	1.2	0.8	1.9	0.45
Smoking*	Quit vs. Never	2.6	0.8	8.6	0.11
	Smoke vs. Never	1.2	0.5	2.6	0.71
Drug abuse	Drug use vs. Never	2.0	0.5	9.2	0.35
	Quit vs. Never	2.2	0.3	18.3	0.47
Alcohol	Quit vs. Never	1.3	0.5	3.5	0.56
	Drink vs. Never	1.0	0.7	1.5	0.85
Anxiety scores*	Continuous	1.1	1.0	1.2	0.05

Covariates considered in unadjusted analysis of attention problems using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Depression	Yes vs. No	1.7	0.8	3.6	0.17
Stress	Yes vs. No	1.2	0.8	2.0	0.38
Overall health of the mother	Poor/Fair/Okay vs. Excellent/Very good/Good	0.9	0.4	1.9	0.72
THREE YEAR AFTER BIRTH (T4)					
Any subsequent pregnancy	Yes vs. No	1.0	0.7	1.5	0.98
Emotional support	Yes vs. No	1.0	0.1	10.9	1.00
Mood disorder scores	Continuous	1.0	1.0	1.1	0.00
Maternal overall health	Excellent/Very good vs. Poor/ Fair/ Okay	1.1	0.5	2.2	0.82
Child overall health	Excellent/Very good vs. Fair/Good	0.7	0.3	1.4	0.28
History of diagnosis & treatment of depression during the study time period	Non-pharmacological methods vs. Not diagnosed	1.5	0.4	5.3	0.55
	Pharmacological methods vs. Not diagnosed	0.7	0.4	1.1	0.11
Satisfaction with the father of the child*	Very satisfied vs. No relationship	1.3	0.5	3.3	0.63
	Not very satisfied vs. No relationship	0.9	0.4	2.2	0.87
Employment status*	Yes vs. No	0.6	0.4	1.0	0.06
Family Income	≥\$40,000/year vs. <\$40,000/ year	0.7	0.4	1.3	0.28
Education status*	Some postsecondary vs. Less than postsecondary	0.6	0.3	1.2	0.15
Marital status	Common law/ Married vs. Single/ Divorced/ Separated	0.9	0.4	1.6	0.64
Gravida status	Multigravida vs. Primigravida	0.9	0.5	1.6	0.76
Exercise	Yes vs. no	0.8	0.4	1.4	0.37
Smoking*	Quit vs. Never	0.8	0.1	5.4	0.82
	Smoke vs. Never	1.2	0.6	2.2	0.66
Drug abuse	Drug use/Quit vs. Never	0.8	0.2	2.9	0.78
Alcohol use	Yes vs. No	1.2	0.6	2.3	0.56
Anxiety scores	Continuous	1.1	1.0	1.3	0.01
Depression	Yes vs. No	0.9	0.4	2.0	0.87

*Unadjusted association (p<0.2)

T1 – Early pregnancy, T2 – Late pregnancy, T3 – Early postpartum, T4 – Three year after birth

6.8.3 Appendix 6-A – Table 3: Unadjusted analysis of high scores for anxious/depressed behaviour ($\geq 93^{\text{rd}}$ percentile).

Covariates considered in unadjusted analysis of anxious/depressed using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Family history of perinatal depression*	Yes vs. No	1.5	1.0	2.3	0.08
	Don't know vs. No	2.7	1.4	4.9	0.00
Previous history of depression	Yes vs. No	1.8	1.2	2.7	0.01
Education level	Some postsecondary vs. Less than postsecondary	0.5	0.3	0.9	0.03
Employment status	Yes vs. No	1.2	0.7	2.1	0.54
Planned pregnancy	Yes vs. No	0.9	0.5	1.6	0.78
Mothers' age cat	25-34 vs. <25	0.8	0.4	1.6	0.55
	≥ 35 vs. <25	0.8	0.3	1.7	0.52
Mothers' ethnicity	Caucasian vs. Non-Caucasian	1.5	0.7	3.4	0.33
	Married/Common Law vs. Single/Divorced	0.5	0.2	1.2	0.11
EARLY AND LATE PREGNANCY MEASURES (T1 & T2)					
Satisfaction with the father of the child at T1	Very satisfied vs. No relationship	1.8	0.4	9.3	0.48
	Not very satisfied vs. No relationship	2.5	0.6	10.9	0.23
Satisfaction with the father of the child at T2*	Very satisfied vs. No relationship	1.3	0.3	5.1	0.67
	Not very satisfied vs. No relationship	1.7	0.5	5.6	0.41
Exercise at T1	Yes vs. No	0.7	0.4	1.3	0.33
Exercise at T2*	Yes vs. No	0.7	0.4	1.3	0.25
Smoking at T1	Quit vs. Never	1.1	0.7	1.8	0.67
	Smoke vs. Never	1.0	0.4	2.3	0.97
Smoking at T2*	Quit vs. Never	0.8	0.4	1.6	0.48
	Smoke vs. Never	1.0	0.5	2.3	0.97
Drug use at T1	Quit vs. Never	0.7	0.4	1.3	0.27
	Drug use vs. Never	1.0	0.2	4.6	0.96
Drug use at T2	Quit vs. Never	1.3	0.4	4.1	0.71
	Drug use vs. Never	2.8	0.2	49.3	0.49
Alcohol at T1	Quite vs. Never	1.1	0.7	1.7	0.69
	Drink vs. Never	1.1	0.5	2.8	0.80
Alcohol at T2	Quit vs. Never	1.6	1.0	2.6	0.07
	Drink vs. Never	1.3	0.6	3.0	0.52
Family Income at T1	$\geq \$40,000/\text{year}$ vs. $< \$40,000/\text{year}$	1.0	0.6	1.6	0.93
Physical abuse at T1	Yes vs. No	1.3	0.8	2.0	0.25
Physical abuse at T2	Yes vs. No	1.6	0.5	5.1	0.38
Overall health of the mother at T1	Poor/Fair/Okay vs. Excellent/Very good/Good	0.5	0.2	1.4	0.19

Covariates considered in unadjusted analysis of anxious/depressed using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Overall health of the mother at T2	Poor/Fair/Okay vs. Excellent/Very good/Good	0.6	0.3	1.3	0.22
Cambridge worry scores at T1	Continuous	1.0	1.0	1.1	0.18
Cambridge worry scores at T2	Continuous	1.0	1.0	1.1	0.11
Stress at T1	Yes vs. No	0.9	0.4	1.7	0.69
Stress at T2	Yes vs. No	1.0	0.5	1.9	0.96
Anxiety scores at T1	Continuous	1.1	1.0	1.2	0.02
Anxiety scores at T2	Continuous	1.1	1.0	1.2	0.07
Depression at T1	Yes vs. No	1.7	0.9	3.1	0.11
Depression at T2*	Yes vs. No	1.0	0.5	2.2	0.99
Pregnancy complications	No vs. Yes	0.9	0.5	1.6	0.79
Type of birth	Assisted vs. Spontaneous	1.8	1.0	3.2	0.05
	C-section vs. Spontaneous	1.1	0.7	1.7	0.57
Gestation period*	Pre-term vs. Term	3.4	1.4	7.8	0.01
	Post-term vs. Term	6.7	1.6	27.2	0.01
Birth complications	No vs. Yes	1.1	0.7	1.6	0.67
One minute Apgar scores	≥ 7 vs. <7	0.8	0.5	1.4	0.47
Five minute Apgar scores	≥ 7 vs. <7	2.9	0.8	10.1	0.10
Neonatal complications	No vs. Yes	1.1	0.7	1.6	0.71
Birth defects	Yes vs. No	1.1	0.6	2.2	0.70
Sex of child	Female vs. Male	0.9	0.6	1.3	0.56
Weight for gestational age (WHO)	SGA vs. AGA	0.6	0.3	1.2	0.14
	LGA vs. AGA	1.0	0.6	1.7	0.98
Weight for gestational age (PHAC)	SGA vs. AGA	0.6	0.3	1.2	0.15
	LGA vs. AGA	1.2	0.6	2.1	0.61
EARLY POSTPARTUM (T3)					
Birth order ordinal	2 nd vs. 1 st	1.2	0.8	1.8	0.47
	3 rd or more vs. 1 st	0.7	0.4	1.2	0.18
Gravida status at T1	Multigravida– Primigravida	1.0	0.6	1.4	0.81
Breastfeeding initiated*	Yes vs. No	1.1	0.6	1.8	0.81
Satisfaction with the partner*	Very satisfied vs. No relationship	1.1	0.3	4.3	0.92
	Not very satisfied vs. No relationship	1.0	0.3	3.7	0.95
Exercise	Yes vs. No	1.4	0.9	2.2	0.13
Smoking*	Quit vs. Never	1.4	0.5	3.9	0.55
	Smoke vs. Never	0.9	0.4	2.1	0.86
Drug abuse	Drug use vs. Never	1.6	0.3	8.2	0.56
	Quit vs. Never	0.8	0.1	5.4	0.80
Alcohol	Quit vs. Never	3.3	1.3	8.6	0.01
	Drink vs. Never	1.0	0.7	1.5	0.96
Anxiety scores*	Continuous	1.2	1.1	1.3	0.00
Depression	Yes vs. No	2.5	1.2	5.1	0.02

Covariates considered in unadjusted analysis of anxious/depressed using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Stress	Yes vs. No	1.3	0.8	2.1	0.29
Overall health of the mother	Poor/Fair/Okay vs. Excellent/Very good/Good	1.3	0.8	2.1	0.29
THREE YEAR AFTER BIRTH (T4)					
Any subsequent pregnancy	Yes vs. No	1.1	0.8	1.7	0.51
Emotional support	Yes vs. No	0.3	0.0	1.9	0.18
Mood disorder scores	Continuous	1.0	1.0	1.0	0.06
Maternal overall health	Excellent/Very good vs. Poor/ Fair/ Okay	1.0	0.5	2.1	0.98
Child overall health	Excellent/Very good vs. Fair/Good	0.2	0.1	0.6	0.00
History of diagnosis & treatment of depression during the study time period	Non-pharmacological methods vs. Not diagnosed	8.8	2.1	36.3	0.00
	Pharmacological methods vs. Not diagnosed	1.5	0.9	2.6	0.09
Satisfaction with the father of the child*	Very satisfied vs. No relationship	2.9	1.0	8.1	0.04
	Not very satisfied vs. No relationship	1.7	0.7	4.3	0.25
Employment status*	Yes vs. No	1.1	0.7	1.9	0.59
Family Income	≥\$40,000/year vs. <\$40,000/ year	0.9	0.5	1.6	0.71
Education status*	Some postsecondary vs. Less than postsecondary	0.5	0.3	1.0	0.05
Marital status	Common law/ Married vs. Single/ Divorced/ Separated	0.8	0.4	1.5	0.49
Gravida status	Multigravida vs. Primigravida	0.9	0.5	1.5	0.62
Exercise	Yes vs. No	1.0	0.6	1.9	0.88
Smoking*	Quit vs. Never	0.4	0.0	4.9	0.46
	Smoke vs. Never	0.8	0.4	1.5	0.47
Drug abuse	Drug use/Quit vs. Never	1.1	0.3	4.0	0.90
Alcohol use	Yes vs. No	1.5	0.8	2.9	0.25
Anxiety scores	Continuous	1.3	1.2	1.4	0.00
Depression	Yes vs. No	2.2	1.0	4.7	0.05

*Unadjusted association (p<0.2)

T1 – Early pregnancy, T2 – Late pregnancy, T3 – Early postpartum, T4 – Three year after birth

6.8.4 Appendix 6-A – Table 4: Unadjusted analysis of high scores for sleep problems ($\geq 93^{\text{rd}}$ percentile).

Covariates considered in unadjusted analysis of sleep problems using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI Lower	95% CI Upper	p-value
Family history of perinatal depression*	Yes vs. No	1.7	1.1	2.7	0.01
	Don't know vs. No	2.0	1.0	3.7	0.04
Previous history of depression	Yes vs. No	1.8	1.2	2.7	0.01
Education level	Some postsecondary vs. Less than postsecondary	0.9	0.4	1.7	0.69
	Employment status	0.9	0.5	1.6	0.75
Planned pregnancy	Yes vs. No	1.1	0.6	1.9	0.76
Mothers' age cat	25-34 vs. <25	1.0	0.5	1.9	0.91
	≥ 35 vs. <25	1.3	0.6	2.8	0.58
Mothers' ethnicity	Caucasian vs. Non-Caucasian	1.1	0.5	2.4	0.77
	Marital status at enrollment	Married/Common Law vs. Single/Divorced	-0.6	-1.3	0.2
EARLY AND LATE PREGNANCY MEASURES (T1 & T2)					
Satisfaction with the father of the child at T1	Very satisfied vs. No relationship	2.8	0.6	14.4	0.21
	Not very satisfied vs. No relationship	2.4	0.5	10.2	0.25
Satisfaction with the father of the child at T2*	Very satisfied vs. No relationship	3.0	0.8	12.3	0.12
	Not very satisfied vs. No relationship	2.5	0.7	8.8	0.16
Exercise at T1	Yes vs. No	0.7	0.4	1.2	0.17
Exercise at T2*	Yes vs. No	0.9	0.5	1.7	0.80
Smoking at T1	Quit vs. Never	1.0	0.6	1.6	0.94
	Smoke vs. Never	0.8	0.3	1.8	0.53
Smoking at T2*	Quit vs. Never	0.7	0.3	1.4	0.27
	Smoke vs. Never	0.7	0.3	1.5	0.35
Drug use at T1	Quit vs. Never	1.3	0.8	2.3	0.34
	Drug use vs. Never	0.9	0.2	5.1	0.97
Drug use at T2	Quit vs. Never	2.3	0.5	12.2	0.31
	Drug use vs. Never	3.7	0.4	34.4	0.25
Alcohol at T1	Quite vs. Never	0.9	0.6	1.3	0.48
	Drink vs. Never	0.9	0.4	2.0	0.73
Alcohol at T2	Quite vs. Never	1.1	0.7	1.9	0.69
	Drink vs. Never	1.9	0.8	4.3	0.15
Family Income at T1	$\geq \$40,000/\text{year}$ vs. < $\$40,000/\text{year}$	1.1	0.7	1.7	0.74
	Physical abuse at T1	Yes vs. No	1.6	1.0	2.5
Physical abuse at T2	Yes vs. No	1.2	0.3	4.8	0.79
Overall health of the mother at T1	Poor/Fair/Okay vs. Excellent/Very good/Good	0.5	0.2	1.2	0.12

Covariates considered in unadjusted analysis of sleep problems using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI	p-value
			Lower	Upper
Overall health of the mother at T2	Poor/Fair/Okay vs. Excellent/Very good/Good	0.7	0.4	1.5
Cambridge worry scores at T1	Continuous	1.0	1.0	1.0
Cambridge worry scores at T2	Continuous	1.0	1.0	1.1
Stress at T1	Yes vs. No	1.1	0.6	2.2
Stress at T2	Yes vs. No	1.3	0.7	2.4
Anxiety scores at T1	Continuous	1.1	1.0	1.2
Anxiety scores at T2	Continuous	1.1	1.0	1.2
Depression at T1	Yes vs. No	1.8	0.9	3.3
Depression at T2*	Yes vs. No	1.7	0.8	3.6
Pregnancy complications	No vs. Yes	1.1	0.6	1.8
Type of birth	Assisted vs. Spontaneous	3.0	1.6	5.6
	C-section vs. Spontaneous	1.1	0.7	1.7
Gestation period*	Pre-term vs. Term	1.6	0.7	3.7
	Post-term vs. Term	3.6	0.9	15.5
Birth complications	No vs. Yes	0.9	0.6	1.3
One minute Apgar scores	≥ 7 vs. <7	0.9	0.5	1.6
Five minute Apgar scores	≥ 7 vs. <7	1.1	0.3	4.0
Neonatal complications	No vs. Yes	0.9	0.6	1.3
Birth defects	Yes vs. No	1.5	0.8	2.7
Sex of child	Female vs. Male	1.0	0.7	1.4
Weight for gestational age (WHO)	SGA vs. AGA	0.8	0.4	1.7
	LGA vs. AGA	1.0	0.6	1.7
Weight for gestational age (PHAC)	SGA vs. AGA	0.7	0.3	1.3
	LGA vs. AGA	0.9	0.5	1.7
EARLY POSTPARTUM (T3)				
Birth order ordinal	2 nd vs. 1 st	0.8	0.5	1.3
	3 rd or more vs. 1 st	0.6	0.4	1.0
Gravida status at T1	Multigravida vs. Primigravida	0.7	0.5	1.1
Breastfeeding initiated*	Yes vs. No	1.7	1.0	2.8
	Very satisfied vs.	1.2	0.3	4.5
Satisfaction with the partner*	No relationship			
	Not very satisfied vs.	1.3	0.4	4.5
	No relationship			
Exercise	Yes vs. No	0.9	0.6	1.3
Smoking*	Quit vs. Never	1.5	0.5	4.6
	Smoke vs. Never	0.7	0.3	1.6
Drug abuse	Drug use vs. Never	2.3	0.5	12.2
	Quit vs. Never	3.7	0.4	34.4
Alcohol	Quit vs. Never	1.5	0.6	3.8
	Drink vs. Never	1.0	0.7	1.6
Anxiety scores*	Continuous	1.1	1.0	1.2

Covariates considered in unadjusted analysis of sleep problems using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI Lower	95% CI Upper	p-value
Depression	Yes vs. No	3.6	1.7	7.6	0.00
Stress	Yes vs. No	1.2	0.8	2.0	0.38
Overall health of the mother	Poor/Fair/Okay vs. Excellent/Very good/Good	0.6	0.3	1.4	0.23
THREE YEAR AFTER BIRTH (T4)					
Any subsequent pregnancy	Yes vs. No	1.2	0.8	1.7	0.37
Emotional support	Yes vs. No	0.3	0.1	1.7	0.19
Mood disorder scores	Continuous	1.0	1.0	1.1	0.01
Maternal overall health	Excellent/Very good vs. Poor/ Fair/ Okay	0.6	0.3	1.1	0.12
Child overall health	Excellent/Very good vs. Fair/Good	0.2	0.1	0.5	0.00
History of diagnosis & treatment of depression during the study time period	Non-pharmacological methods vs. Not diagnosed	0.5	0.1	2.5	0.42
	Pharmacological methods vs. Not diagnosed	1.6	1.0	2.8	0.07
Satisfaction with the father of the child*	Very satisfied vs. No relationship	2.2	0.8	5.8	0.11
	Not very satisfied vs. No relationship	1.3	0.5	3.0	0.57
Employment status*	Yes vs. No	0.9	0.6	1.5	0.80
Family Income	≥\$40,000/year vs. <\$40,000/ year	1.0	0.5	1.8	0.94
Education status*	Some postsecondary vs. Less than postsecondary	0.9	0.5	1.9	0.86
Marital status	Common law/ Married vs. Single/ Divorced/ Separated	0.6	0.3	1.2	0.16
Gravida status	Multigravida vs. Primigravida	0.7	0.4	1.2	0.24
Exercise	Yes vs. No	0.7	0.4	1.2	0.20
Smoking*	Quit vs. Never	1.2	0.2	6.8	0.81
	Smoke vs. Never	0.8	0.4	1.6	0.58
Drug abuse	Drug use/Quit vs. Never	0.8	0.2	3.4	0.80
Alcohol use	Yes vs. No	1.3	0.7	2.5	0.47
Anxiety scores	Continuous	1.2	1.0	1.3	0.01
Depression	Yes vs. No	2.7	1.2	6.0	0.02

*Unadjusted association (p<0.2)

T1 – Early pregnancy, T2 – Late pregnancy, T3 – Early postpartum, T4 – Three year after birth

6.8.5 Appendix 6-A – Table 5: Odds ratios, p-values and 95% confidence limits for the predictors (with proportional odds assumption was not true) of children with high scores for sleep problems ($\geq 93^{\text{rd}}$ percentile) at three years of age.

Table 5: Odds ratios, p-values and 95% confidence limits for the predictors (with proportional odds assumption was not true) of children with high scores for sleep problems ($\geq 93^{\text{rd}}$ percentile) at three years of age.

Variables		Odds ratio	95% CI		p-value
			Lower	Upper	
Estimates for sleep category 4 vs. category 0, 1, 2, and 3					
Family history of perinatal depression	Yes vs. No	2.7	1.4	5.2	0.002
	Don't know vs. No	1.6	0.7	3.8	0.23
Physical abuse at T1	Yes vs. No	1.7	0.9	3.2	0.09
Type of birth	Assisted vs. Spontaneous	2.6	1.1	5.9	0.02
	C-section vs. Spontaneous	1.8	1.0	3.1	0.04
Breastfeeding initiated	Yes vs. No	2.5	1.2	4.8	0.009
Child's overall health at three years of age	Excellent/good vs. Poor/Fair	3.94e-07	0	0	0.97
Estimates for sleep category 4 & 3 vs. category 0, 1, and 2,					
Family history of perinatal depression	Yes vs. No	1.9	1.1	3.4	0.03
	Don't know vs. No	2.1	0.9	4.6	0.07
Physical abuse at T1	Yes vs. No	1.2	0.6	2.1	0.62
Type of birth	Assisted vs. Spontaneous	3.6	1.7	7.6	0.001
	C-section vs. Spontaneous	1.2	0.7	2.1	0.51
Breastfeeding initiated	Yes vs. No	4.8	2.1	10.7	<0.0001
Child's overall health at three years of age	Excellent/good vs. Poor/Fair	0.2	0.1	0.6	0.003
Estimates for sleep category 4, 3 & 2 vs. category 0 & 1					
Family history of perinatal depression	Yes vs. No	1.1	0.6	2.2	0.72
	Don't know vs. No	1.3	0.5	3.3	0.58
Physical abuse at T1	Yes vs. No	1.3	0.7	2.5	0.42
Type of birth	Assisted vs. Spontaneous	3.2	1.5	7.1	0.004
	C-section vs. Spontaneous	1.4	0.8	2.7	0.27
Breastfeeding initiated	Yes vs. No	6.0	2.1	17.0	0.001
Child's overall health at three years of age	Excellent/good vs. Poor/Fair	0.5	0.2	1.5	0.22
Estimates for sleep category 4, 3, 2, 1 vs. category 0					
Family history of perinatal depression	Yes vs. No	1.4	0.5	3.8	0.50
	Don't know vs. No	9.3	2.9	30	<0.0001
Physical abuse at T1	Yes vs. No	5.0	1.8	13.5	0.002
Type of birth	Assisted vs. Spontaneous	16.7	5.6	49.6	<0.0001
	C-section vs. Spontaneous	1.1	0.4	2.8	0.81
Breastfeeding initiated	Yes vs. No	1.1	0.3	4.2	0.87
Child's overall health at three years of age	Excellent/good vs. Poor/Fair	0.1	0.0	0.2	<0.0001

6.8.6 Appendix 6-A – Table 6: Unadjusted analysis of high scores for withdrawn behaviour ($\geq 93^{\text{rd}}$ percentile).

Covariates considered in unadjusted analysis of withdrawn behaviour using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Family history of perinatal depression*	Yes vs. No	1.4	0.9	2.2	0.20
	Don't know vs. No	1.0	0.5	1.9	0.95
Previous history of depression	Yes vs. No	0.9	0.6	1.4	0.79
Education level	Some postsecondary vs. Less than postsecondary	1.3	0.6	2.6	0.50
Employment status	Yes vs. No	1.1	0.6	2.0	0.70
Planned pregnancy	Yes vs. No	0.8	0.4	1.4	0.38
Mothers' age cat	25-34 vs. <25	1.4	0.7	2.6	0.38
	≥ 35 vs. <25	0.9	0.4	2.0	0.79
Mothers' ethnicity	Caucasian vs. Non-Caucasian	1.5	0.6	3.6	0.35
	Married/Common Law vs. Single/Divorced	0.7	0.3	1.6	0.42
EALY AND LATE PREGNANCY MEASURES (T1 & T2)					
Satisfaction with the father of the child at T1	Very satisfied vs. No relationship	0.4	0.1	1.8	0.24
	Not very satisfied vs. No relationship	0.7	0.2	2.6	0.62
Satisfaction with the father of the child at T2*	Very satisfied vs. No relationship	1.6	0.4	6.5	0.51
	Not very satisfied vs. No relationship	1.5	0.4	5.2	0.55
Exercise at T1	Yes vs. No	1.2	0.6	2.2	0.57
Exercise at T2*	Yes vs. No	1.2	0.6	2.2	0.64
Smoking at T1	Quit vs. Never	1.0	0.6	1.6	0.84
	Smoke vs. Never	1.0	0.4	2.4	0.93
Smoking at T2*	Quit vs. Never	1.0	0.5	2.1	0.99
	Smoke vs. Never	1.0	0.4	2.3	0.98
Drug use at T1	Quit vs. Never	0.7	0.4	1.3	0.27
	Drug use vs. Never	1.2	0.2	5.9	0.84
Drug use at T2	Drug use/Quit vs. Never	1.0	0.3	4.0	0.96
Alcohol at T1	Quite vs. Never	1.1	0.7	1.8	0.58
	Drink vs. Never	2.2	0.9	5.4	0.09
Alcohol at T2	Quit vs. Never	1.5	0.9	2.5	0.16
	Drink vs. Never	1.5	0.6	3.4	0.36
Family Income at T1	$\geq \$40,000/\text{year}$ vs. $<\$40,000/\text{year}$	0.8	0.5	1.3	0.31
Physical abuse at T1	Yes vs. No	1.0	0.6	1.5	0.86
Physical abuse at T2	Yes vs. No	0.8	0.2	3.0	0.77
Overall health of the mother at T1	Poor/Fair/Okay vs. Excellent/Very good/Good	0.5	0.2	1.3	0.17

Covariates considered in unadjusted analysis of withdrawn behaviour using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Overall health of the mother at T2	Poor/Fair/Okay vs. Excellent/Very good/Good	1.1	0.5	2.3	0.82
Cambridge worry scores at T1	Continuous	1.0	1.0	1.1	0.07
Cambridge worry scores at T2	Continuous	1.0	1.0	1.1	0.06
Stress at T1	Yes vs. No	1.2	0.6	2.5	0.53
Stress at T2	Yes vs. No	1.6	0.8	3.2	0.16
Anxiety scores at T1	Continuous	1.1	1.0	1.2	0.18
Anxiety scores at T2	Continuous	1.1	1.0	1.2	0.19
Depression at T1	Yes vs. No	0.7	0.4	1.4	0.36
Depression at T2*	Yes vs. No	1.0	0.4	2.4	0.96
Pregnancy complications	No vs. Yes	1.1	0.6	2.0	0.67
Type of birth	Assisted vs. Spontaneous	1.2	0.6	2.1	0.61
	C-section vs. Spontaneous	0.9	0.6	1.4	0.60
Gestation period*	Pre-term vs. Term	1.6	0.7	3.5	0.29
	Post-term vs. Term	0.5	0.1	2.9	0.42
Birth complications	No vs. Yes	1.2	0.8	1.7	0.45
One minute Apgar scores	≥ 7 vs. <7	0.7	0.4	1.2	0.22
Five minute Apgar scores	≥ 7 vs. <7	1.2	0.3	4.4	0.80
Neonatal complications	No vs. Yes	0.9	0.6	1.4	0.65
Birth defects	Yes vs. No	1.1	0.6	2.0	0.86
Sex of child	Female vs. Male	0.9	0.6	1.3	0.53
Weight for gestational age (WHO)	SGA vs. AGA	0.2	1.3		0.26
	LGA vs. AGA	1.2	0.7	2.0	0.56
Weight for gestational age (PHAC)	SGA vs. AGA	0.6	0.3	1.3	0.19
	LGA vs. AGA	0.9	0.5	1.7	0.75
EARLY POSTPARTUM (T3)					
Birth order ordinal	2 nd vs. 1 st	2.0	1.2	3.1	0.00
	3 rd or more vs. 1 st	1.0	0.6	1.6	0.89
Gravida status at T1	Multigravida vs. Primigravida	1.5	1.0	2.2	0.06
Breastfeeding initiated*	Yes vs. No	1.3	0.7	2.2	0.41
	Very satisfied vs. No relationship	1.6	0.3	7.4	0.55
Satisfaction with the partner*	Not very satisfied vs. No relationship	1.9	0.5	7.7	0.38
Exercise	Yes vs. No	0.8	0.5	1.3	0.44
Smoking*	Quit vs. Never	0.4	0.1	1.8	0.25
	Smoke vs. Never	0.8	0.4	1.9	0.67
Drug abuse	Drug use vs. Never	0.7	0.1	4.1	0.68
	Quit vs. Never	3.6	0.5	24.3	0.19
Alcohol	Quit vs. Never	0.7	0.2	1.9	0.47
	Drink vs. Never	1.0	0.7	1.6	0.87
Anxiety scores*	Continuous	1.1	1.0	1.2	0.18

Covariates considered in unadjusted analysis of withdrawn behaviour using ordinal regression (n= 338)	Variable category	Odds ratio	95% CI		p-value
			Lower	Upper	
Depression	Yes vs. No	1.3	0.6	2.9	0.54
Stress	Yes vs. No	1.6	1.0	2.7	0.06
Overall health of the mother	Poor/Fair/Okay vs. Excellent/Very good/Good	1.4	0.6	3.3	0.46
THREE YEAR AFTER BIRTH (T4)					
Any subsequent pregnancy	Yes vs. No	1.1	0.7	1.6	0.62
Emotional support	Yes vs. No	1.5	0.1	18.2	0.76
Mood disorder scores	Continuous	1.0	1.0	1.0	0.07
Maternal overall health	Excellent/Very good vs. Poor/ Fair/ Okay	1.3	0.6	2.9	0.50
Child overall health	Excellent/Very good vs. Fair/Good	0.7	0.3	1.6	0.36
History of diagnosis & treatment of depression during the study time period	Non-pharmacological methods vs. Not diagnosed	0.8	0.2	3.7	0.79
	Pharmacological methods vs. Not diagnosed	0.7	0.4	1.1	0.14
Satisfaction with the father of the child*	Very satisfied vs. No relationship	1.8	0.6	5.3	0.27
	Not very satisfied vs. No relationship	1.8	0.7	4.7	0.21
Employment status*	Yes vs. No	1.1	0.7	1.9	0.67
Family Income	≥\$40,000/year vs. <\$40,000/ year	0.9	0.5	1.6	0.61
Education status*	Some postsecondary vs. Less than postsecondary	0.9	0.5	1.9	0.86
Marital status	Common law/ Married vs. Single/ Divorced/ Separated	0.7	0.3	1.4	0.30
Gravida status	Multigravida vs. Primigravida	1.1	0.6	2.0	0.72
Exercise	Yes vs. No	0.8	0.5	1.5	0.50
Smoking*	Quit vs. Never	5.5	0.4	68.4	0.18
	Smoke vs. Never	0.9	0.5	1.8	0.82
Drug abuse	Drug use/Quit vs. Never	3.0	0.6	15.2	0.18
Alcohol use	Yes vs. No	1.4	0.7	2.8	0.39
Anxiety scores	Continuous	1.1	1.0	1.3	0.04
Depression	Yes vs. No	0.8	0.3	1.9	0.60

*Unadjusted association (p<0.2)

T1 – Early pregnancy, T2 – Late pregnancy, T3 – Early postpartum, T4 – Three years after birth

CHAPTER 7: CONCLUSION AND POLICY IMPLICATIONS

7.1 Overview of thesis objectives

The primary goal of this study was to examine the course of depression and anxiety scores in women from early pregnancy to three years postpartum and to identify predictors of depression and anxiety scores across this period. The secondary goal was to examine the role of maternal mental health and high-risk behaviours, as well as other important socio-demographic factors, on early childhood physical, cognitive, personal-social, and emotional-behavioural development at three years of age. Based on previous analysis of the first three rounds of data collected from the Feelings in Pregnancy (FIP) study, policy recommendations for perinatal screening of depression and anxiety and improved support services to the mothers have been made to the Government of Saskatchewan ([Bruce et al., 2012](#)). The present study supports the previous recommendations and extends this initial analysis by further examining the long-term impacts on the mother and her child. This analysis identifies both significant predictors and the most sensitive time periods during and after pregnancy to be targeted when designing and implementing interventions to prevent long-term sequelae for maternal mental health and child development.

7.2 Maternal depression and anxiety

The long-term effects of maternal depression are widely recognized. Some Canadian jurisdictions have developed guidelines and recommendations for screening and prevention of perinatal and postpartum depression, as well as for follow-up of mothers who screen positive for depression ([BCRMHP, 2006](#); [Bowen, 2010](#); [Bruce et al., 2012](#); [Glauser et al., 2016](#); [Hull, 2007](#)). However, there is need to develop national recommendations and guidelines for the screening and treatment of both perinatal depression and anxiety ([Haran et al., 2014](#)).

We examined the time course of depression and anxiety in mothers during pregnancy through to three years after birth. Across the study population, maternal depression and anxiety scores declined over the study time points. Pre-pregnancy maternal mental health was a significant predictor of both longitudinal depression and anxiety scores (Figure 7-1). Stress at T3 (early postpartum period) and affective lability (mood disorder) scores at T4 were associated with higher longitudinal depression and anxiety scores in the study (Figure 7-1). However, the effects of a previous history of depression on longitudinal depression and anxiety scores varied with study time points as well as with stress experienced by the mother during early pregnancy (T1).

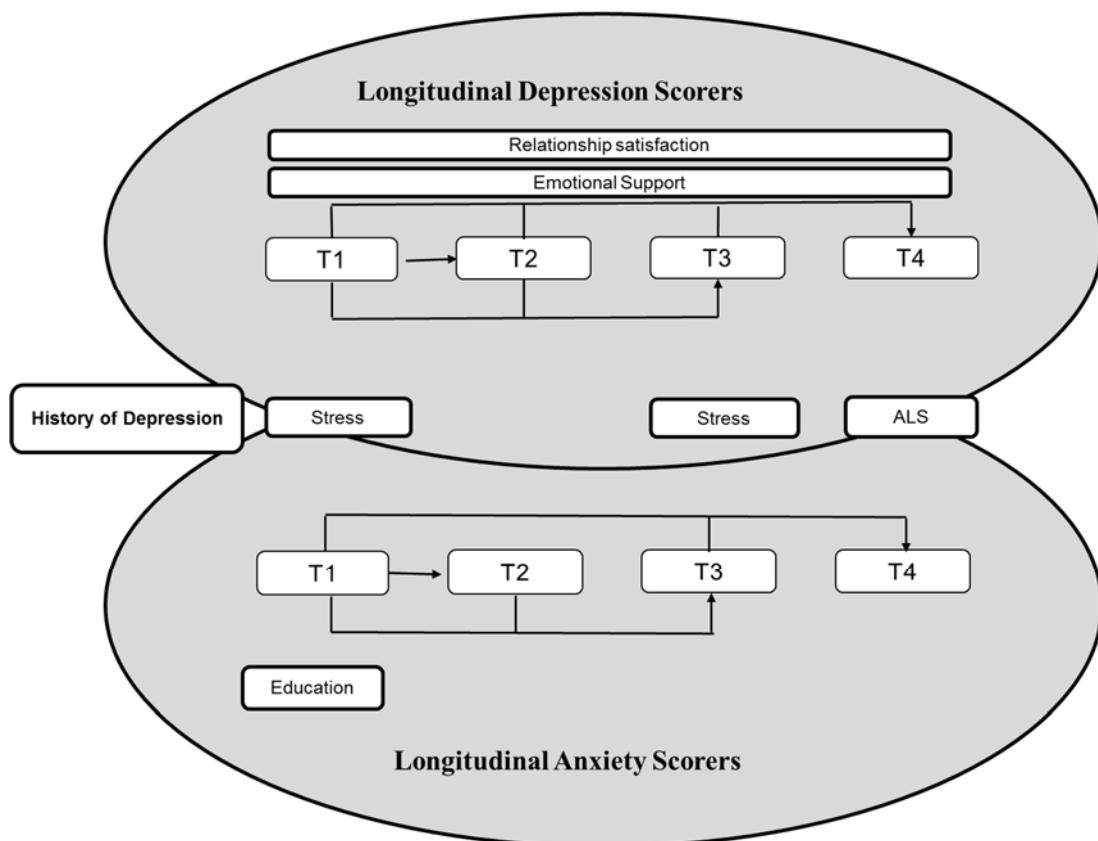


Figure 7-1: Predictors of depression and anxiety from early pregnancy to three years after childbirth. Arrows represent time points that significantly predict subsequent depression or anxiety scores. T1 – Early pregnancy, T2 – Late pregnancy, T3 – Early postpartum, T4 – Three years after childbirth. ALS – Affective lability scores measuring mood disorders in the mothers.

Mothers with the previous history of depression had significantly higher depression and anxiety scores during early pregnancy (T1) and three years after childbirth (T4) as compared to mothers with no history of depression. For mothers who reported being stressed at T1, the previous history of depression significantly increased the average depression and anxiety scores over the study time points as compared to mothers with no previous history of depression. Whereas, for mothers who did not report being stressed at T1, the previous history of depression had no significant effects on the depression and anxiety scores over the study time points. Stress at T1 (early pregnancy) was a partial mediator and moderator with respect to the effects of the history of depression on anxiety scores over time. However, stress at T1 (early pregnancy) was only a moderator (not a mediator) with respect to the effects of the history of depression on depression scores over time.

The presence of emotional support in all stages of pregnancy and after birth significantly and consistently lowered the average depression scores by more than three points and having a not very satisfactory relationship with the father of the child as compared to no relationship significantly increased the depression scores over the study time points (Figure 7-1). Different from the longitudinal depression scores, having some post-secondary education at T1 (early pregnancy) lowered the average longitudinal anxiety scores.

To the best of our knowledge, this is the one of the kind study to use lagged variable analysis to study the effects of previous depression and anxiety scores on the subsequent depression and anxiety scores at all study time points using linear regression ([Rabe-Hesketh & Skrondal, 2012](#)). These models are sometimes called ‘transitional models’([Rabe-Hesketh & Skrondal, 2012](#)). After considering both prior depression and anxiety scores lagged depression scores were the only significant predictor of subsequent depression scores. This suggested that

previous depression scores were a more important predictor of subsequent depression scores as compared to previous anxiety scores. Both anxiety scores at T3 and depression scores at T1 were, however, significant predictors of anxiety scores- three years after childbirth (T4). Whereas for late pregnancy (T2) and early postpartum (T3) anxiety scores, only previous anxiety scores remained as the significant predictors. The critical finding from this analysis was that depression scores in early pregnancy were significant predictors for both depression and anxiety scores at three years of age in mothers.

7.3 Early childhood development

Academic and financial success in adult life has been linked with early childhood development ([Victora et al., 2008](#)). Interventions before age three have been shown to be more effective than later remediation for addressing developmental delays ([Karoly et al., 2006](#)). The ‘first 1,000 days’ (conception through to 24 months of age) provide opportunities for interventions during sensitive windows to minimize early threats and lifelong consequences ([Doyle et al., 2009](#)).

7.3.1 Physical, cognitive, and personal-social development of the children

Gross motor and fine motor skills measure the physical development of the child. Gross motor skills (walking, crawling, and balance) employ large muscle groups whereas fine motor skills (writing, drawing, playing an instrument) employ the use of small muscles ([Bosma et al., 2000](#)). Gross motor skills develop before the fine motor skills ([Berk, 2003](#); [Cools et al., 2009](#)). Cognitive skills include thinking, reading, learning, remembering, reasoning, and paying attention ([Dyer, 2002](#); [Oakley, 2004](#)). These skills help us to develop critical thinking and to understand cause and effect ([Oakley, 2004](#)). Cognitive skill development is believed to be partly inherited but mostly learned, and thus it can be improved with practice and training ([Campbell et](#)

[al., 2001](#)). Personal - social development is about how children learn the life skills necessary to take care of themselves and develop healthy social networks and relationships ([Bee, 1985](#)). The physical, cognitive, and personal-social development of children at three years of age was measured by Ages and Stages Questionnaire (ASQ®) ([Squires et al., 2009](#)).

We examined the determinants of the physical, cognitive, personal-social, emotional, and behavioural development of children at three years of age. The only maternal mental health measure associated with physical development was early postpartum depression (Figure 7-2). The sex of the child and postpartum influences such as breastfeeding, early postpartum (T3) depression, and having some relationship with the father of the child at T4 were associated with physical development scores (Figure 7-2). Female children performed better at attaining high fine motor skills at three years of age as compared to male children.

None of the maternal mental health measures in this study was significantly associated with the cognitive development (Figure 7-2). Child factors (one minute Apgar scores, weight for gestation age) and breastfeeding were associated with communication skills, and birth order and gestation period were associated with problem-solving skills. Type of birth was a mediator for birth order, and neonatal complications were mediators for gestation period in predicting problem-solving skills at three years of age (Figure 7-2). Late pregnancy smoking and drug use were confounders with respect to the gestation period in predicting the higher problem-solving skill scores.

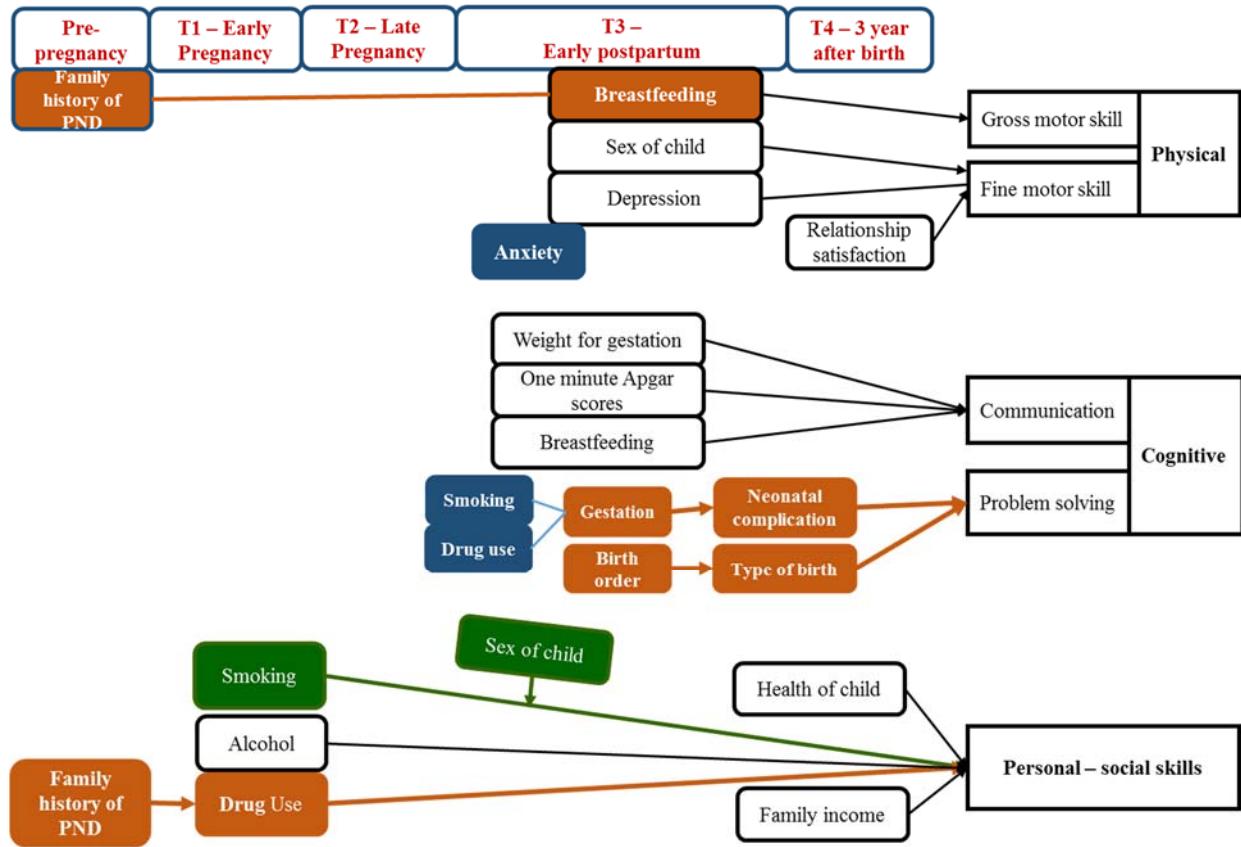


Figure 7-2: Predictors of physical, cognitive, and personal – social skills of children at three years of age. Orange represents the mediation effects in the model, green represents interaction effects, blue represents the confounders, and black represents significant predictors.

Family history of perinatal depression and alcohol consumption in early pregnancy (T1) both decreased the odds of high scores for personal-social skills (Figure 7-2). Drug use in early pregnancy mediated the effects of family history of perinatal depression, suggesting that transgenerational effects of postpartum depression were mediated through maternal high-risk behaviours.

High family income and good overall health of the child were associated with higher personal-social skills after controlling for family history of perinatal depression, prenatal exposure to alcohol and smoking. Female children were found to be resilient to the effects of

prenatal smoking and had better odds of higher personal-social development scores as compared to the male children (Figure 7-2).

Along with the pregnancy and postpartum period, the pre-pregnancy period was also associated with the physical and personal-social development of children at three years of age. However, for cognitive development, the post pregnancy period was the most sensitive time period (Figure 7-2). In our study, maternal prenatal high-risk behaviours (smoking, alcohol, drug use), pregnancy outcomes (weight for gestation, Apgar scores, gestation period), and maternal early postpartum depression were associated with lower odds of high physical, cognitive, and personal-social skill development. Thus, mother- and child-oriented programs that decrease child poverty, improve nutrition and the health of the baby, and help the mother refrain from high-risk behaviours could help improve the long-term cognitive and personal-social development of children born into higher risk environments.

7.3.2 Emotional and behavioural development of children at three years of age

Five syndrome scales of the Child Behaviour Checklist (CBCL) (1.5–5 years) developed through Item Factor Analysis (IFA) were used to measure aggression, attention problems, anxiety/depression, sleep problems, and withdrawn behaviour at the fourth time point of the study ([Achenbach & Rescorla, 2000](#)). To our knowledge this is the first study to use IFA to examine the factor analytic structure of CBCL (1.5 – 5 years) among three-year-old Canadian children and measure the reliability of the syndrome scales using factor loadings (FL), thresholds (t), item characteristic curves (ICCs) and item information curves (ICs). Despite the loss of the syndrome scales for emotionally reactive and somatic problems, we were able to establish the second-order correlated factor structure of the model and use it to identify the predictors of the emotional and behavioural development of children at three years of age.

Most of the literature on emotional and behavioural development focuses on the determinants of internalizing and externalizing behaviour among preschoolers and early childhood ([Carneiro et al., 2016](#); [Connell & Goodman, 2002](#); [Liu et al., 2013](#); [Slemming et al., 2010](#); [Stene-Larsen et al., 2009](#); [Wright et al., 1999](#)). Except for aggression, all the remaining syndromes of anxiety, sleep problems, withdrawn behaviour, and attention deficit were observed to be largely underreported in the literature. Emotional development and social competence begin in infancy and emotions of joy, anger, sadness, and fear are first to develop. Emotional development and social competency are important for a child to adapt to school and form relationships ([Cassidy & Shaver, 1999](#); [Collins, 1999](#); [Dunn, 1993](#)). Physical reactions, including stomach aches and changes in breathing, are typical emotional responses of children in infancy and early childhood ([Kenardy et al., 2010](#); [Saarni, 2008](#)). However, as they become more aware of their feelings their emotional responses become more complex. Parent-child interactions, family culture, and child temperament rooted in biological makeup guide the development of emotions and behaviour ([Denham et al., 2003](#)).

Our study examined the determinants of specific syndromes of emotional, and behavioural development at three years of age and explored the role of maternal mental health, maternal high-risk behaviours, and pregnancy outcome factors, on specific syndromes of anxiety/depression, sleep problems, withdrawn behaviour, aggression and attention problems at three years of age (Figure 7-3).

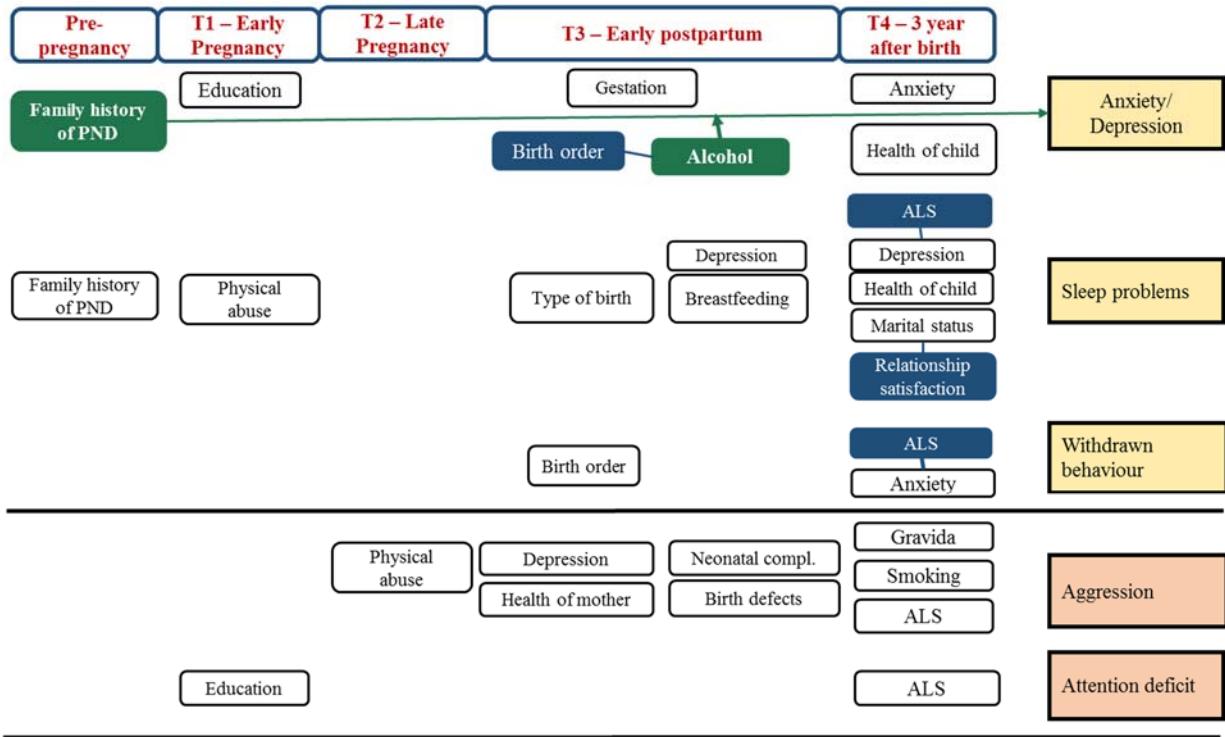


Figure 7-3: Predictors of emotional and behavioural development of children at three years of age. Green represents interaction effects, blue represents the confounders, and black represents significant predictors.

Along with the pregnancy and postpartum period, the pre-pregnancy period was also associated with the emotional and behavioural development of the child at three years of age. Pre-pregnancy family history of perinatal depression was associated with higher odds of anxiety/ depression and sleep problems (Figure 7-3). Further maternal alcohol consumption in the early postpartum period moderated the effects of family history of perinatal depression in increasing the odds of higher of anxiety/ depression scores at three years of age (Figure 7-3).

During pregnancy, rather than maternal mental health and high-risk behaviours, socio-demographic factors were significantly associated with the emotional and behavioural development of the child at three years of age. Mother's education had a protective role in preventing the higher odds of anxiety/depression and attention deficit problems, and physical

abuse increased the odds of sleep problems and aggressive behaviours in children at three years of age.

Similarly, during the early postpartum period, mostly pregnancy outcome factors of pre-term or post-term pregnancy, assisted or Caesarean section births, the presence of birth defects and neonatal complications were associated with higher odds of emotional and behavioural problems (Figure 7-3). However, maternal depression was associated with high sleep problems and aggression behaviour scores at three years of age.

At three years after childbirth, maternal mental health factors including depression, anxiety, and affective lability were associated with emotional and behavioural development in children at three years of age. Along with maternal mental health, maternal socio-demographic factors of marital status, gravida status, smoking, perceived health of the child, and relationship satisfaction levels were also associated with the emotional and behavioural development of the child at three years of age (Figure 7-3).

Thus, in our study post-pregnancy maternal mental health (depression, anxiety, and affective lability) and maternal high-risk behaviours (smoking and alcohol consumption) were associated with lower odds of attaining higher behavioural development scores in children at three years of age. However prenatal mental health and high-risk behaviours had no significant direct effect on the emotional and behavioural development in children at three years of age (Figure 7-3).

7.4 Summary of the long-term implications of maternal depression and anxiety

Overall maternal depression and anxiety scores showed a decline from early pregnancy to three years after birth (T1 to T4). Maternal history of depression, stress, and affective lability scores were significant predictors of both longitudinal depression and anxiety scores. The study

also provided evidence that the previous depression and anxiety scores predict subsequent depression and anxiety scores.

In this study cohort, prenatal (T1 and T2) maternal mental health factors (depression, anxiety, stress) did not have any significant effects on the physical, cognitive, personal-social, emotional, and behavioural development of the child at three years of age. However, several measures of maternal mental health measured after pregnancy were associated with early childhood development. Early postpartum (T3) depression was a significant predictor of fine motor skills and aggressive behaviours at three years of age. Maternal depression three years after birth was also a significant predictor of sleep problems in these children, while maternal anxiety at three years after birth was a significant predictor of early childhood anxiety/depression and withdrawn behaviours. Finally, affective lability scores in the mothers at three years after birth were significant predictors of childhood aggression and attention deficit behaviours at three years.

Maternal high-risk behaviours (smoking, alcohol consumption, and drug use), independently and in association with the maternal family history of perinatal depression were associated with early childhood development. Maternal smoking three years after the birth of the baby was also a significant predictor of aggression in children at three years of age (Figure 7-3). Prenatal drug use mediated the effects of family history of perinatal depression in predicting personal-social skills in children at three years of age (Figure 7-2). Similarly, alcohol use moderated the effects of family history of perinatal depression in predicting the anxiety/depression scores in children at three years of age (Figure 7-2, Figure 7-3). However, no mediation effects of maternal high-risk behaviours on maternal depression or anxiety or vice versa were observed in predicting the early childhood development scores in the study.

7.5 Contributions of this research and suggestions for future work

The analysis described in Chapter 3 represents the primary study in Canada to examine the validity of CBCL among normal three-year-old children. The chapter also contributes by using the correct terminology of IFA rather than CFA for categorical observed items and continuous latent variables. This is the first study to date, to report reliability using information scores and item difficulty scores of each item of a re-specified CBCL. CBCL is a 100-item tool to measure the emotional and behavioural development of children from 1.5 years to 5 years of age ([Achenbach & Rescorla, 2000](#)). Out of these 100 items, 77 items are divided into seven first-order subscales and two second-order subscales ([Achenbach & Rescorla, 2000](#)). Our re-specified 29 item CBCL scales includes five first-order subscales and two second-order subscales. The 29 item CBCL scale is easier to administer and the risk of missing information is lower. However, the re-specified tool needs further validation. The fifth round of FIP data (5 year) provides a unique opportunity to validate the tool for the healthy 3- to 5-year-olds in Saskatchewan, Canada.

Chapters 4 – 6 examine the role of social factors on the course of depression and anxiety in mothers and their effects on children at three years of age. Chapter 4 represents the first study identified to date in Canada to examine the longitudinal time course of depression and anxiety from prenatal period to three years after birth. One of the strengths of the study was the same two research assistants were used for all rounds of data collection which minimized the risk of bias due to measurement differences over time. The relevance of individual social factors on the course of depression and anxiety scores during and after pregnancy was explored using linear mixed models with a random intercept for the mother and exponential correlation structure to account for unequal periods between measurements. We also examined mediation effects in the multilevel data with categorical mediating and independent variables based on *a priori*

hypothesis. Another distinctive methodology used in the chapter was ‘lagged variable analysis’ to study the effects of previous depression and anxiety scores on subsequent depression and anxiety scores.

One of the initial objectives of the FIP study was to identify different trajectories of depression and anxiety scores over time. We tried using ‘traj’ command in STATA 12.0 to perform trajectory analysis for the maternal depression and anxiety scores over time ([Jones & Nagin, 2013](#); [Nagin, 1999](#)). However, there was not enough power to examine various trajectories using four data points. Future larger studies are required to identify different trajectories for depression and anxiety based on the previous history of depression and prenatal depression and anxiety scores and examine the role of the identified social factors on the each of the trajectories thus identified.

The research summarized in Chapter 5 identified resilience factors that were associated with increasing physical, cognitive, and personal-social development scores in children at three years of age. This is the first study identified to date in Canada to examine the role of social factors including maternal mental health and high-risk behaviours on attaining high early physical, cognitive, and personal-social development at three years of age. This analysis was limited to data from children above the cut-off ASQ® scores as there were insufficient numbers of children in this cohort who had ASQ® scores below the cut-off for a meaningful examination. We used proportional odds and partial proportional odds methods in developing the models. This is the first study identified to date in which more parsimonious partial proportional odds model was used instead of multinomial or logistic regression. We used the Sobel-Goodman test to measure mediation effects of previously identified risk factors on categorical dependent variables in the presence of other covariates in the model.

Previous research has shown that mothers with mental health problems tend to have higher rate of exposures to high-risk behaviours in the prenatal period ([Linares Scott et al., 2009](#)), poor mother-child relationships ([CPS, 2004b](#); [Paris et al., 2009](#)) with poor interactive playing ([Hart et al., 1998](#)); thus, resulting in poorer cognitive and personal-social development in the early childhood period ([CPS, 2004a](#); [Murray et al., 1996](#)). We evaluated the potential for moderating and confounding effects of these prenatal mental health and high-risk factors on pregnancy outcomes in predicting the development skills scores. Although our study was able to highlight the confounding, mediating, and moderating effects of some maternal prenatal and postnatal high-risk behaviours, we did not identify the effects of maternal prenatal mental health on the cognitive and personal-social development of the child at three years of age. The study results provide the impetus for future research using ‘path analysis’ to elucidate the strength and significance of proposed pathways and to inform theories of early childhood development.

Chapter 6 presents the first study identified to date in Canada to assess the determinants of aggression, attention problems, anxiety, sleep problems, and withdrawn behaviours among three-year-old children evaluated using a re-specified CBCL. Based on published recommendations, the 93rd percentile served as a cut-off to identify children with borderline/clinical behavioural disorders. Original score categories above the 93rd percentile were collapsed to obtain a manageable number of categories to perform ordinal regression. Thus, the odds of attaining the highest category scores in the model also represents the odds of being borderline/clinical for the specific syndrome.

In this study population, post-pregnancy maternal mental health and maternal high-risk behaviours were most influential for the emotional and behavioural development of the children at three years of age. Study results support the social theories of child development that focus on

the role of parents, caregivers, and other social influences on early childhood emotional and behavioural development and are an important step forward in limiting the long-term effects of maternal depression and anxiety.

We evaluated the potential mediating, moderating, and confounding effects of prenatal mental health and high-risk factors on pregnancy outcomes in predicting the emotional and behavioural development of the children at three years of age. Although we did not identify any mediating effects of maternal prenatal mental health or high-risk behaviours, post-pregnancy maternal mental health and high-risk behaviours were significant predictors of the emotional and behavioural development of the child at three years of age. The study results provide the impetus for future research using path analysis to elucidate the strength and significance of proposed pathways.

7.6 Limitations of the research

Longitudinal studies have a unique advantage in being able to detect and analyze change over time. However, attrition or loss to follow-up over time is a common drawback ([Caruana et al., 2015](#)). Our study had an attrition rate of approximately 50% for the fourth round of data collection. The low retention rate for the fourth round of data collection is one of the most important limitations of this study. Based on the analysis described in Chapter 2, mothers lost to follow-up were significantly younger, had poorer overall health, were more likely to be single or non-Caucasian, and depressed during pregnancy. The selective attrition of mothers with higher EPDS scores in pregnancy may have resulted in some loss of power to look at the effects of depression on long-term mental health in the mothers and child development outcomes. The study results can be best generalized to predominantly Caucasian mothers with above average family income, and who have some post-secondary education. Despite the limited retention rate,

we were able to examine the average change in the depression and anxiety scores over the duration of pregnancy up to three years after childbirth and examine the effects of previous depression and anxiety scores on the subsequent depression and anxiety in 333 women with singleton pregnancies.

The study relied on self-reported information on maternal overall health and maternal high-risk behaviours such as smoking, alcohol, and drug use both during and after pregnancy. Self-reported health status is the most commonly used health measure in Canada and other developed countries ([CBC, 2013](#)). The Conference Board of Canada (CBC), describes self-reported health as ‘physical, emotional, and social wellbeing’ of the individual ([CBC, 2013](#)). There is evidence that women tend to report poorer self-reported overall health as compared to men which is attributed to greater female health sensitivity ([NRCCP, 2006](#)). Self-reported health in longitudinal studies is also affected by the ‘ceiling effect’ where further improvement in health status after initial attainment of the highest level of health is un-recordable ([Benítez-Silva & Ni, 2008](#); [Gunasekara et al., 2012](#)). Similarly, small changes in the health status over time are also difficult to measure using the self-reported health ([Benítez-Silva & Ni, 2008](#); [Gunasekara et al., 2012](#)).

Changes in pregnancy and the postpartum period add to variability in the physical, psychological and emotional state of the mother which might have affected the validity of the self-reported health. Mothers may not have had a frame of reference to answer some questions objectively ([Fayers & Sprangers, 2002](#)). For example, mothers facing gestational diabetes or hypertension or severe nausea and vomiting may refer self-reported health status to her specific health problems associated with pregnancy rather than overall health status. Lastly, the

personality of the individual and socio-demographic factors like age and education can bias the self-reported health status ([Jylhä, 2009](#)).

The potential consequences of high-risk behaviours in pregnancy have been well-established. Self-reported smoking, alcohol consumption, and drug use are usually under-reported especially in pregnancy due to social desirability bias ([Patrick et al., 1994](#); [Tourangeau & Yan, 2007](#); [Yeager & Krosnick, 2010](#)). Social desirability is the tendency to over or under-report behaviours that are considered socially unacceptable ([Tourangeau, 2000](#)). There was some discrepancy observed in the number of mothers who reported having never smoked and never consumed alcohol between the first and subsequent rounds of data collection which might have affected the strength of association that were observed between maternal high-risk behaviours and early childhood development (Chapter 5 and 6) and longitudinal depression and anxiety (Chapter 4). Thus, assessments of plasma, saliva, urine, or expired air may be better suited to provide objective assessments of exposure to high-risk behaviours among pregnant women ([Patrick et al., 1994](#); [Yeager & Krosnick, 2010](#)).

One of the limitations of the findings from the Ages and Stages Questionnaire (ASQ[®]) scores (Chapter 5) was that the scores from the children below the cut-off for normal physical, cognitive, and personal – social development represented only 5% of all of the observations. Given that there was insufficient power to assess factors associated with scores below the cut-off for 343 three-year-old children, the analysis was restricted to examining risk factors for variation among children above the cut-off. Scores above the cut-off were categorized into three equal categories labelled as ‘high’, ‘intermediate’, and ‘low’ early childhood development to measure and identify predictors of highest physical, cognitive, and person-social skills. The results of the

ordinal regression models represented the odds of attaining highest one-third of scores as compared to the remaining two-thirds of the scores.

We used IFA to test the hypothesized factor structure of CBCL (1.5 – 5 years) (Chapter 3). Missing data were inconsequential for the IFA since it represented 0.02% of all the data points. The missing data had no systematic pattern across participants or items, i.e., missing data were observed across 12 different items and 12 subjects had at least one missing data point and Little's MCAR test ($\chi^2 = 84$, $p\text{-value} = 0.99$) was not significant ([Little, 1988](#)). Hence, the data were considered to be missing completely at random (MCAR), and manual imputation by median scores was chosen over the multiple imputation methods to utilize the full capacity of the Mplus program to perform IFA.

One of the challenges in analyzing the individual syndromes of emotional and behavioural development using CBCL for three-year-children in Chapter 6 was the non-normal score distribution for individual syndromes of aggression, attention problems, anxiety/depression, sleep problems, and withdrawn behaviour. Thus, the outcome scores were retained as ordinal variables for analysis and the variables were categorized by collapsing all the categories above the proposed cut-off of 93rd percentile (for diagnosing borderline/clinical cases). This was done to obtain a manageable number of categories for the outcome variables for ordinal regression. Thus, the original dependent variable structure was retained as far as possible. The results presented in Chapter 6 represent the odds of having borderline/clinical behavioural scores as compared to a lower score.

Throughout all risk factors analyses in this thesis, there was also the potential for type 1 error due to a large number of predictors considered (Chapters 4 – 6). This risk was managed by choosing risk factors for evaluation based on peer-reviewed literature and also by screening

variables using unadjusted analysis at $p < 0.2$ prior to considering them in building the multivariable models. Models were built systematically giving careful consideration to the role of confounders, mediators, and effect modifiers and temporal order in the associations between risk factors and outcomes of interest.

Recall and information bias were likely limitations to this research. Due to three-year gap between the third and fourth round of data collection, there was a risk of recall bias regarding episodes of respiratory or gastrointestinal illnesses in their children or regarding information on prescription or over the counter drug use among children or the mothers ([Bryant et al., 1989](#)). However, due to the longitudinal nature of the study, data regarding high-risk behaviours, relationship satisfaction, marital status, and measures of depression and anxiety were collected by the same interviewers over the four-year study period and recall time for most behaviours ranged between one week to one month before the interview. Thereby, minimizing the risk of recall or information bias.

7.7 Policy implications for maternal and child health

The results presented in this thesis provide evidence to public health practitioners, healthcare providers, policy makers, government, and non-governmental agencies to help refine maternal health programmes in Saskatchewan and provide the basis of comparative research for other provinces across Canada.

Our research builds on previous reports ([Bowen et al., 2012](#); [Heron et al., 2004](#)) that maternal depression and anxiety scores are highest during pregnancy and decline thereafter. Mothers with a history of depression are at higher risk of depression and anxiety during pregnancy and the postpartum period. Also, early pregnancy depression scores were significant predictors of both depression and anxiety scores at three years after the birth of the child. Thus,

highlighting the long-term effects of early pregnancy depression on the later life depression and anxiety scores.

Family history of perinatal depression was also independently associated with anxiety/depression and sleep problems in children at three years of age and maternal prenatal drug use mediated the effects of family history of perinatal depression in predicting the personal – social development of the children at three years of age. Together these findings suggest the potential for transgenerational effects of postpartum depression on early childhood development. Whether these effects are genetic or environmental in origin could be assessed in further research. However, mothers with the family history of perinatal depression and previous history of depression should be considered high-risk and screened for prenatal depression and anxiety early in the pregnancy (Figure 7-4).

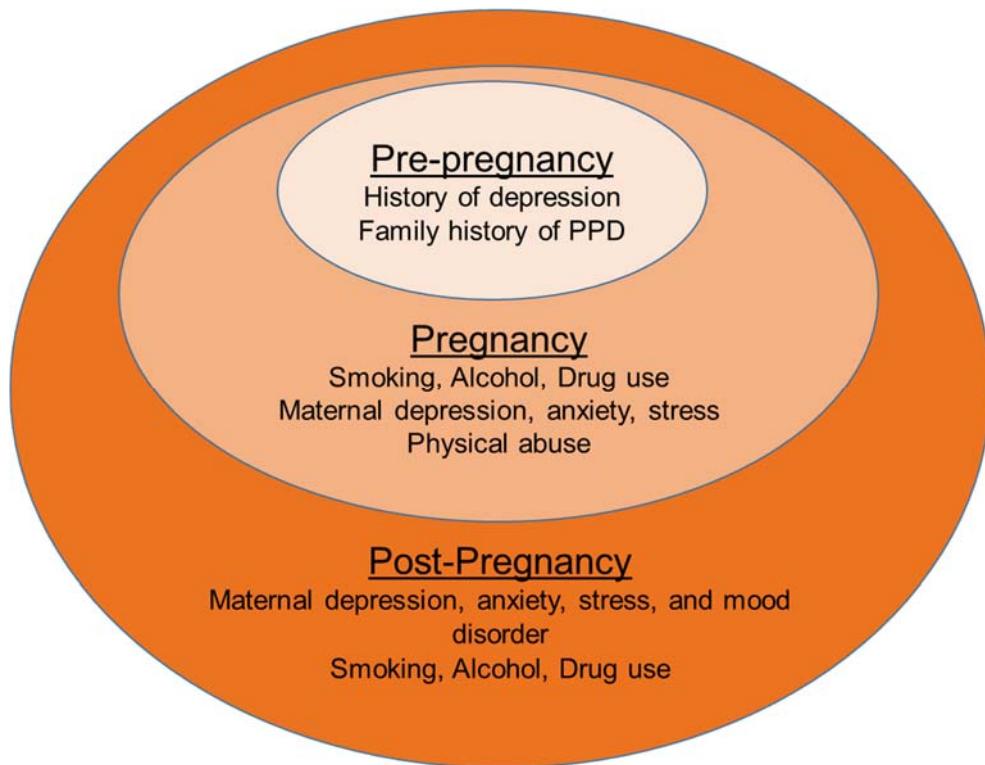


Figure 7-4: Representation of the focus of screening and support programs recommended to prevent the development of chronic depression and anxiety and reduce developmental delays in the children at three years of age.

Other literature supports the observation that maternal high-risk behaviours and stressful life conditions appear to have vicious cycle effects on maternal mental health. Mothers who lacked social support, were physically or emotionally abused, living in economic disadvantage, and who participated in high-risk behaviours such as smoking, alcohol consumption, or drug use had a higher risk of developing perinatal depression ([Norbeck & Anderson, 1989](#); [Norbeck & Tilden, 1983](#)). At the same time, depressed mothers are more likely to smoke, consume alcohol, use drugs, and have a history of physical or sexual abuse in pregnancy ([Evans et al., 2001](#)). Thus, information and education programs to screen, counsel, and help prenatal mothers quit high-risk behaviours should decrease the long-term impacts on early childhood emotional and behavioural development (Figure 7-2, Figure 7-3). Similarly, screening high-risk mothers in early pregnancy will help to prevent the development of chronic depression and anxiety and similarly help to prevent developmental delays in their children.

Our research indicates that birth to three years of age is a critical period for the effects of maternal mental health on early childhood development skills and behaviours (Figure 7-2, Figure 7-3). Whereas, pregnancy and postpartum are both sensitive time periods to mitigate the effects of maternal high-risk behaviours such as smoking, alcohol consumption, and drug use on early childhood development skills and behaviours (Figure 7-2, Figure 7-3). Stable family environments and higher income levels were associated with higher early childhood development scores at three years of age (Figure 7-2, Figure 7-3). Our study reiterates the benefits of providing financial, emotional, and educational support to mothers in the postpartum period and the role of this support in mitigating the long-term developmental delays in their children (Figure 7-4).

The study provides additional evidence to support the ‘MothersFirst’ strategy from Saskatchewan ([Bruce et al., 2012](#)). ‘MotherFirst’ strategy recommends: 1) education to increase awareness about the risks associated with perinatal depression and anxiety and de-stigmatize the diagnosis of depression and anxiety; 2) universal screening for both perinatal depression and anxiety, especially in conjuncture with the routine immunization visits of their babies to aid in early diagnosis; 3) provision of appropriate early treatment to minimize the detrimental effects on self, infant, and families; and 4) evaluation of the impact of the services and programs through feedback and consistent data collection ([Bruce et al., 2012](#)). In addition, we also recommend using validated tools for early screening of children of mothers who were depressed or anxious during or after pregnancy and those who exhibit high-risk behaviours. The ‘KidsFirst’ program in Saskatoon, Saskatchewan is in place to provide support to high-risk families through home visitation ([Stadnyk et al., 2005](#)). Families of children who screen positive for emotional and behavioural problems can be referred to the ‘KidsFirst’ program.

7.8 References

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