Effects of Preconception Disordered Eating on Next Generation Birth Outcomes

By
Rhian Waitapu Coram (BA, GDipPsych)

Submitted in partial fulfilment of the requirements for the degree of Doctor of Psychology (Clinical)

Deakin University, June 2015
I am the author of the thesis entitled “Effects of Preconception Disordered Eating on Next Generation Birth Outcomes”

Submitted for the degree of Doctor of Psychology (Clinical)

This thesis may be made available for consultation, loan and limited copying in accordance with the Copyright Act 1968.

'I certify that I am the student named below and that the information provided in the form is correct'

*Full Name:* Rhian Waitapu Coram

*Signed:* 

*Date:* 13th November, 2015
CANDIDATE DECLARATION

I certify the following about the thesis entitled “Effects of Preconception Disordered Eating on Next Generation Birth Outcomes”

Submitted for the degree of:

Doctor of Psychology (Clinical)

a. I am the creator of all or part of the whole work(s) (including content and layout) and that where reference is made to the work of others, due acknowledgment is given.

b. The work(s) are not in any way a violation or infringement of any copyright, trademark, patent, or other rights whatsoever of any person.

c. That if the work(s) have been commissioned, sponsored or supported by any organisation, I have fulfilled all of the obligations required by such contract or agreement.

I also certify that any material in the thesis, which has been accepted for a degree or diploma by any university or institution, is identified in the text.

'I certify that I am the student named below and that the information provided in the form is correct'

Full Name: Rhian Waitapu Coram

Signed: .......................................................... ..........................................................

Date: 22nd June, 2015
This thesis draws on 20 years of prospective intergenerational data, obtained from the Australian Temperament Project (ATP), to examine effects of adolescent disordered eating on risk of low birth weight, preterm or small for gestational age births. This thesis also aimed to investigate the potential mediating effect of adolescent disordered eating on transmission of adverse birth outcomes across generations. The ATP and ATP Generation Three (G3) study comprises of data obtained across three generations. Generation Two (G2) participants were recruited at 4 to 8 months of age during the initial wave of recruitment in 1983 and followed during adolescence, adulthood and pregnancy. The current sample comprised of data from 188 female G2 ATP participants who had given birth to 83 male and 105 female G3 infants. The first study of this thesis, a systematic literature review, provided early indications of risk for women with a history of an eating disorder, particularly AN, yet revealed a significant gap in relation to available prospective studies that examined the effects of adolescent disordered eating on later pregnancy outcomes. The second and third studies aimed to address noted gaps in the literature by examining the hypothesis that drive for thinness scores or being At Risk of an eating disorder in adolescence would predict subsequent risk of low birth weight, preterm and small for gestational age offspring. In contrast, it was hypothesised that Bulimia scores would not be associated with these adverse birth outcomes. It was further hypothesised that a relationship would exist between G2 and G3 low birth weight and small for gestational age births and that intergenerational transmission would be mediated by adolescent disordered eating. Findings from adjusted logistic regression analyses partially supported these hypotheses, revealing a significantly increased risk of small for gestational age births to women reporting higher drive for thinness scores or those At Risk of an eating disorder in adolescence (OR: 1.104, CI: 1.027-1.188; OR: 3.473, CI: 1.241-9.722). Adolescent disordered eating behaviour did not result in a significant increase in risk of low birth weight or preterm births. Findings from this thesis revealed a significant correlation between maternal (G2) and infant (G3) birth weight. G2 women born low birth weight were also found to be at a significantly increased risk of having a low birth weight birth. Furthermore, maternal low birth weight and preterm status was found to significantly predict risk of small for gestational age births in offspring. Significant mediation effects were not revealed, although the indirect effect of
adolescent disordered eating on intergenerational risk of small for gestational age births was significant based on 90% Confidence Intervals. These findings, in the context of the Developmental Origins of Health and Disease theory, underscore the importance of the adolescent period in developing positive health trajectories into adulthood and pregnancy and have implications for the prevention and management of small for gestational age births. This provides support for recommendations of a lifespan approach to reproductive care and the extension of the preconception period to include adolescence.
ACKNOWLEDGEMENTS

First and foremost, I would like to acknowledge and express my warmest gratitude to my supervisors, Dr Jacqui Macdonald and Professor Craig Olsson, who have provided me with invaluable insights and knowledge, whilst guiding and supporting me throughout the research process. I would also like to acknowledge the members of the Australian Temperament Project (ATP) for offering their time and sharing their extensive knowledge of the ATP. I would like to acknowledge George Youssef, for his willingness to share his time and statistical expertise, particularly during the final stages of research. I would also like to thank Dr Ross King for sharing his knowledge in this field of research. I wish to express my gratitude to the Nursing and Allied Health Scholarship and Support Scheme (NAHSSS) for their generous financial contribution, which helped to lighten the financial burden and stress associated with undertaking this research.

I would like to also thank and show my appreciation to my family and friends for their ongoing encouragement and kind words. In particular, I am grateful for my parents who have provided me with the financial support and practical assistance, which has enabled me to undertake and complete my current studies. I want to thank Stella Coram for her keen editing eye and advice. This has been exceedingly helpful and will not be forgotten. I would also like to express my gratitude and appreciation to Gerard Winter for his dedicated support, encouragement and humour throughout the research process.
## TABLE OF CONTENTS

CANDIDATE DECLARATION ................................................................. ii  
ABSTRACT .................................................................................. iii  
ACKNOWLEDGEMENTS ................................................................. v  
TABLE OF CONTENTS ................................................................. vi  
LIST OF TABLES ................................................................. xi  
LIST OF FIGURES ................................................................. ix  
GLOSSARY ........................................................................ xl  

**CHAPTER 1: INTRODUCTION** .................................................. 1  
1.1 Low birth weight, preterm and small for gestational age births .......... 1  
1.2 Developmental Origins of Health and Disease (DOHaD) ................. 2  
1.3 Disordered eating and pregnancy outcomes ........................................ 3  
1.4 Research aims ............................................................................ 4  
1.5 Thesis overview ........................................................................ 5  

**CHAPTER 2: EPIDEMIOLOGY AND AETIOLOGY OF LOW BIRTH WEIGHT, PRETERM AND SMALL FOR GESTATIONAL AGE BIRTHS** .......... 7  
2.1 Chapter overview ........................................................................ 7  
2.2 Epidemiology of low birth weight, preterm and small for gestational age births .................................................. 7  
2.3 Implications of IVF use and multiple births .................................... 10  
2.4 Impact of low birth weight, preterm and small for gestational age births ........ 11  
2.5 Aetiology of low birth weight, preterm and small for gestational age births .... 15  
  2.5.1 Biological determinants .................................................................. 15  
  2.5.2 Psychosocial determinants ................................................................. 16  

**CHAPTER 3: DEVELOPMENTAL ORIGINS OF HEALTH AND DISEASE** ...... 18  
3.1 Chapter overview ........................................................................ 18  
3.2 Developmental Origins of Health and Disease (DOHaD) .................... 19  
3.3 Epigenetic vulnerability and gestational exposure ................................ 20  
3.4 Theoretical limitations of the DOHaD approach ................................. 22  
3.5 Future directions and recommendations ......................................... 23  
3.6 Developmental risk and psychosocial exposure in adolescence .......... 24  
3.7 A preconception approach to reproductive health ............................ 28  

**CHAPTER 4: DISORDERED EATING AND PREGNANCY** .................. 31  
4.1 Chapter overview ........................................................................ 31
4.2 Epidemiology of disordered eating................................................................. 31
  4.2.1 Prevalence of eating disorders ................................................................. 33
  4.2.2 Course and recovery rates ........................................................................ 34
  4.2.3 Physical, psychological and emotional outcomes in disordered eating popula
tions .................................................................................................................. 35
  4.2.4 Comorbidity amongst eating disorder populations .................................. 36
4.3 Disordered eating behaviours in adolescence ................................................. 37
4.4 Reproductive and biological consequences of disordered eating .................. 39
4.5 Pregnancy and birth outcomes in women with eating disorders .................... 42
4.6 The effects of preconception disordered eating on adverse birth outcomes ..... 45

CHAPTER 5: SYSTEMATIC LITERATURE REVIEW ........................................... 48
  5.1 Chapter overview .......................................................................................... 48
  5.2 Objectives ..................................................................................................... 49
  5.3 Methods ......................................................................................................... 49
    5.3.1 Criteria for considering studies for this review ....................................... 49
    5.3.2 Search methods for identification of studies .......................................... 50
    5.3.3 Data extraction and quality assessment .................................................. 51
  5.4 Results ........................................................................................................... 51
    5.4.1 Country ................................................................................................... 54
    5.4.2 Sample size ............................................................................................. 54
    5.4.3 Design ...................................................................................................... 54
    5.4.4 Measures ................................................................................................ 55
    5.4.5 Analytic methodology ............................................................................ 57
    5.4.6 Relevant findings .................................................................................... 57
  5.5 Discussion ...................................................................................................... 62
    5.5.1 Substantive limitations in the studies reviewed ...................................... 65
    5.5.2 Methodological limitations ..................................................................... 72
    5.5.3. Sampling and demographic limitations ................................................ 74
    5.5.4 Review limitations ................................................................................ 76
    5.5.5 Future directions .................................................................................... 76
  5.6 Aims and hypotheses for empirical analyses in this thesis ......................... 77

CHAPTER 6: METHODS ...................................................................................... 79
  6.1 The current study: The Australian Temperament Project- Generation 3 Study
  (ATPG3) ............................................................................................................. 79
8.4 Mediating role of disordered eating on intergenerational patterns of low birth weight, preterm and small for gestational age births ............................................. 125
8.5 Aims and hypotheses ..................................................................................... 128
8.6 Methods: ATP G3 Study 3 ............................................................................. 130

CHAPTER 9: RESULTS AND DISCUSSION OF INTERGENERATIONAL BIRTH RISK AND MEDIATING EFFECTS OF ADOLESCENT DISORDERED EATING
.................................................................................................................................... 130
9.1 Chapter overview .......................................................................................... 130
9.2 Rationale and research aims........................................................................... 130
9.3 Statistical assumption testing ......................................................................... 131
9.4 Descriptive statistics: Maternal and infant adverse birth outcomes ............... 134
9.5 Preliminary analyses: Continuity of adverse birth outcomes between Generation Two mothers and Generation Three infants ........................................................... 136
9.6 Mediation analyses ......................................................................................... 138
  9.6.1 Direct effects of maternal birth outcomes and adolescent disordered eating on infant small for gestational age births ........................................................... 139
  9.6.2 Indirect effects of adolescent disordered eating on transmission of risk of adverse birth outcomes from mother to infant ................................................... 139
9.7 Post-hoc analyses: Effects of preconception disordered eating and maternal birth outcomes on risk of small for gestational age births ............................................. 142
  9.7.1 Statistical assumption testing .................................................................... 143
  9.7.2 Post hoc logistic regression results ........................................................... 144
9.8 Discussion of findings regarding the mediating role of adolescent disordered eating on intergenerational transmission of adverse birth outcomes ............... 147
  9.8.1 Continuity of low birth weight, preterm and small for gestational age births ............................................................................................................................ 147
  9.8.2 Mediating effect of adolescent disordered eating on intergenerational patterns of adverse birth outcomes ................................................................. 150
  9.8.3 Post-hoc analyses: Effects of adolescent disordered eating and maternal birth outcomes on risk of small for gestational age births .......................................... 152

CHAPTER 10: OVERALL DISCUSSION ..................................................................... 155
10.1 Chapter overview ........................................................................................ 155
10.2 Literature review ......................................................................................... 156
10.3 Aims and research questions........................................................................ 157
10.4 Key study findings and implications .............................................................. 158
10.5 Strengths and limitations ........................................................................... 163
10.6 Recommendations and future directions ..................................................... 167
10.7 Conclusions ............................................................................................... 169
REFERENCES .................................................................................................. 171
APPENDICES ................................................................................................. 227
<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 1</td>
<td>Search strategy and search terms</td>
</tr>
<tr>
<td>Table 2</td>
<td>Summary of reviewed studies’ population, design, and retained sample characteristics</td>
</tr>
<tr>
<td>Table 3</td>
<td>Summary of exposure and outcome measures, analytic methods and major findings</td>
</tr>
<tr>
<td>Table 4</td>
<td>Comparison of retained sample at Wave 11 and the original cohort on characteristics at recruitment in 1983</td>
</tr>
<tr>
<td>Table 5</td>
<td>Analysis of normality for predictor and outcome variables; Kolmogorov-Smirnov, Skew and Kurtosis</td>
</tr>
<tr>
<td>Table 6</td>
<td>Analysis of normality for covariates; Kolmogorov-Smirnov, Skew and Kurtosis</td>
</tr>
<tr>
<td>Table 7</td>
<td>Missing data, percentage missing in the sample and mean scores</td>
</tr>
<tr>
<td>Table 8</td>
<td>Frequencies of birth outcomes</td>
</tr>
<tr>
<td>Table 9</td>
<td>Frequencies of IVF use, multiple births, first births, disordered eating ‘Risk’ and low birth weight, preterm and small for gestational age births</td>
</tr>
<tr>
<td>Table 10</td>
<td>Demographics of adolescent sample at 15 and 16 years of age</td>
</tr>
<tr>
<td>Table 11</td>
<td>Pearson’s r correlations between continuous predictor variables, outcomes and potential covariates</td>
</tr>
<tr>
<td>Table 12</td>
<td>Chi Square Analyses and Fischer’s Exact Test</td>
</tr>
<tr>
<td>Table 13</td>
<td>Independent samples T-Test comparing birth weight between disordered eating ‘Risk’ and not at risk groups</td>
</tr>
<tr>
<td>Table 14</td>
<td>Independent samples T-test comparing gestational age between disordered eating ‘Risk’ and not at risk groups</td>
</tr>
<tr>
<td>Table 15</td>
<td>Independent samples T-test comparing Drive for Thinness and Bulimia scores between low birth weight and normal weight births</td>
</tr>
<tr>
<td>Table 16</td>
<td>Independent samples T-test comparing Drive for Thinness and Bulimia scores between preterm and term births</td>
</tr>
<tr>
<td>Table 17</td>
<td>Independent samples T-test comparing Drive for Thinness and Bulimia scores between small for gestational age and appropriate weight for age births</td>
</tr>
<tr>
<td>Table 18</td>
<td>Independent sample t-tests between continuous covariates and categorical predictor and outcome variables</td>
</tr>
</tbody>
</table>
Table 19 Unadjusted logistic regression analyses assessing the effects of adolescent 
disordered eating on low birth weight, preterm and small for gestational age 
births .................................................................111
Table 20 Adjusted logistic regression analyses assessing the effects of adolescent 
disordered eating on risk of small for gestational age births ......................111
Table 21 Hypothesised mediated pathways ...................................................129
Table 22 Analysis of normality of G2 and G3 birth outcomes and G2 adolescent 
disordered eating based on the Kolmogorov-Smirnov statistic, Skew and 
Kurtosis ..............................................................................................132
Table 23 Missing data for G2 and G3 predictor and outcome variables ............133
Table 24 Frequencies of maternal (G2) and infant (G3) birth outcomes ..........135
Table 25 Frequencies of low birth weight, preterm and small for gestational age 
infants in mothers born low birth weight, preterm and small for gestational age 
........................................................................................................136
Table 26 Pearson's r correlations between maternal (G2) and infant (G3) birth 
outcomes ..................................................................................................137
Table 27 Logistic regression analyses assessing G2 maternal low birth weight, 
preterm and small for gestational age births on G3 low birth weight, preterm and 
small for gestational age births ...............................................................138
Table 28 Standardised and unstandardized direct effects of G2 birth outcomes and 
disordered eating risk on G3 small for gestational age births ..................140
Table 29 Indirect effects of G2 disordered eating on G2 and G3 birth outcomes ....141
Table 30 Chi Square analyses of independence for maternal birth outcomes ........144
Table 31 Logistic regression assessing G2 Drive for Thinness and disordered eating 
‘Risk’ on G3 infant small for gestational age births adjusting for categorical 
indicators of G2 maternal low birth weight, preterm and small for gestational age 
births .......................................................................................................146
Table 32 Logistic regression analyses assessing G2 Drive for Thinness and disordered 
eating ‘Risk’ on G3 infant small for gestational age births adjusting for 
continuous indicators of G2 maternal birth weight in kilograms and gestational 
age in weeks ..........................................................................................146
LIST OF FIGURES

Figure 1: Prisma diagram outlining exclusion criteria and process for inclusion of articles in this review .......................................................... 53

Figure 2: Generation Two (G2) and Generation Three (G3) participants and ATP and ATP-G3 study waves .......................................................... 85

Figure 3 Sample size requirements for logistic regression analyses based on power analyses using G Power 3.1 ......................................................... 92

Figure 4 Mediating effects of adolescent Drive for Thinness and eating disorder ‘Risk’ on transmission of risk of small for gestational age births from G2 to G3. Indirect models are significant within 90% confidence intervals ............... 142
**GLOSSARY**

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AN</td>
<td>Anorexia Nervosa clinical diagnosis based on DSM diagnostic criteria.</td>
</tr>
<tr>
<td>ATP</td>
<td>The Australian Temperament Project is a prospective longitudinal study that followed the psychosocial development of a community sample in Victoria from infancy to adulthood. Participants were recruited in 1983 from 67 Local Government Authority areas (LGA’s) selected by the Australian Bureau of Statistics.</td>
</tr>
<tr>
<td>ATP G3</td>
<td>The Australian Temperament Project Generation Three (ATP G3) study is a prospective longitudinal study examining psychosocial development in a sample of Victorian participants across three generations from generation One (G1) grandparents to Generation Three (G3) grandchildren.</td>
</tr>
<tr>
<td>BN</td>
<td>Bulimia Nervosa clinical diagnosis based on DSM diagnostic criteria.</td>
</tr>
<tr>
<td>Bulimia</td>
<td>Bulimia scores represent summed scores from the Bulimia subscale of the Eating Disorder Inventory (EDI) measured at 15 and 16 years of age.</td>
</tr>
<tr>
<td>Drive for Thinness (DFT)</td>
<td>Drive for thinness scores represent summed scores from the Drive for Thinness subscale of the Eating Disorder Inventory (EDI) measured at 15 and 16 years of age.</td>
</tr>
<tr>
<td>ED ‘At Risk’</td>
<td>Disordered eating ‘Risk’ at 15 and 16 years of age. Disordered eating risk was coded dichotomously based on Drive for Thinness and Bulimia scores of the EDI and Body Mass Index (BMI).</td>
</tr>
<tr>
<td>EDI</td>
<td>Eating Disorder Inventory (Garner, Olmstead, &amp; Polivy, 1983) designed to measure psychological and behavioural traits consistent with AN and BN.</td>
</tr>
<tr>
<td>G1</td>
<td>Generation One participants recruited in the initial ATP study. Generation One participants represented the parents of Generation Two infants recruited during the initial waves of data collection in 1983.</td>
</tr>
<tr>
<td>G2</td>
<td>Generation Two participants were recruited during the initial ATP study in 1983 during infancy.</td>
</tr>
<tr>
<td>G2 Birth weight</td>
<td>Birth weight of the Generation Two mother when she was born. Birth weight was measured continuously in kilograms to the nearest 100 grams.</td>
</tr>
<tr>
<td>G2 Gestational age</td>
<td>Gestational age of the Generation Two mother when she was born. Gestational age was measured continuously in number of week’s gestation.</td>
</tr>
<tr>
<td>-------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>G2 LBW</td>
<td>Low birth weight status of the Generation Two mother when she was born. Coded dichotomously, with low birth weight defined as being born less than 2500 grams.</td>
</tr>
<tr>
<td>G2 Preterm births</td>
<td>Preterm birth status of the Generation Two mother when she was born. Coded dichotomously, with preterm births defined as being born less that 37 weeks.</td>
</tr>
<tr>
<td>G2 SGA</td>
<td>Small for gestational age status of Generation Two mothers at birth. Coded dichotomously with small for gestational age defined as being below the 10th percentile for age and weight based on 1999 Australian norms.</td>
</tr>
<tr>
<td>G3</td>
<td>Generation Three participants. Generation Three participants represent participating infants born to Generation Two mothers.</td>
</tr>
<tr>
<td>G3 Birth weight</td>
<td>Generation Three infant birth weight reported at 12 months of age. Birth weight was measured continuously in kilograms to the nearest 100 grams.</td>
</tr>
<tr>
<td>G3 Gestational age</td>
<td>Generation Three infant gestational age reported at 12 months of age. Gestational age was measured continuously in number of week’s gestation.</td>
</tr>
<tr>
<td>G3 LBW</td>
<td>Generation Three infant low birth weight status. Coded dichotomously with low birth weight births defined as those weighing less than 2500 grams at birth.</td>
</tr>
<tr>
<td>G3 Preterm births</td>
<td>Generation Three infant preterm birth status. Coded dichotomously with preterm births defined as being born less than 37 weeks gestation.</td>
</tr>
<tr>
<td>G3 SGA</td>
<td>Generation Three infant small for gestational age births. Coded dichotomously with small for gestational age births defined as those below the 10th percentile for age and weight based on Australian normed percentiles.</td>
</tr>
<tr>
<td>SES</td>
<td>Socioeconomic status was measured using data obtained during wave 11 of the ATP at 15 and 16 years of age. SES was based on parent reported level of education and occupation and ranged from 1 to 8 with higher scores indicating lower SES.</td>
</tr>
</tbody>
</table>
CHAPTER 1: INTRODUCTION

Low birth weight, preterm and small for gestational age births remain a significant problem, with rates of low birth weight and preterm births in developed countries cited at approximately 8% and 6% respectively (Blencowe et al., 2012; Martin et al., 2011). Even during periods of optimal reproductive health these adverse birth outcomes remain prevalent, indicating that biological risks to offspring associated with increasing maternal age are not wholly attenuated (Davidoff et al., 2006). This raises the possibility that other psychosocial factors are contributing to proportions of risk (Hemminki & Forssas, 1999; Rai & Regan, 2006). This thesis investigates the proposition that some risk factors for low birth weight, preterm and small for gestational age births may originate well before conception. In particular, an examination is presented here of disordered eating in adolescence as an aetiiological factor in subsequent pregnancy outcomes. Findings may contribute to current understandings of maternal and infant risk and reduce preventable instances of adverse birth outcomes.

1.1 Low birth weight, preterm and small for gestational age births

Despite continued attempts to address the issue of low birth weight and preterm births a gradual rise in rates of low birth weight and preterm births among western countries have been observed over the past two decades (Department of Health, 2005; Donahue, Kleinman, Gillman, & Oken, 2010). Findings based on US data from 2010 revealed that low birth weight births had remained stable at approximately 8% of live births (Martin, Hamilton, and Ventura et al., 2012). Low birth weight, preterm, and small for gestational age births are reported to account for approximately 75% of neonatal morbidity and mortality (Goldenberg, Culhane, Lams, & Romero, 2008). Australian data from 2009 indicated early gestational age and restricted foetal growth accounted for 31.3% of all perinatal deaths (Australian Bureau of Statistics, 2009, cat. no. 3304.0). The long-term consequences of these outcomes include physical, psychological, cognitive and developmental complications for the infant, as well as significant financial and psychological consequences for the mother and family (Hack et al., 2003; Kersting et al., 2004; Petrrou, 2003). Adverse birth outcomes of this kind may also result in changes in the social and developmental
timing of consequent births, potentially altering women’s choices with respect to the family cycle or developmental stage at which subsequent births occur (Singer et al., 1999).

Hence, further investigation of potential determinants of these outcomes represents an important area of research, with the aim of reducing preventable instances of low birth weight, preterm and small for gestational births and alleviating some of the associated morbidity and mortality. Increasing trends in the context of advanced reproductive and medical care infer that a greater focus towards more psychological or social determinants, compared to biological influences, is warranted (Valero de Bernabe et al., 2004). Examination of early psychosocial indicators of risk may provide a target for preventative intervention and expand upon current theories of maternal and infant health that, to date, have focused primarily on risks occurring during pregnancy.

1.2 Developmental Origins of Health and Disease (DOHaD)

Developmental Origins of Health and Disease (DOHaD) theory presupposes that early life experiences during gestation and infancy have long-term impacts on health and disease later in life (Newnham, 2007). In particular, maternal diet and nutrition has been identified as an important determinant of adverse pregnancy and birth outcomes, including low birth weight, preterm and small for gestational age births. Under nutrition in pregnancy is proposed to contribute to adaptive processes and altered gene expression during gestation that may increase the risk of disease throughout the lifespan (Godfrey, Lillycrop, Burdge, Gluckman, & Hanson, 2007). However, the effects of preconception diet and eating behaviour on later pregnancy outcomes remain speculative.

Adolescence is identified as a critical period of development that is marked by more social, psychological and environmental changes than any other developmental stage apart from infancy (Choudhury, Blakemore, & Charman, 2006; Christie & Viner, 2005). Significant changes associated with the onset of puberty and sexual maturation occurring in adolescence confers a degree of vulnerability and sensitivity to a range of environmental and psychosocial risks (Cichetti & Rogosch, 2002).
Developmental notions of vulnerability in adolescence have contributed to understandings of atypical developmental and psychopathology, with many mental health diagnoses, including eating disorders, emerging in adolescence (Merikangas et al., 201). What happens during this time may therefore impact on long-term trajectories of health and wellbeing in adulthood and later pregnancies (Holmbeck, 2002). It is proposed that outcomes in adulthood and pregnancy may therefore develop from distal factors emerging during early development in adolescence.

1.3 Disordered eating and pregnancy outcomes

Eating disorders are estimated to effect approximately 5% to 7% of women of childbearing age and represent the third most common chronic disease in adolescence (Micali, Treasure & Simonoff, 2007). Findings based on community surveys in South Australia revealed a two-fold increase in the prevalence of binge eating, purging behaviour and restrictive dieting from 1995 to 2005 (Hay, Mond, Buttner, & Darby, 2008). Eating disorders are associated with significant physical and biological consequences, including reproductive and endocrine complications (Sidiropoulos, 2007). Reproductive complications resulting from physical starvation and disordered eating during pregnancy, including AN and BN, have been linked to an increased risk of low birth weight, preterm and small for gestational age births (Bansil et al., 2008; Pasternak et al., 2012). The impacts of malnutrition and diet during pregnancy appear well established (Ehrenberg, Dierker, Milluzzi, & Mercer, 2003; Franko & Spurrell, 2000; Naeya, 1990). Yet, the impacts of adolescent disordered eating on pregnancy outcomes remain speculative, representing an important area for future research.

Adolescent disordered eating behaviours have been associated with poorer trajectories of physical and psychological health in adulthood and pregnancy (Graber, Brooks-Gunn, Paikoff, & Warren, 1994; Johnson, Cohen, Kasen, & Brook, 2002). It may be proposed that disordered eating behaviours in adolescence or the period of sexual maturation may incur hormonal and physical changes that have long-term impacts for pregnancy and birth outcomes in adulthood. Increases in the proportion of disordered eating and sub clinical symptoms, particularly in adolescent populations, increases potential for ongoing harms (Chamay-Weber, Narring, & Michaud, 2005; Sancho, Arija, Asorey, & Canals, 2007). Improving understanding of the potential
consequences of adolescent disordered eating behaviours and attitudes may allow for the development of specific programs aimed at mitigating these risks. This may have positive flow on effects in reducing adverse birth outcomes for next generation offspring.

1.4 Research aims

The central objective of this thesis is to extend on current theories of developmental health and disease by examining the effects of preconception disordered eating on next generation birth outcomes. The first study of this thesis represents a systematic literature review that aims to summarise and review the current literature base examining the effects of preconception disordered eating on low birth weight, preterm and small for gestational age births. This thesis draws on rare ‘early release’ prospective intergenerational data obtained from the Australian Temperament Project (ATP). The second and third studies of this thesis utilised data obtained from the first 188 female participants with Generation Three infant data to test the hypothesis that adolescent disordered eating, at 15 to 16 years of age, would increase the risk of low birth weight, preterm or small for gestational age births in adulthood. Furthermore, this thesis aimed to examine intergenerational patterns of low birth weight, preterm and small for gestational age births and the role of adolescent disordered eating in potentially mediating the transmission of risk from mother to offspring.

This study represents one of only a small number of studies in the world that can prospectively examine the effects of preconception disordered eating in adolescence on next generation birth outcomes. To date, little research has examined the effects of preconception disordered eating on pregnancy outcomes, with the main focus to this point largely on exposures occurring during the gestational period. The long-term impacts of adolescent disordered eating on pregnancy outcomes, therefore, remain somewhat unknown. Methodological limitations and differences in study design of those studies that have examined the effects of preconception disordered eating infer a need for further replication and examination of these associations. The ATP aims to recruit 1000 Generation Three offspring in the coming years so that larger replication, using community based prospective data, may be conducted. It is
anticipated that examination of preconception risks, specifically adolescent disordered eating, may facilitate the development of targeted interventions aimed at reducing preventable instances of low birth weight, preterm or small for gestational age births.

1.5 Thesis overview

Chapter two provides an overview of the outcomes examined in this thesis. This chapter reviews the epidemiology and aetiology of low birth weight, preterm and small for gestational age births, with specific reference to the morbidity and mortality associated with these outcomes.

Chapter three provides a description of the theoretical and empirical basis underlying the Developmental Origins of Health and Disease (DOHaD) approach. This chapter discusses the potential limitations associated with current approaches to health and disease so as to provide a framework for future models of preconception health and wellbeing.

Chapter four examines the epidemiology of eating disorders, including AN and BN, as well as the biological and reproductive consequences of disordered eating behaviours in adolescence and pregnancy. This chapter also reviews the empirical evidence examining the link between eating disorders, including AN and BN, prior to and during pregnancy and consequent pregnancy and birth outcomes, including low birth weight, preterm and small for gestational age births.

Chapter five presents the first study, which is a systematic review of literature examining pregnancy and birth outcomes of women with a history of disordered eating, including An or BN. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and methodology were used examine the literature in relation to disordered eating, including AN and BN, as potential exposures associated with subsequent offspring outcomes, low birth weight, preterm and small for gestational age births.
Chapter six presents the methodology for the empirical analyses reported in this thesis. This chapter outlines the participants, materials and procedures undertaken as part of the study and the methodological procedures for the larger longitudinal study from which data were obtained; the Australian Temperament Project Generation Three (ATPG3) study. This chapter also describes the statistical approaches adopted to assess the hypotheses developed in this thesis.

Chapter seven presents the results from the second study that examined the effects of adolescent disordered eating on risk of low birth weight, preterm and small for gestational age births. Findings obtained from logistic regression analyses are presented followed by a discussion of the findings in the context of DOHaD theory.

Chapter eight provides a review of intergenerational theory and research in relation to patterns of low birth weight, preterm or small for gestational age births from parent to offspring. This chapter presents the rationale for the examination of the role of adolescent disordered eating in the transmission of adverse birth outcomes from one generation or the next.

Chapter nine presents the results from the third study that investigated continuity of low birth weight, preterm and small for gestational births from mother to offspring and the mediating effect of adolescent disordered eating on intergenerational transmission of risk. This chapter includes a discussion of reported findings in the context of previous literature.

Chapter ten provides a discussion of the results revealed in this thesis. This chapter includes an overview of key findings, in the context of DOHaD theory and previous research. Strengths and limitations of this thesis will be discussed as well as the clinical implications of reported findings. Recommendations for future research are presented in light of the current findings.
CHAPTER 2: EPIDEMIOLOGY AND AETIOLOGY OF LOW BIRTH WEIGHT, PRETERM AND SMALL FOR GESTATIONAL AGE BIRTHS

2.1 Chapter overview

This chapter discusses the issue of low birth weight, preterm and small for gestational age births so as to provide a context for further examination of such factors in epidemiological research. In particular, the epidemiology for these birth outcomes is summarised and their impact on the infant and family at birth, and throughout development, are explored. In addition, aetiological determinants of low birth weight, preterm and small for gestational age births are reviewed from a biopsychosocial perspective.

2.2 Epidemiology of low birth weight, preterm and small for gestational age births

Low birth weight and preterm births are leading causes of infant morbidity and mortality in both developing and developed countries (Lumley, 2003; Petrou, 2003). The World Health Organisation has defined low birth weight births as those less than 2500g (Wardlaw, 2004). This is a dually defined process incorporating both the duration of gestation and rate of foetal growth (Kramer, 2003). Pre-term deliveries are defined as those occurring before 37 weeks gestational age and are estimated to account for 12% of all live births in the United States (Glynn, Schetter, Hobel, & Sandman, 2008; Goldenberg et al., 2008). An important distinction is whether preterm births are medically induced, where preterm labour or early caesarean section is indicated due to foetal or maternal factors such as premature rupture of the membrane, or whether this has occurred spontaneously as a result of spontaneous labour (Feldman, Woolcott, O’Connell, & Jangaard, 2012; Moutquin, 2003). Whilst the majority of preterm births are associated with spontaneous labour, approximately 25% of preterm births, occurring without premature rupture of the membrane, are reported to be medically induced preterm births (Moutquin, 2003).
Birth weight and gestational age are not mutually exclusive outcomes, with approximately two thirds of low birth weight births also presenting as preterm (Tucker & McGuire, 2004). Premature births are associated with early cessation of foetal development and intrauterine growth that results in under developed or smaller infants of lower birth weight (Goldenberg & Culhane, 2007). Despite some concordance between underlying categories of preterm birth and low birth weight births, these outcomes are not interchangeable. Whilst preterm births predispose infants to lower birth weights, this in itself does not represent a singular cause for low birth weight births thereby inferring the importance of other related maternal and environmental factors, such as maternal age or parity, in the development of these outcomes (Aldous & Edmonson, 1994; Kramer, 1987).

A proportion of low birth weight births are also described as being small for gestational age (Tucker & McGuire, 2004). Small for gestational age births are typically classified as those below the 10th percentile for the general population or two standard deviations below the mean for gestational age (Lee, Chernausek, Hokken-Koelega, & Czernichow, 2003). Small for gestational age births are classed after birth as either small for weight, length or both based on population percentiles of birth weight distribution for gestational age (Clayton et al., 2007; Roberts & Lancaster, 1999). The likelihood of being small for gestational age is significantly increased if born premature yet small for gestational age births can occur at full term and result in small although normal weight infants (Groom, Poppe, North, & McCowan, 2007). Although the majority of small for gestational age infants demonstrate catch-up growth by the age of two years, approximately 13% to 40% fail to demonstrate such growth (Hokken-Koelega et al., 1995; Saenger et al., 2007). This suggests potential long-term effects stemming from diminished growth during gestation.

The global proportion of low birth weight births is cited at approximately 17%, of which 19% are from developing and 5% to 7% from developed countries (Valero de Bernabe et al., 2004). Data obtained from the US in 2010 revealed that the incidence of low birth weight births was approximately 8% (Martin et al., 2012). For nations with high estimates of low birth weight births a significant majority are reported to occur as a result of intrauterine growth restriction (Kramer, 2003). Global estimates of preterm births in 2010 revealed that approximately 14.9 million infants
were born premature, with approximately 5% in European countries, 12% in the US and 6% of infants in Australia born premature (Blencowe et al., 2012; Goldenberg et al., 2008). Population estimates obtained from low and middle-income countries in 2012 revealed that 32.4 million infants were born small for gestational age, which accounted for 27% of all live births (Lee et al., 2013). Increases in rates of low birth weight and preterm births have been reported in most industrialised countries over the last 25 years (Ananth et al., 2005; Bada et al., 2005; Glynn et al., 2008; Goldenberg et al., 2008). This represents a real concern given ongoing advances in reproductive knowledge and clinical and community based interventions designed to target and prevent these outcomes (Green et al., 2005).

Efforts so far to reduce the incidence of low birth weight, preterm and small for gestational age births appear to have limited impact. Data published by the Victorian Department of Health in 2004 from the perinatal data collection unit revealed a gradual rise in low birth weight and preterm births of approximately 1.5% and 1.8% respectively since 1985 (Department of Health, 2005). Analysis of changes in birth weight and gestational age, from 1990 to 2005 in the US, revealed an overall decrease (52 grams) in infant birth weight (Donahue et al., 2010). The proportion of small for gestational age births were approximately 1% higher in 2005 compared to 1990 (Donahue et al., 2010). Similarly, epidemiological data in the US has revealed a shift in the average gestational age from 40 weeks to 39 weeks (Damus, 2008). US data from 2010 indicated that whilst a relative decrease in preterm births was observed, low birth weight births remained stable over the previous ten years accounting for 8% of live births (Martin, Hamilton & Osterman, 2012). Whilst some improvements have been observed in extending the gestational age of infants who may have previously been at risk of earlier stages of prematurity, rates of low birth weight and small for gestational age births appear relatively unchanged.

Trends in low birth weight, preterm and small for gestational age births have been associated with higher rates of assisted reproductive techniques and rising maternal age (Goldenberg et al., 2008; Tucker & McGuire, 2004; Wisborg, Ingerslev, & Henriksen, 2010). Increasing maternal age has been identified as an independent risk factor for low birth weight and preterm births, with the likelihood of medically indicated preterm deliveries increasing through attempts to reduce incidences of
perinatal mortality (Henderson et al., 2012; Kenny et al., 2013). Rising trends may also be due, in part, to increased survival rates for infants who may have been previously classified as being unviable (Beck et al., 2010; Lawn et al., 2013). The determinants of preterm births are thought to vary as a function of subtype, with only 20% to 30% of preterm births medically indicated (Ananth et al., 2005; Green et al., 2005). By implication, approximately 70% of preterm birth may be interpreted as not medically indicated. Examination of psychosocial determinants of spontaneous preterm births represents an area of further research. The implications of extending current understandings in relation to the causes of these adverse outcomes may lie in the identification of psychosocial and behavioural determinants and the development of targeted interventions aimed at addressing more specified psychosocial risks. These risks will be explored in detail in Chapter three and four.

2.3 Implications of IVF use and multiple births

Rates of multiple births and use of advanced assisted reproduction techniques such as In Vitro Fertilisation (IVF) have been associated with increasing rates of low birth weight and preterm births (Blondel et al., 2002; Kulkarni et al., 2013; McDonald et al., 2010; Jain, Missmer & Hornstein, 2004; Mathews & MacDorman, 2010). US data from 2009 indicated that one in every thirty infants was a twin, which represented a rise from 68,339 to more than 137,000 births from 2006 to 2009 (Martin, Hamilton & Osterman, 2012). Blondel, Macfarlane, Gissler, Breart, and Zeitlin, (2006) examined rates of preterm births in a European sample from the PERISTAT project. They reported that approximately 20% of all preterm births were attributable to multiple births. Increasing trends in multiple births have been linked to use of assisted reproductive technology (McDonald et al., 2010). Given low success rates of IVF treatment, multiple embryos are typically transferred in turn increasing the likelihood of multiple births (Tough, Greene, Svenson, & Belik, 2000). More than 40% of triplets born in the US in 1997 were associated with assisted reproductive techniques (Schieve, Ferrie, Peterson, Jeng, & Wilcox, 2002). Kallen, Finnstrom, Nygren, and Olausson (2005) reported that reductions in multiple births as a result of changing standards in the numbers of embryo’s transferred resulted in a reduction in the number of preterm births.
Risks associated with IVF use are not wholly accounted for by rates of multiple births, with independent risks also observed in singleton births (Helmerhorst, Perquin, Donker, & Keirse, 2004; Jackson, Gibson, Wu, & Croughan, 2004). A systematic review and meta-analysis, conducted by Pandey, Shetty, Hamilton, Bhattacharya, and Maheshwari (2012), examined birth outcomes in women undergoing IVF treatment. They revealed a significant increase in risk of low birth weight (OR: 1.65, CI: 1.56-1.75), preterm (OR: 1.54, CI: 1.47-1.62) and small for gestational age births (OR: 1.39, CI: 1.27-1.53) in singleton pregnancies conceived through IVF. Findings from current literature indicate that IVF use and multiple births are important variables to consider when examining these adverse birth outcomes.

Rates of low birth weight, preterm and small for gestational age births may also be explained by an upward shift in the age distribution of first and consequent pregnancies associated with IVF use (Engmann et al., 2001; Tough et al., 2002). Furthermore, one fourth to one third of multiple births have been associated with a simultaneous increase in maternal age (Blondel & Kaminski, 2002). Poorer birth outcomes to women undergoing IVF are reported in women over 35 years compared to women aged between 20 to 30 years (Yan, Wu, Tang, Ding, & Chen, 2012). However, maternal factors, such as tobacco use and indicators of under or over eating including BMI, have also shown to alter the risk of low birth weight, preterm or small for gestational age births in women undergoing IVF (Sazonova, Kallen, Thurin-Kjellberg, Wennerholm, & Bergh, 2011). Maternal factors are important in understanding trends in adverse birth outcomes for such women. The influence of psychosocial and environmental factors may be particularly important for women where risks associated with IVF and multiple births are not present. The significance of this comes to light in the discussion to follow on the impact of these outcomes.

2.4 Impact of low birth weight, preterm and small for gestational age births

Birth weight represents one of the major determinants of neonatal mortality in the developed world (Lee, Paneth, Gartner, & Pearlman, 1980). Lemons et al. (2013) investigated mortality and morbidity rates for very low birth weight births. They reported that mortality rates were as high as 89% for infants weighing 401 to 500g at birth and 71% for infants weighing 501 to 600g. Similarly, preterm births have been
identified as one of the leading causes of perinatal morbidity, accounting for more than 75% of perinatal mortality (Goldenberg et al., 2008; Lawn et al., 2014). Australian data from 2009 indicated that early gestational age and restricted foetal growth accounted for approximately 31% of all perinatal deaths, over one third ($n = 1011$) of which were attributed to non-specific causes (Australian Bureau of Statistics, 2009, cat. no. 3304.0). This emphasises a significant gap in understandings of the determinants of these outcomes and a need for further analysis of potential maternal psychosocial causes.

Low birth weight infants as well as small for gestational age births infants are thought to be at greatest risk due to both shortened gestational age and restricted intrauterine growth (Gutbrod, Wolke, Soehne, Ohrt, & Riegel, 2000). For these infants, higher prenatal and perinatal complications are observed. Giapros, Drougia, Krallis, Theocharis, and Andronikou (2012) cited the mortality rate for preterm small for gestational age births at 33% compared to 17% for preterm births that met the appropriate size for gestational age. Low birth weight, preterm and small for gestational births not only result in physical risks to the infant at birth, requiring immediate and ongoing care, but also result in ongoing complications leading to later infant mortality (Saigal & Doyle, 2008). These outcomes pose a strong risk to the survival of infants and their ongoing physical and developmental wellbeing (Petrou, Sach, & Davidson, 2001). Survival of low birth weight or preterm births might well be a function of postnatal care during the months following birth that may in turn be mediated by number of social variables such as socio economic status and indices of class (Lee et al., 1980).

Morbidity and mortality associated with low birth weight and preterm births are generally observed to vary based on the severity of these outcomes (Lee et al., 1980; Moster, Lie, & Markestad, 2008). This is represented by an inverse relationship, with the level of risk increasing as birth weight and age decreases (Darlow et al., 2005; Saigal & Doyle, 2008). A meta-analysis of observational studies, conducted by Risnes et al. (2011), revealed an inverse although moderate relationship between birth weight and adult mortality, in particular cardiovascular mortality. An emerging body of evidence has examined associated risk based on subtypes of these outcomes, reporting higher risks of morbidity in infants born near to full term, or later preterm;
that of 34 to 36 weeks gestation (Davidoff et al., 2006; Wang, Dorer, Fleming, & Catlin, 2004). The last six weeks of gestation represents a critical period of foetal growth and brain development, meaning that even late preterm infants can incur significant long-term effects compared to those born full term (Loftin et al., 2010). In this sense, there are no categories of birth weight or gestational age that are exempt from risk, with ongoing consequences observed within even those infants born marginally premature or of a relatively normal birth weight (Saigal & Doyle, 2008). These findings highlight the extent of the problem with even pregnancies considered only marginally discrepant from the ideal experiencing adverse consequences.

An important body of evidence has identified a range of ongoing physical, cognitive, social and emotional consequences as a result of these adverse birth outcomes (Hack et al., 2003; Kok, Lya den Ouden, Verloove-Vanhorick, & Brand, 1998; Levy-Marchal & Jaquet, 2004; Moster et al., 2008; O’Keeffe, O’Callaghan, Williams, Najman, & Bor, 2003). Wood, Marlow, Costeloe, Gibson, and Wilkinson (2000) examined outcomes of 283 preterm births admitted to a neonatal intensive care in the United Kingdom and Ireland between 1998 and 1999. Findings from short-term follow up indicated that 53 (19%) children had severely delayed development, 28 (10%) children had severe neuro-motor disability, 7 (2%) were blind and 8 (3%) had hearing loss requiring some form of hearing aid. Overall, 138 children (49%) had some form of disability, with 64 of these (23%) meeting criteria for a severe disability. Significant differences in mean Intelligence Quotient (IQ), academic achievement and professional attainment have also been revealed in children born with low birth weight compared to normal weight term births (Hack et al., 2002; Strauss, 2000). The long-term consequences extend beyond birth, occurring throughout the lifespan. Prevention of these outcomes may therefore incur positive flow on effects for health and wellbeing throughout development.

Furthermore, the consequences of low birth weight, preterm and small for gestational age births are not limited to the infant but have implications for the mother and extended family. For mothers, such incidences represent traumatic and distressing experiences that in turn predispose women to ongoing psychological morbidity (Singer et al., 1999; Vigod, Villegas, Dennis & Ross, 2010). Kersting et al. (2004) examined the psychological impact of 50 mothers of very low birth weight births.
across four time points; one to three days, 14 days, six months and 14 months post
birth. They found that mothers of very low birth weight births reported significantly
higher rates of trauma symptoms at all measured time points compared to mothers of
full term, normal weight infants. Furthermore, mothers of very low birth weight births
were found to have significantly higher rates of depressive and anxiety symptoms
compared to mothers of full term, normal weight infants, at 14 days and 14 months
post birth. This suggests that such outcomes are greatly traumatic necessitating
emotional support, beyond the period immediately following birth (Kersting et al.,
2004). Likewise, Davis, Edwards, Mohay, and Wollin (2003) examined the impact of
preterm births on the psychological health of mothers. Analysis of scores on the
Edinburgh Postpartum Depression Scale (EPDS) indicated that 40% of women
experiencing a preterm birth reported significant depressive symptoms. Depressive
symptoms were significantly higher amongst women following a preterm birth
compared with population norms estimated at between 10% and 15% (Davis et al.,
2003). Furthermore, it has been suggested that post partum psychopathology may
contribute to changes in the social and developmental timing of consequent
pregnancies (Ellis, Figueredo, Brumbach, & Schlomer, 2009; Singer et al., 1999). It
stands to reason that anxiety about the prospect of a subsequent adverse birth may
inhibit decision making in this regard. The impact of this thereby extends to the whole
family unit as a whole.

Economic costs associated with low birth weight, preterm and small for
gestational age births contribute to substantial global burden to health, special
education and family services (Petrou, 2003). Stevenson, McCabe, Pharoah, and Cook
(1996) investigated the economic consequences of low birth weight births in the UK
for children aged between 8 to 9 years. The lowest birth weight births were found to
incur an average health service cost of £14, 510, with intermediate birth weight births
costing approximately £12,051, and £7,178 for the highest birth weight group. Russell
et al. (2007) also examined the economic costs of hospitalisation and care for low
birth weight and preterm births in a nationwide in-patient sample in the US. They
reported that, in 2001, 8% of the total 4.6 million infant stays included a diagnosis of
preterm or low birth weight. Total costs for these infants was estimated at around $5.8
billion US dollars, representing approximately 47% of the costs for all infant
hospitalisations and 27% of all paediatric stays (Russell et al., 2007). From a financial
perspective, preventative interventions targeting determinants of low birth weight and preterm births may be crucial in deterring related economic health costs and burden.

2.5 Aetiology of low birth weight, preterm and small for gestational age births

2.5.1 Biological determinants

The aetiological determinants of low birth weight, preterm and small for gestational age births are classed into one or more of the following three broad categories; factors originating from the foetus, factors originating from the mother, and placental factors (Tucker & McGuire, 2004; Valero de Bernabe et al., 2004). Two primary determinants of low birth weight have been identified; the duration of gestation and intrauterine growth rate, which have been linked to uterine malnutrition produced through problems in circulation of the placenta (Kramer, 1987; Valero de Bernabe et al., 2004). Most commonly, preterm births are associated with spontaneous or unexplained preterm labour occurring as a result of premature rupture of the amniotic membrane (Steer, 2005). Approximately 15% to 25% of preterm births are attributed to maternal or foetal complications, related primarily to hypertensive disorders and severe intrauterine growth restriction (Tucker & McGuire, 2004). Genetic factors have also been associated with low birth weight and preterm births with these outcomes observed to repeat within families (Goldenberg et al., 2008; Muglia & Katz, 2010). However, a proportion of low birth weight, preterm and small for gestational age births occur without clear biological causes.

Maternal determinants of low birth weight, preterm and small for gestational age births include, but are not limited to, individual medical and obstetric history, parity, maternal age and socioeconomic status (Brown, Andera & Masho, 2008; Heaman et al., 2013; Ota et al., 2014; Scott, Moar, & Ounsted, 1981). A study conducted by Hirve and Ganatra (1994) set out to identify and quantify risk for low birth weight in a community based prospective cohort of women. They found that the relative risk of low birth weight was significantly higher for women of lower socioeconomic status (RR=1.71) and for women in their first pregnancy (RR=1.32). Importantly, low socioeconomic factors were correlated with haemoglobin less than 9 g/dl (RR=1.53) and third trimester bleeding (RR=1.87). The correlation between
socio economic status and severe anaemia was estimated to have substantial attributable risk for low birth weight births, accounting for 41% and 34% of low birth weight births respectively. This finding suggests that a variety of biological and social risks are likely to be interrelated.

A factor that has received some attention is the impact of maternal age (Cleary-Goldman et al., 2005; Newburn-Cook & Onyshkiw, 2005). Tough et al. (2002) examined the impact of delayed childbearing and increasing maternal age on rates of low birth weight, preterm, multiple births and small for gestational age births. Among women aged 35 years and over, low birth weight and preterm births increased by 11% and 14% respectively. Delayed childbearing was reported to account for approximately 78% and 36% of this change, with significant findings remaining when controlling for environmental factors such as maternal smoking. This provides some weight to biological perspectives and explanations of reproductive risk, with changes in risk associated with maternal age thought to occur as a result of impaired reproductive functioning and quality. Such biological risks are likely to be reduced for women aged in their 20s and 30s, who may nevertheless experience low birth weight, preterm and small for gestational age births. Examination of other potential determinants may shed some light into the causal pathway of these adverse birth outcomes for women where this type of biological risk may be attenuated.

2.5.2 Psychosocial determinants

Traditional explanations of low birth weight, preterm and small for gestational age births have adopted a biologically oriented perspective; however, medical knowledge and interventions have fallen short of wholly preventing or explaining these outcomes (Goldenberg et al., 2008). Genetic explanations remain important although are they too are thought to account for only 40% of these outcomes (Valero de Bernabe et al., 2004). The remaining 60% is attributed to a range of environmental and psychosocial factors including socio demographic and disadvantage, culture and race (Ananth, Joseph, Oyelese, Demissie, & Vintzileos, 2005; Reagan & Salsberry, 2005). Broadening the scope to examine further social and psychological explanations of risk may be particularly pertinent for women where
traditional biological risks, generally associated with increasing maternal age, may not apply.

Large disparities are observed in trends of low birth weight, preterm and small for gestational age births among various racial and ethnic groups, with a two-fold risk reported in African American women compared to Caucasian women in the US (Goldenberg & Culhane, 2007; Green et al., 2005; James, 1992; Saigal & Doyle, 2008). It is argued that these differences occur as a result of social determinants, including socioeconomic status, income and occupation, which vary as a function of race and ethnicity (Parker, Schoendorf, & Kiely, 1994). Yet, studies controlling for social factors such as education and occupation have revealed significant effects suggesting that birth outcomes have complex genetic, social and psychological determinants (Green et al., 2005). That is to say, biological risks associated with low birth weight, preterm and small for gestational age births may also be mediated by underlying psychological and social determinants (Misra, O’Campo & Strobino, 2001).

Psychosocial determinants, such as maternal nutrition, stress, mental health and substance use during pregnancy, have been associated with adverse birth outcomes (Bada et al., 2005; Chiolero, Bovet, & Paccaud, 2005; Muthayya, 2009). Misra et al. (2001) examined the influence of social factors in the development of preterm birth in a sample of 822 women delivering in an urban hospital. Taking into account the inclusion of biomedical factors, maternal stress (OR=1.86, CI: 1.21-2.86, \(p = .005\)) and locus of control (OR=1.75, CI: 1.17-2.63, \(p = .007\)) were found to be strongly associated with preterm births. These findings draw on the relative importance of psychological and social factors in the development of these outcomes. Maternal mental health, including depression and anxiety, has been associated with an increased risk of preterm and low birth weight births (Diego et al., 2006; Fransson, Ortenstrand, & Hjelmstedt, 2011; Glynn et al., 2008). Maternal nutrition is also recognised as an important determinant of intrauterine growth restriction and low birth weight births (Raisanen et al., 2013). Environmental conditions or exposures during gestation therefore have strong implications for outcomes in offspring. The influence of maternal nutrition and weight, in particular, on the development of adverse birth outcomes will be discussed in more detail in the Chapters to follow.
The determinants of low birth weight, preterm and small for gestational age births are multifactorial and heterogeneous in nature, marked by a number of potential pathways of risk (Ananth & Vintzileos, 2006; Villar et al., 2004). The causes of these outcomes are thought to vary according to subtype, although a number of commonalities and variations exist between and within each subtype. With such heterogeneity comes a degree of uncertainty regarding the underlying causes or precipitating factors, with some outcomes remaining unexplained in their origin. Continued investigation of potential causes, particularly those representing preventable sources of risk, will be important in addressing the problem of low birth weight, preterm and small for gestational age births.

The chapter to follow will discuss relevant psychosocial determinants of low birth weight, preterm and small for gestational age births in the context of the Developmental Origins of Health and Disease (DOHaD) framework. In particular, theoretical and empirical evidence regarding the influence of psychosocial factors, such as maternal weight and disordered eating behaviour, on these outcomes will be discussed and reviewed. Emphasis will be given to a developmental framework as an important means to understand trajectories of adolescent risk and preconception disordered eating behaviour. This is indicative of an alternative approach to traditional theories that have focused on risk occurring during gestation.

CHAPTER 3: DEVELOPMENTAL ORIGINS OF HEALTH AND DISEASE

3.1 Chapter overview

The previous chapter provided a context for examination of the potential predictors of low birth weight, preterm and small for gestational age births. This chapter outlines the theoretical basis for the Developmental Origins of Health and Disease (DOHaD) approach. The purpose of which is to develop a framework for understanding the development of adverse infant outcomes; low birth weight, preterm and small for gestational age births, from adolescence to adulthood. The focus in this chapter is to identify potential adolescent determinants for subsequent offspring low birth weight, preterm and small for gestational age births.
3.2 Developmental Origins of Health and Disease (DOHaD)

The Developmental Origins of Health and Disease (DOHaD) approach is a scientific framework to come out of a number of epidemiological studies derived from large perinatal cohort studies on infant and adult mortality (Wadhwa, Buss, Entringer, & Swanson, 2009). Examination of extensive perinatal data from England and Wales revealed high geographical correlations between infant birth weight and adult heart disease and Type II diabetes (Barker, Osmond, Forsen, Kajantie, & Eriksson, 2005; Barker, 2007). Observations from these studies lead to the theory that the geographic relationship between infant outcomes and adult disease reflected variations in poor gestational nutrition, which was an indicator of low birth weight births and an early source of cardiac and metabolic disorders in adulthood (Gluckman, Hanson, & Pinal, 2005). These findings gave rise to the foetal origins hypothesis or ‘Barker’s hypothesis which proposed that the risk of developing chronic disease in later life is not only influenced by genetic and environmental factors during adulthood but also by environmental conditions in early life (Barker, 1995).

Specifically, under-nutrition at different stages of gestational development, middle or late pregnancy, was associated with different birth phenotypes and consequent adaptations associated with disease in adulthood (Barker, 1995; Wadhwa et al., 2009). It was hypothesised that in utero stress, stemming from under-nutrition, leads to a process of adaptation whereby the development of non-essential organs are compromised in preference for essential organs such as the brain (Gluckman, Hanson & Bukligas, 2010; Rinaudo, Piane, & Revelli, 2012). The short-term effects of this trade off, for the foetus, include suboptimal in utero growth and infants born with low birth weight. Adaptations of this kind during gestation are thought to permanently change the body’s structure and function, resulting in later health risks in environments where these adaptations are no longer advantageous (Wadhwa et al., 2009). The long-term consequences include increased risk of cardiovascular disease in adulthood (Rinaudo et al., 2012). This pattern has also been associated with insulin resistance in adulthood (Eriksson, Forsen, Tuomilehto, Osmond, & Barker, 2001; Ong & Dunger, 2004).
3.3 Epigenetic vulnerability and gestational exposure

‘Barker’s hypothesis’ generated worldwide debate on the subject of developmental plasticity, epigenetic processes, and the influence of environment on the development of mature phenotypes and risk of later disease (Godfrey et al., 2007). It is suggested that aspects of maternal developmental environment may modify non-imprinted genes and gene expression without altering DNA sequences, through heritable changes in DNA methylation within embryonic cells (Sinclair & Singh, 2007; Swanson, Entringer, Buss, & Wadhwa, 2009). In other words, gestation is thought to be a critical period of development, marked by a degree of plasticity, adaptation and vulnerability to the surrounding environment and epigenetic processes (Gomes & Pelosi, 2013). The “foetal programming” hypothesis proposes that these changes serve an adaptive function in optimising infant survival by programing infants to experience and adapt to similar, potentially harsh, conditions of the mother (Remacle, Bieswal, & Reusens, 2004). These adaptive functions may have disadvantageous effects if conditions following birth no longer match those experienced by the infant during gestation.

Inconsistencies between foetal development, gene expression and maternal environmental conditions following birth are hypothesised to result in increases in the risk of disease throughout the lifespan, such as obesity and diabetes (Gluckman et al., 2005; Godfrey et al., 2007; Newnham, 2009). These adaptions were found to be detrimental when nutrition was more abundant following birth, in comparison to conditions during gestation (Hales & Barker, 2001). Periods of early rapid catch-up growth following birth, due to an abundance of nutrients, may contribute to dramatic modifications in foetal programming leading to the development of risk and disease (Barker, 2005; Remacle et al., 2004). This process may be relevant within eating disorder populations, where symptoms of restriction and starvation in mothers potentially emulate vulnerable conditions that trigger adaptations impacting on foetal development (Campbell, Mill, Uher, & Schmidt, 2011). Research on adaptive foetal responses to a range of environmental cues has led to additional benefits in extending understandings of adult health and disease (Langley-Evans, Alexander, McArdle, & Sloboda, 2012). The foetal programming hypothesis provides a rationale for
preconception care in optimising health and wellbeing prior to conception before these adaptive processes occur (Atrash et al., 2008).

In uterine growth restriction, associated with maternal under-nutrition, is thought to be associated with epigenetic modifications and foetal programming (Delisle, 2002; Sinclair & Singh, 2007; Swanson et al., 2009). Research into long-term outcomes of infants born to mothers during the Dutch Hunger Winter provides support for DOHaD theory and patterns of disease from birth to adulthood (Schulz, 2010). Women exposed to famine during mid to late gestation gave birth to infants with significantly reduced birth weight. Exposure to famine during pregnancy altered the developmental trajectories of the children born to these mothers, with their infants experiencing long-term developmental problems, including obesity and impaired glucose tolerance as adults (De Boo & Harding, 2006; Schulz, 2010). Offspring of mothers exposed to famine during early gestation were born on average at a normal birth weight but experienced a threefold increase in risk of coronary heart disease as adults (De Boo & Harding, 2006). These findings may be indicative of programming during gestation, with changing conditions following birth representing a mismatch in environmental conditions and an increase in long-term risks.

The DOHaD framework has provided a foundation for a number of studies investigating maternal exposures or conditions, particularly maternal nutrition, in the aetiology of adverse birth outcomes (Wadhwa et al., 2009). The objective of DOHaD is to further understand the broader scope of developmental cues and extrapolate maternal conditions that may have consequences for infant health and development. It is anticipated that deeper examination of potential psychosocial determinants of low birth weight, preterm and small for gestational age births may help to broaden understandings of health and disease. It has been proposed that environmental factors impact on epigenetic patterns throughout the lifespan and not only in gestation (Gomes & Pelosi, 2013). Given that a number of potential psychosocial indicators of risk develop long before the gestational period, investigation of these influences prior to conception, especially during adolescence, represents a novel area for future research. It is predicted that this will inform the development of preventative interventions aimed at circumventing risks in pregnancy as well as long-term developmental risks for offspring.
3.4 Theoretical limitations of the DOHaD approach

Whilst contributing to important understandings of health and disease, the DOHaD framework has largely focused on the gestational period (Yajnik & Deshmukh, 2008). In doing so, current theory is yet to adequately address the influence of potential risks occurring prior to pregnancy. Emerging evidence has begun to recognise the relative importance of developmental processes prior to conception. For example, Tobi et al. (2009) revealed that women exposed to famine in the peri-conception period, defined broadly as the period prior to and including conception, also experienced alterations of methylation profiles of loci implicated in growth, metabolic and cardiovascular disease. This suggests that a proportion of individual vulnerability to disease occurs prior to conception. Expanding on traditional DOHaD theory by examining potential preconception risks will contribute to understandings of health and disease through identification of early risks. This may permit women sufficient time to adopt positive behavioural change (Bhutta, Dean, Imam, & Lassi, 2011). The theoretical underpinnings of preconception reproductive care will be discussed in greater detail later in this chapter.

Critics of the DOHaD framework have suggested that its theoretical foundations are based merely on phenomenological associations with limited theoretical and mechanistic explanations of how early life experiences affect disease vulnerability (Gluckman et al., 2010). There is the potential for these associations to be explained by confounding variables related to exposures or conditions occurring throughout development or prior to conception (Godfrey, 2006; Huxley, Neil, & Collins, 2002). It has consequently been argued that a number of studies have not adequately accounted for potential confounding variables, with a number of environmental conditions, such as preconception psychosocial influences, or genetic factors potentially relevant in the development of these adverse birth outcomes (Gluckman et al., 2010). Hence, conclusions in relation to trajectories of risk may be limited. This is indicative of the need for methodologically sound studies, particularly prospective longitudinal designs, in which environmental influences and potential confounding variables can be measured and accounted for. However, it is argued that reduced foetal growth is not necessarily representative of an indicator of long-term
trajectories of health and disease but more a marker of foetal responses to conditions imposed during gestation, such as under-nutrition (Gluckman & Hanson, 2004; Hanson & Gluckman, 2008). Further investigation of potential preconception mechanisms that may predict adaptive processes, reflected by low birth weight births, may be indicated as a method of reducing long-term risks.

A narrow focus towards gestational exposures and early infancy has meant that a relatively short-term perspective of neonatal health has been adopted (Misra, Guyer, & Allston, 2003). Foundations in epigenetic mechanisms and developmental plasticity have influenced a focus on early maternal and gestational exposures in the development of later disease (Gluckman et al., 2009). Preconception health is thought to be a precondition for health and wellbeing during pregnancy and for future generations (Korenbrot, Steinberg, Bender, & Newberry, 2002). In fact, recent recommendations have suggested that the preconception period extend to include the beginning of puberty or sexual maturation so that optimal reproductive outcomes may be achieved (Johnson et al., 2006). The DOHaD approach emphasises the importance of gestational conditions, particularly maternal nutrition, in the development of adverse birth outcomes and later disease. Yet, significant gaps exist in relation to understandings of the relative influence of the preconception period on pregnancy outcomes, such as low birth weight, preterm and small for gestational age births.

3.5 Future directions and recommendations

A lifespan approach to prenatal health that addresses a range of biological, psychological, and social influences, has been proposed as a way of addressing current gaps in reproductive health. The rationale for this model is based on the underlying principle that most influential predictors of maternal health occur long before pregnancy (Misra et al., 2003). This perspective posits that maternal behaviour prior to conception, during times of potential risk, impact on reproductive success later in life (Lu & Halfon, 2003). From a life course perspective, risks occurring during early life, especially adolescence, are likely to result in an increase or accumulation of risk across the lifespan. A developmental perspective with this in mind can be expected to broaden current understandings of reproductive health through identification of windows of opportunity where preventative treatment or
interventions may be particularly effective (Werner-Wilson & Morrissey, 2005). Despite providing important recommendations for maternal care, research to date has mostly focused on biological proximal risk factors, with less research expanding into earlier developmental stages.

The incidence of low birth weight, preterm and small for gestational births remain relatively unchanged despite advancements in reproductive care and knowledge (Martin, Hamilton & Osterman, 2012; Rai & Regan, 2006). Currently, reproductive and maternal interventions are primarily described as secondary, aimed at eliminating or reducing existing risk, or tertiary, intended to improve outcomes for infants (Iams, Romero, Culhane, & Goldenberg, 2008). Unfortunately such interventions have been only partially successful in reducing rates of these outcomes. Further research into primary intervention is required to prevent early risks, such as poor nutrition and diet, and reduce an accumulation of risk and the need for secondary interventions during pregnancy. Otherwise, behavioural change becomes much harder to achieve (Iams et al., 2008). Examination of critical periods of development occurring prior to pregnancy may help to identify early indicators of risk and provide targets for preventative reproductive interventions aimed at circumventing preventable instances of low birth weight, preterm and small for gestational age births. The discussion to follow outlines a number of unique vulnerabilities and risks associated with the adolescent period that are, in turn, considered relevant to the development of disordered eating behaviour and adverse outcomes later in life.

### 3.6 Developmental risk and psychosocial exposure in adolescence

It is well recognized that early life experiences shape trajectories into adulthood (Newnham, 2007). It is proposed that periods of developmental plasticity extend from preconception to gestation, with epigenetic responses to environmental changes exerting their effects throughout the lifespan (Hochberg et al., 2010; Pembrey et al., 2006). Adolescence is considered a critical period of development, marked by more biological, psychological, social and cognitive changes than any other stage of the lifespan apart from infancy (Bordini & Rosenfield, 2011; Choudhury, Blakemore, & Charman, 2006). Notions of vulnerability during adolescence have provided important insights into atypical development and psychopathology. Mental health
diagnoses account for a large proportion of the global burden of disease in young people, with many common mental health diagnoses seen in adulthood first emerging in childhood and adolescence (Merikangas et al., 2010; Petal, Flisher, Hetrick, & McGorry, 2007; Saluja et al., 2004). Lewinsohn, Hops, Roberts, Seeley, and Andrews (1993) reported that 33% of school students in their sample had experienced mental illness of some type over their lifetime, with 31% of these individuals also suffering comorbid disorders. Eating disorders and subclinical patterns of disordered eating remain prevalent within the general adolescent population (Neumark-Sztainer, Wall, Larson, Eisenberg & Loth, 2011). In a school-based study of 1739 adolescent females between the ages of 12 to 18 years, almost one third were found to present with disordered eating attitudes or behaviours (Jones, Bennett, Olmsted, Lawson & Rodin, 2001). Furthermore, disordered eating attitudes and behaviours, including dieting, bingeing and purging, were found to increase gradually throughout adolescence (Jones et al., 2001). What happens during this time may therefore alter long-term trajectories of health and wellbeing, with environmental and psychosocial risks in adolescent having lasting effects (Holmbeck, 2002).

The onset of puberty and sexual maturation results in significant physiological changes, including the maturation of gametogenesis, secretion of gonadal hormones and the development of secondary sexual characteristics (Bordini & Rosenfield, 2011). Hormonal and biological changes in adolescence may drive changes in adolescent behaviour and influence the expression of psychopathology including variations in emotional states such as anger and depression (Irwin et al., 1997; Martel, Klump, Nigg, Breedlove, & Sisk, 2009; Petersen et al., 1993). This suggests a degree of vulnerability to psychosocial influences during adolescence. The onset of puberty is proposed to moderate genetic risks, with hereditability of risk increasing linearly across pubertal development (Klump, McGue, & Lacono, 2003; Klump, Perkins, Burt, McGue, & Iacono, 2007). Gonadal hormones are thought to play a role in the development of disordered eating either directly through organisation and activation of genetic predispositions, or indirectly through changes in body fat compositions and appetite characteristics (Klump et al., 2005). Pubertal development may therefore contribute to specified risks unique to the adolescent period.
Adolescence is also associated with significant changes in neurogenesis, cortical development and neurotransmitters (Crews & Hodge, 2007). Developmental changes, in particular, growth in the frontal cortex, have been linked to the refinement of higher order functioning such as reasoning, goal and priority setting, impulse control as well as evaluations of long and short-term rewards (Steingberg, 2005). These changes are linked to increased risk taking behaviour, poor decision-making, and a decreased ability to cope with developmental changes and expectations (Steingberg, 2005). In lieu of adaptive coping skills, individuals may turn to maladaptive coping behaviours, such as avoidance or maladaptive emotion-focused behaviours, in an attempt to manage such demands (Compas, Orosan, & Grant, 1993; Wilson, Pritchard, & Revalee, 2005). All of these physiological and biological changes contribute to an accumulation of potential vulnerabilities that predispose individuals to risk of disease in later life.

Developmental notions of vulnerability in adolescence have important implications for understanding atypical development and psychopathology. Adolescence requires that individuals exert greater control in regulating their affect and behaviour in line with long-term goals and consequences whilst also individuating and distancing from the guidance and structure typically provided by primary care givers (Steinberg, 2005). A relative lack of preparedness for these responsibilities presents a potential source of internal and external conflict (Cichetti & Rogosch, 2002). Adolescence involves changes in almost every aspect of life including, education, peer friendships and stressful life events such as parental divorce. Given this, adolescence is described as a period of “storm and stress”, with problems of adjustment generalised as a normative experience during this period (Cicchetti & Rogosch, 2002). For some individuals, these periods can represent distressing situations, significantly impacting on positive development and wellbeing (Petersen et al., 1993). Without developed coping skills or supports, some may follow a trajectory towards disease and psychopathology, such as disordered eating (Martyn-Nemeth, Penckofer, Gulanick, Velsor-Friedrich, & Bryant, 2009).
Individuation from the family network is often associated with a greater influence of peer interactions and attitudes on adolescent behaviour and decision-making (Gardner & Steinberg, 2005). Adolescence involves the development and consolidation of the social self in relation to the social world, with individuals becoming increasingly aware of the perspectives and attitudes of others (Choudhury et al., 2006). A peer process model of adolescent transition and peer influence asserts that dual paths of risk exist for normative and high-risk populations (Leung, Toumbourou, & Hemphill, 2014). For high-risk populations, early risk factors cumulate to have a snowball effect, resulting in a degree of developmental vulnerability and early antisocial peer selection. For normative adolescent populations, the snowstorm effect may occur, where threatening environmental conditions may exacerbate individual vulnerabilities to peer influence (Leung et al., 2014). This model has been applied to adolescent alcohol use, however may also be relevant in explaining the development of maladaptive eating behaviours. Peer selection processes, associated with peer influence and perceived pressure to be thin, have all been linked to the development of disordered eating behaviours in adolescence (Shomaker & Furman, 2009; Zalta & Keel, 2006).

Psychosocial risks in adolescence, including disordered eating, may predispose individuals to poorer trajectories of health and wellbeing (Floyd et al., 2008; Graber et al., 1994; Johnson et al., 2002; Patton, Coffey, Carlin, Sanci, & Sawyer, 2008; Petal et al., 2007; Weissman et al., 1999). Stice et al. (2013) examined disordered eating diagnoses in a community sample of 496 adolescent females. They found that youth diagnosed with an eating disorder reported greater functional impairment, distress, suicidality and unhealthy BMIs compared to participants without an eating disorder. Recurrence rates, at eight year follow up, were cited at 25% for AN, 23% for BN, 21% for atypical AN and 27% for sub threshold BN. Findings from the Western Australian Pregnancy Cohort (Raine) Study revealed that one quarter of participants who met criteria for a binge eating or purging disorder at 14 years of age also met criteria for an eating disorder at 20 years of age (Allen, Byrne, Oddy, & Crosby, 2013a).
These findings indicate that risks occurring during adolescence are not exclusive to the adolescent period and may contribute to poorer long-term outcomes in adulthood. Adolescent risk may exert a twofold effect by exposing individuals to direct harms or increasing the risk of similar eating patterns in adulthood and pregnancy. It may be that early exposure, particularly during adolescence, predisposes individuals to ongoing patterns of maladaptive eating throughout development and increases the potential for accumulative effects (Neumark-Sztainer et al., 2011). Poor outcomes in adulthood and pregnancy may therefore develop from distal factors emerging during early development. The long-term effects of adolescent psychosocial exposures on adulthood and pregnancy remain speculative. High prevalence rates of disordered eating behaviours and attitudes during adolescence, however, indicate a need for further examination of the long-term effects (Allen, Byrne, Oddy & Crosby, 2013b). The next chapter will extend on understandings of development of health and disease through further discussion of the potential relationship between adolescent risks, specifically disordered eating, and the development of adverse birth outcomes later in life.

3.7 A preconception approach to reproductive health

The preconception approach is underscored by the premise that adverse birth outcomes may have psychosocial aetiological roots prior to pregnancy. A preconception approach to reproductive health emphasises an integrated and preventative strategy to understand and potentially reduce the occurrence of adverse pregnancy outcomes (Dean, Lassi, Imam, & Bhutta, 2014). Preconception interventions are defined as any number of strategies that set out to identify and modify biomedical, behavioural, and social risks related to women’s reproductive health in order to maximise optimal birth outcomes (Johnson et al., 2006). Conservative definitions of the preconception period indicate that this begins at a minimum of three menstrual cycles prior to conception (Dean et al., 2013). This definition, however, does not account for developmental risks occurring prior to this time. More liberal definitions stipulate that preconception begins a minimum of one year prior to conception. But, this still does not wholly reflect the broader scope of preconception care that extends to adolescents and all women of reproductive age (Dean et al., 2013).
The Centre for Disease Control and Prevention (CDC) recommendations indicate that preconception should extend to include the beginning of reproductive functioning or the onset of puberty (Johnson et al., 2006). Moreover, high rates of unplanned pregnancies mean that a large proportion of women are becoming pregnant during periods of sub optimal reproductive health (Johnson et al., 2012-2014). This has been associated with risks of low birth weight, preterm and small for gestational age births (Johnson et al., 2012-2014). Extending the preconception framework to include puberty has the potential to improve reproductive awareness and facilitate the development of reproductive life plans aimed at optimising birth outcomes (Johnson et al., 2006). This can minimise early risks and provide women with sufficient time to adopt positive behavioural changes, ensuring that all women of reproductive age enter pregnancy with optimal health (Bhutta et al., 2011). Support for preconception interventions, though, is reliant on the emergence of further empirical evidence, which at present represents a gap in the literature (Jack et al., 2008; Korenbrot et al., 2002).

Although remaining an under researched area of study, the importance of the preconception period is becoming increasingly apparent. Preconception mental illness, such as depression, has been linked to risk of low birth weight and preterm births (Gavin, Chae, Mustillo, & Kiefe, 2009; Witt, Wisk, Cheng, Hampton, & Hagen, 2012). This finding is crucial for justifying the application of preconception models to other modifiable psychosocial influences, such as disordered eating (Atrash, Johnson, Adams, Cordero, & Howse, 2006). It may be that early prenatal care and intervention is too late for some, with identifiable risks forming well before women are pregnant (Atrash, Jack, & Johnson, 2008). A review of the evidence supporting recommendations of preconception care have endorsed early assessment and annual review of weight status, Body Mass Index (BMI) and nutrition for women of reproductive age (Jack et al., 2008). They recommended counselling and early intervention for women identified at risk, including those with eating disorders (Jack et al., 2008). Despite this, the quality of evidence regarding the effects of preconception disordered eating is relatively low, inferring a need for further methodologically sound studies.
Improved maternal and birth outcomes have been observed as a result of the implementation of effective preconception intervention (Atrash et al., 2006; Elsinga et al., 2008; Iams et al., 2008). Czeizel and Vereczkey (2012) examined the effects of preconception screens and health interventions at three months prior to conception as part of their primary health care. They reported significantly reduced rates of preterm births and congenital abnormalities. These outcomes were also identified as the two major determinants of infant mortality and morbidity within that cohort. A systematic review conducted by Whitworth and Dowswell (2009) examined the effectiveness of pre-pregnancy health promotion and intervention on pregnancy outcomes. They found that pre-pregnancy interventions, ranging from brief advice through to ongoing psycho-education, were associated with positive maternal behaviour change and significant improvements in mean birth weight (-97.00; CI: -168.05 to -25.95). These results are mixed, though, with only limited data available for review. They noted the potential for the efficacy of interventions to have differed depending on maternal age, developmental stage, and intent to conceive. This is illustrative that findings should be interpreted with caution.

Bhutta et al. (2011) evaluated the effectiveness of preconception interventions for maternal, perinatal and newborn outcomes. Their review consisted of 516 studies and included all available and unpublished studies investigating the impact of preconception care on maternal, neonatal and infant outcomes in women of reproductive age. Results indicated that interventions promoting adolescent health, such as optimal weight and micronutrient status, contraceptive use and screening for chronic conditions, were efficacious in reducing adverse infant outcomes. This provides a sound basis for the provision of adolescent preconception intervention in improving birth outcomes. Early evidence of the efficacy of preconception intervention underscores the hypothesis that maternal and reproductive risk factors may be rooted in childhood and adolescence (Weisman, Hillemeier, et al., 2011).

Preconception intervention is recommended for the promotion of optimal reproductive health and care. The development of effective preconception interventions is dependent on the emergence of empirical evidence, which currently represents a significant gap in the literature. Further examination of specific preconception influences, such as adolescent disordered eating, may facilitate the
development of selective interventions targeting individuals identified as being at an elevated risk. Adolescent intervention will be crucial for circumventing the development or accumulation of risk thereby contributing to adverse birth outcomes (Munoz, Mrazek, & Haggerty, 1996). The next chapter will expand on DOHaD theory described in this chapter by examining the effects of disordered eating, including AN and BN, occurring prior to conception in adolescence, on the development of adverse birth outcomes in adulthood.

CHAPTER 4: DISORDERED EATING AND PREGNANCY

4.1 Chapter overview

The previous chapter presented a theoretical framework, drawing on the Development Origins of Health and Disease (DOHaD) approach, to understand the development of adverse pregnancy outcomes such as low birth weight, preterm and small for gestational age births. A number of biopsychosocial determinants were discussed as gestational and preconception predictors of risk. This chapter examines the potential impact of disordered eating on the development of adverse birth outcomes. It provides a discussion on the epidemiology of disordered eating behaviour as well as a review of the impact and consequences of such behaviour throughout development from adolescence and into pregnancy.

4.2 Epidemiology of disordered eating

Eating disorders are predominant in young women and can result in significant psychological and medical consequences (Reijonen, Pratt, Patel, & Greydanus, 2003). According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) there are three subtypes of disordered eating, Anorexia Nervosa (AN), Bulimia Nervosa (BN) and binge eating disorder (American Psychiatric Association, 2013). DSM-5 criteria for AN requires that individuals experience marked restriction in energy intake leading to significantly low body weight relative to age, sex and developmental stage. AN is marked by intense fears of gaining weight as well as disturbances in perceptions of body weight and shape (American Psychiatric Association, 2013). Severity is based on Body Mass Indices (BMI), with a BMI <15 classified as extreme, 15 to 15.99 severe, 16 to 16.99 moderate and >17 mild
(American Psychiatric Association, 2013). A sub group of binge-eating/purging AN has been identified and characterised by the presence of purging, binge eating, and compensatory behaviour in attempts to facilitate weight loss. Binge-eating/purging subtypes have been associated with greater impulsivity, emotional disturbance, a greater predisposition to depression, and poorer prognostic outcomes (Garfinkel, Moldofsky, & Garner, 1980; Garner, Garner, & Rosen, 1993).

BN is marked by recurrent episodes of binge eating, occurring at least once a week for three months, and is characterised by the consumption of large quantities of food, a lack of control or inability to stop eating, high levels of secrecy, shame, and attempts to conceal behaviour (American Psychiatric Association, 2013). Episodes of binge eating are followed by compensatory behaviours, such as purging or excessive exercise, as a means of preventing weight gain. BN is associated with fears around weight gain, body dissatisfaction and a desire for weight loss as well as a tendency to make self-evaluations which are unduly influenced by body weight and shape (American Psychiatric Association, 2013). The severity of disorder is based on the frequency of inappropriate compensatory behaviours, with an average of fourteen or more episodes of compensatory behaviours classed as extreme, eight to thirteen classed as severe, four to seven moderate, and one to three mild in severity.

Binge eating disorder is defined as recurrent episodes of binge eating, occurring at least once a week for three months, which are characterised by consuming amounts of food that is definitively larger than what is expected or observed in others during a discrete period of time (American Psychiatric Association, 2013). These episodes are marked by a degree of lack of control or an inability to stop eating as well as three or more associated symptoms, including rapid food consumption, feeling uncomfortably full, eating large amounts without feelings of physical hunger and feelings of shame, embarrassment, disgust or guilt. Binge eating episodes are distinguished from episodes of binge eating characteristic in women with BN, as they are not accompanied by inappropriate compensatory behaviours (American Psychiatric Association, 2013). A diagnosis of Other Specified Feeding or Eating Disorder (OSFED) or Unspecified Feeding or Eating Disorder (UFED) may be made where clinically significant symptoms or behaviours are
present, which result in distress or impairment, but do not necessarily meet the full criteria for any diagnostic class.

There is a high degree of overlap across clinical subtypes, with many behaviours such as restrictive eating and purging, commonly experienced by women with AN and BN (Peat, Mitchell, Hoek, & Wonderlich, 2009; Tozzi et al., 2005). A seven-year prospective study of 216 women diagnosed with An or BN revealed that more than half of these women crossed between restricting and binge/purge subtypes over time and that one third crossed from AN to BN (Eddy et al., 2008). Regardless, significant differences exist between clinical subtypes, with bulimic women, for example, identified as being within a healthy weight range or being overweight compared to women with AN who present with significantly low body weight (Garner, Garfinkel, & O’Shaughnessy, 1985).

4.2.1 Prevalence of eating disorders

Prevalence rates of diagnosed eating disorders are reported to have increased significantly from the 1990’s to 2000’s, although are now reported currently remain relatively stable overall (Smink, Van Hoeken, & Hoek, 2012). A register-based study in the UK reported that the incidence of diagnosed eating disorders, for individuals aged between 10 to 49 years, rose from 32.3 per 100 000 to 37.2 per 100 000 between 2000 and 2009 (Micali, Hagberg, Petersen, & Treasure, 2013). It should be noted that increasing prevalence rates described in their study may not truly reflect current population prevalence due to the inclusion of identified diagnosed cases in their study. Lifetime prevalence rates for AN and BN have been cited at between 0.5% and 4% and 0.2% to 7% respectively (Glaeske, & Bachmann, 2013; Jaite, Hoffmann, Makino, Tsuboi, & Dennerstein, 2004; Keski-Rahkonen et al., 2007; Smink, Van Hoeken, & Hoek, 2013; Wade et al., 2006). Although rates of diagnosed eating disorder appear to have stabilized, significant increases in the prevalence of partial syndromes or sub clinical symptoms have been reported, with sub clinical presentations now hypothesised to surpass the number of clinical diagnoses (Sancho et al., 2007). Results from community surveys in South Australia indicated a two-fold increase in the prevalence of sub clinical symptoms, including binge eating, purging behaviour and restrictive dieting from 1995 to 2005 (Hay et al., 2008).
The highest incidence rates for AN and BN are among girls in middle and late adolescence (Portela de Santana, da Costa Ribeiro, Mora, & Raich, 2011). The prevalence of AN and BN in adolescent females has been cited between 0.3% and 0.7% and 1% to 2% respectively (Ackard, Fulkerson, & Neumark-Sztainer, 2007; Herpertz-Dahlmann, 2008; Hoek & Van Hoek, 2003; Hoek, 2006; Swanson, Crow, Le Grange, Swendsen, & Merikangas, 2011). Swanson et al. (2011) examined the prevalence and correlates of diagnosed eating disorders, such as AN and BN, using a cross sectional sample of 10,123 adolescents from the general population in the US. Lifetime prevalence of AN and BN were reported at 0.3% and 0.9% respectively.

The prevalence of partial syndromes and sub clinical symptoms in adolescence remain high and appear to remain constant from adolescence to young adulthood (Neumark-Sztainer et al., 2011). Patton, Coffey and Sawyer (2003) reported that the mean point prevalence (from 1992 to 1995) of partial syndrome eating disorders in females aged between 15 and 18 years, in a sample of 982 Victorian students, was 2.4% (1.8% to 3.1%). The point prevalence at follow up, at 20 years of age, was 3% (1.9% to 4.1%). Chamay-Weber et al. (2005) on the other hand, reported that the proportion of subclinical symptoms or partial eating disorders in adolescence is more than double the rates for full diagnoses, reported as 0.8% and 14% for AN and BN. More recent findings signify a relative increase in disordered eating behaviours, with 15.2% of female participants included in the population sample (n=1,383) reporting sub clinical disordered eating symptoms (Allen et al., 2013b). These findings indicate that disordered eating behaviours remain prevalent, inferring a growing potential for harms with the general population.

4.2.2 Course and recovery rates

AN and BN are often conceptualised as developmental disorders given that they commonly begin during adolescence or young adulthood (Steiner & Lock, 1998). Recovery rates for individuals engaged in treatment are estimated at 50% in relation to AN and 70% for BN (Wade, Bergin, Tiggemann, Bulik, & Fairburn, 2006). Despite the existence of effective evidence based treatments, a proportion of women experience lifelong symptoms, relapse or periods of altered or sub clinical eating behaviours (Keel, Mitchell, Miller, Davis, & Crow, 1999). The course of AN is quite
variable and may be characterised by single episodes, ongoing fluctuations in weight gain, relapse or a chronic long-term pattern of disordered eating (Pike, 1998). High levels of partial recovery and low rates of long-term full recovery are often observed in women with AN, compared to BN, for which full recovery rates are significantly higher (Herzog et al., 1999). Even among women who have recovered from an eating disorder, relatively low body weight and cognitive features consistent with an eating disorder are reported (Sullivan, Bulik, Fear, & Pickering, 1998).

Herzog et al. (1999) conducted a longitudinal study that followed 246 women, ranging in age between 13 to 45 years (mean age 24.8 years), over 7.5 years. The average duration of illness was 6.7 years, with nearly all women engaged in treatment during some point in the study. They found that 74% women with BN, compared to 33% of women with AN, achieved full recovery at 90 months follow up. Reported remission rates are observed to increase in line with the length of observed follow up, with remission rates at 4 to 20 years follow up cited as 84% and 70% for AN and BN respectively (Keel & Brown, 2010). Jayasinghe, Grover and Zacharin (2008) reported that full recovery of weight, growth and menstruation occurred in approximately 50% to 70% of women in their sample of adolescents who sought treatment. Regardless, there appears to be a significant proportion of people who go on to experience chronic lifelong conditions.

4.2.3 Physical, psychological and emotional outcomes in disordered eating populations

Eating disorders, particularly AN, have been associated with the highest mortality rates among all mental health diagnoses, cited at approximately 5% (Crow et al., 2009; Herzog et al., 2000; Hoek, 2006). A meta-analysis conducted by Arcelus, Mitchell, Wales, and Nielsen (2011) reviewed 36 studies examining morbidity and mortality in women with AN and BN. Standardized mortality rates for AN were reported at approximately 6% and 2% for BN. Increased mortality is generally associated with severe starvation, although is also related to increased rates of suicide (Papadopoulos, Ekbom, Brandt, & Ekselius, 2009; Zerwas et al., 2015). One in five deaths, for women with AN, are reported to occur as a result of suicide (Arcelus et al., 2011). The medical consequences for women diagnosed with an eating disorder are
extensive and place women at a significantly increased risk of physical and biological harm, including endocrine, reproductive, cognitive, cardiovascular, skeleton-muscular, gastrointestinal, metabolic and haematological complications (Gendall & Bulik, 2005; Kaplan & Woodside, 1987; Sidiropoulos, 2007). The severity of medical complications is generally dependent on the degree of weight loss, length of disorder and rate of weight loss (Herpertz-Dahlmann, 2008). This points to the influence of interrelated, although differing, risks which require careful consideration.

Eating disorders are also associated with significant psychological distress that impacts on social, familial and psychological domains (Hilleg, Beale, & McMaster, 2006). Hsu (1980) conducted a systematic review examining various physical, emotional, psychological and social outcomes in women with an eating disorder. He found that they were less likely to marry and have children, or were more likely to experience marriage or children later in life, compared to individuals who had recovered. Berkman, Lohr, and Bulik (2007) found that a substantial portion of individuals continued to suffer from an eating disorder over time as well as comorbid conditions such as depression and anxiety. These findings imply that the women diagnosed with an eating disorder incur poorer social and psychological outcomes long-term.

4.2.4 Comorbidity amongst eating disorder populations

High comorbidity rates are observed among disordered eating populations, with depression, anxiety and substance use representing common coexisting conditions (Gandalla & Piran, 2008; Hudson, Harrison, & Kessler, 2007; Kaye, Bulik, Thornton, Barbarich, & Masters, 2004; Santos, Richards, & Bleckley, 2007). A study of 229 female patients seeking treatment for an eating disorder revealed that 73% of women with AN and 60% of women with BN had a current Axis I comorbid condition (Herzog, Kellerm Sacks, Yeh, & Lavori, 1992). Overall, 82% of women with an eating disorder had a comorbid Axis I diagnosis. O’Brien and Vincent (2003) examined comorbidity among women diagnosed with AN and BN. Major depression was found to be the most common comorbid diagnosis, with Obsessive Compulsive Disorder (OCD) and substance use found to be highly comorbid with AN and BN. Blinder, Cumella, and Sanathara (2006) investigated correlations of 27 DSM-IV
comorbidities in a clinical sample of 2436 women with an eating disorder. Findings from their study were consistent with previous comorbid rankings, with mood (94%), anxiety (56%) and substance use disorders (22%) highest for women with an eating disorder. Patterns of comorbidity in subclinical populations remain similar to those in clinical samples, indicating significant risks even for those experiencing symptoms at the lower end of the spectrum (Chamay-Weber et al., 2005).

Complex aetiological determinants and common risk factors are thought to predispose individuals to a number of co-morbid mental health conditions. Similar neurological profiles have been observed in individuals with eating disorders and OCD, suggesting that common determinants may contribute to the development of one disorder or both (O’Brien & Vincent, 2003). In a number of cases, comorbid conditions, such as depression or anxiety, have been shown to pre date the onset of disordered eating, implying that similar genetic or psychosocial determinants may exist for both conditions (Bulik, Sullivan, Fear, & Joyce, 1997; O’Brien & Vincent, 2003). The peak onset for disordered eating, and a number of common comorbid conditions, occurs during adolescence suggesting that some determinants may be associated with unique influences occurring during this period (Stice, Presnell, & Bearman, 2001). Alternatively, comorbid diagnoses that present as secondary to a primary eating disorder diagnosis may occur as a result of increased distress and psychological impairment (Altemus & Gold, 1992).

4.3 Disordered eating behaviours in adolescence

As discussed in Chapter three, the adolescent period represents a critical period of early development. Eating disorders remain prevalent in adolescence, with the adolescent period typically marking the onset of disordered eating symptoms (Stice, Marti & Rohde, 2013). Swanson et al. (2011) reported that in their sample of 10,123 adolescents, the majority of participants reporting disordered eating behaviours also met criteria for at least one other disorder, such as Oppositional Defiant Disorder (ODD), mood and anxiety disorders, with comorbidity rates estimated at 55% and 88% for AN and BN. The adolescent period represents a time of increased risk for disordered eating behaviour, which may also predispose individuals to additional risks that in turn may accumulate across the lifespan.
Early indicators of disordered eating risk, in particular the onset of puberty, have been identified within child and adolescent populations (Johnson et al., 2002; Keel, Fulkerson, & Leon, 1997; Klump et al., 2007). This association has largely been explained by a combination of biological, social, physical and psychological changes associated with the onset of puberty, which were described in Chapter three of this thesis (Culbert, Burt, McGue, Iacono, & Klump, 2009). Body dissatisfaction and low self-esteem, which are known to peak during periods of pubertal change, have also been linked to the development of disordered eating behaviour (Andrist, 2003; Bearman, Presnell, Martinez, & Stice, 2006; Littleton & Ollendick, 2003; O’Dea & Abraham, 1999; Stice, 2002). Conclusions around the influence of hormonal changes and developmental processes in the development of disordered eating remain limited, although it appears that these factors create a degree of vulnerability for young women (Harden, Kretsch, Moore & Mendle, 2014). Yet, the presence of early maladaptive eating behaviours has also been associated with significant developmental outcomes including decelerated growth, delays in puberty and pubertal regression (Campbell & Peebles, 2014). Adolescence may represent a critical period where early intervention can be pertinent in circumventing later risk.

Striegel-Moore and Cachelin (1999) proposed a theoretical model describing dual pathways of risk in the development of disordered eating in youth. One pathway, described as the ‘restraint’ pathway, relates to the internalisation of societal ideals regarding beauty and thinness (Striegel-Moore & Cachelin, 1999). The second pathway, the ‘interpersonal vulnerability’ pathway, relates to the development of disturbances in self-image and social functioning that may arise in the context of decreased parental nurturing (Striegel-Moore & Cachelin, 1999). Although both paths likely lead to the development of disordered eating in young people, it is thought that greater risk is associated with the interactional effects of both paths. Another model that has been well established and validated is the dual pathway model of bulimic pathology (Stice & Agras, 1998; Stice, 2001). This model posits that internalisation of unattainable thin ideals projected through family, peers and the media, contribute to increased body dissatisfaction in women. Body dissatisfaction is hypothesised to then foster dieting or weight control behaviours and chronic negative affect, both of which result in a greater risk of developing bulimic pathology. Dieting behaviours, however,
are also hypothesised to promote negative affect due to perceived failures associated with weight control efforts and low mood resulting from reduced calorie intake (Stice & Agras, 1998). The onset of bulimic behaviours may therefore be precipitated by either extreme dieting behaviours or chronic negative affect, or a combination of these two risk factors. Described pathways represent unique risks associated with the adolescent period, with adolescents potentially more vulnerable to the internalisation of social pressures and attitudes (Choudhury et al., 2006). Such models may help to explain increased onset and prevalence rates of disordered eating behaviours and attitudes during adolescence (Stice, Marti, Shaw & Jaconis, 2009).

Disordered eating behaviours in adolescence have been associated with the continuation of similar maladaptive eating patterns throughout the lifespan, including pregnancy (Kotler, Cohen, Davies, Pine, & Walsh, 2001; Rastam, Gillberg, & Wentz, 2003). Neumark-Sztainer et al. (2011) examined long-term trajectories of disordered eating behaviours in a sample of 2,287 adolescents at 15 years of age. They found, at ten-year follow-up, that eating behaviour remained constant or had increased from adolescence to young adulthood. Slane, Klump, McGue and Iacono (2014) also examined developmental trajectories of disordered eating behaviours and attitudes from 11 years to 25 years of age. They reported significant increases in overall levels of disordered eating and cognitive symptoms across all ages. However, they found that bulimic behaviours were found to increase during adolescence but then level off and become stable from 18 to 25 years of age (Slane et al., 2014). Given that adolescent onset disordered eating is associated with a longer course compared to adult onset, it has been argued that earlier disordered eating behaviours may be associated with greater risks (Hebebrand & Remschmidt, 2001). This emphasises the importance of recognising and attending to disordered eating behaviours presenting in adolescence.

4.4 Reproductive and biological consequences of disordered eating

Eating disorders are associated with significant physical and biological consequences including, endocrine, cardiovascular, skeleton-muscular, gastrointestinal, metabolic and reproductive problems (Kaplan & Woodside, 1987; Sidiropoulos, 2007). In the short-term, these changes serve an adaptive function in
attempts to conserve energy following decreased calorie intake; however, long-term symptoms can be detrimental to overall functioning and wellbeing (Herpertz-Dahlmann, 2008). Biological and reproductive complications are thought to be dependent on the time of onset in relation to puberty, with symptoms occurring prior to or during puberty, associated with pubertal delays, primary amenorrhea and pubertal arrest (Jayasinghe et al., 2008). The long-term impact of these changes for women experiencing persistent symptoms remains unclear. For instance, individuals presenting with fewer symptoms that are lesser in severity have been reported to experience similar risks to those presenting with clinical diagnoses (Austin et al., 2008; Kreipe, Strauss, Hodgman, & Ryan, 1989). This means that even at the lower end of the spectrum, dietary factors and restricted eating patterns may be impacting adversely on positive outcomes and wellbeing (Chamay-Weber et al., 2005).

In some cases, reduced fat levels and resultant decreases in oestrogen production may lead to amenorrhea in women. It is estimated that approximately 68% to 89% of women with AN experience amenorrhea for at least three months during the course of their condition (Hoffman, Zerwas, & Bulik, 2011). Crow, Thursa, Keel, and Mitchell (2002) examined the long-term effects of menstrual cycle abnormalities in 173 women diagnosed with an eating disorder. They found that 60.2% of women had full term births, 5% were premature, 11.2% miscarried and 23.6% experienced induced abortions in later pregnancies. There is some debate around the long-term impacts of menstrual abnormalities or disturbances, with some evidence suggesting that such women may be at an increased risk of fertility problems (Easter, Treasure, & Micali, 2011; Hoffman et al., 2011; Stewart, Robinson, Goldbloom, & Wright, 1990). Empirical findings have since indicated that fertility rates are comparable for women with eating disorders to those in the general population (Bulik et al., 1999; Crow et al., 2002; Kreipe, Churchill, & Strauss, 1989). Nevertheless, findings indicating comparable fertility rates between women with an eating disorder and the general population do not infer an absence of reproductive risks for mothers and infants.

Endocrine abnormalities associated with disordered eating are thought to occur as secondary effects of physical starvation and low caloric intake. Low leptin levels, occurring as a function of physical starvation, are associated with an adaptive response by the hypothalamus and neuroendocrine axis, which in turn result in a
decrease in reproductive and thyroid function (Jayasinghe et al., 2008). This process can result in altered gonadotropin hormone pulsatility, which can contribute to insufficient ovarian stimulation and oestrogen production (Usdan, Khaodhiar, & Apovian, 2008). Furthermore, women with an eating disorder have been shown to have high cortisol levels independent of body mass index (Lawson et al., 2011). Lawson et al. (2011) found that psychological factors, including restraint, eating concerns and body image disturbance, were positively associated with cortisol and peptide levels in women with an eating disorder, independent of individual BMI (Lawson et al., 2011). Resultant decreases in luteinizing hormone and follicle-stimulating hormone may resemble secretory patterns of pre pubertal children (Jayasinghe et al., 2008). Studies utilising ultrasonography in post pubertal women have found that hormonal changes can impact on reproductive functioning and contribute to decreases in ovary and uterus size and length to that observed prior to puberty (Hoffman et al., 2011; Mason, Key, Allan, & Lask, 2007). Hormone levels in women diagnosed with an eating disorder, such as AN, may emulate those observed in prepubescent girls.

Comorbid conditions, such as depression or anxiety, have been shown to contribute to maladaptive changes in the HPA axis and increased maternal corticotrophin-releasing hormone (CRH) leading to greater risks of obstetric complications (Wadhwa et al., 2004). Yet, changes in corticotrophin-releasing hormone (CRH) resulting from physical starvation effects, associated with AN and BN, have also been identified as playing a role in the development of depression (Altemus & Gold, 1992). Some studies have since demonstrated an increase in depressive symptomatic in women undergoing calorie-restricted diets, suggesting that biological or hormonal changes associated with an eating disorder may have dual effects in the development of other conditions (Laessle, Platte, Schweiger, & Pirke, 1996; O’Brien & Vincent, 2003). Whilst promising, further research is required to empirically test this hypothesis so as to better understand the underlying mechanisms of risk. Disordered eating may incur direct biological harms but also predispose women to an accumulation of secondary risks.
It may be argued that biological and reproductive outcomes vary depending on clinical subtypes, with differential pathways of risk potentially existing for AN and BN. In some women, bulimic symptoms have been associated with higher rates of polycystic ovaries, which have been linked to complications during pregnancy including premature births and perinatal mortality (Boomsma et al., 2006; Wolfe, 2005). Changes in glucose metabolism and homeostasis resulting from patterns of binging and purging behaviour can contribute to rapid increases and decreases in blood sugar levels (Micali & Treasure, 2009). Altered glucose metabolism during pregnancy has been associated with increased risks of adverse infant outcomes such as cardiac abnormalities and gestational diabetes (Ong et al., 2008). Women with BN, who may be within a healthy weight range, may be at a higher risk of experiencing cardiac problems in offspring. This is associated with greater metabolic dysfunction compared to underweight women who may be susceptible to problems of foetal growth and growth restriction. Further examination of eating disorder subtypes is required to identify specified pathways of risks.

A tentative model of risk has been proposed by Micali and Treasure (2009) in an attempt to explain pathways from maternal eating disorder to later adverse birth outcomes. They suggested that two potential pathways of risk exist, either through nutritional factors such as poor nutrition, malnourishment and protein deficiency, or through comorbid psychopathology, including anxiety and depression. Poor or under nutrition was hypothesised to restrict protein intake and increase glucocorticoids in foetal circulation, which are thought to increase the risk of low birth weight births. Further research is required to empirically test this hypothesis and develop further understandings of the mechanisms underlying risk of adverse birth outcomes.

4.5 Pregnancy and birth outcomes in women with eating disorders

A recent study revealed that at least one in twenty women experience some form of disordered eating or sub clinical symptoms during pregnancy (Easter et al., 2013). Reproductive and biological complications resulting from disordered eating and physical starvation effects mean that these women may be at an increased risk of adverse birth outcomes. Findings from a large prospective study of Norwegian mothers and infants revealed that women with a current eating disorder were, on
average, younger at the time of birth (26.2 years, SD=4.76) compared to individuals without an eating disorder (29.9 years, SD=4.60) and significantly more likely to report having an unplanned pregnancy (RR: 2.11, CI: 1.64-2.72) (Bulik et al., 2010). This finding indicates that a number of women may be unaware of the potential risks and may experience reduced opportunities for positive behavioural change and nutritional or emotional support (Hoffman et al., 2011).

Physical starvation during pregnancy has been linked to surges in levels of corticotrophin-releasing hormone (CRH) concentrations and consequent changes in the timing of delivery (Herrmann, Siega-Riz, Hobel, Aurora, & Dunkel-Schetter, 2001). Similarly, prenatal stress has been associated with increases in levels of glucocorticoids in infants and changes in CRH associated with an increased risk of adverse birth outcomes (Hales & Barker, 2001; Seckl, 2008; Wadhwa et al., 2004). The prospect of pregnancy, including associated weight gain and physical changes, for women with an eating disorder can represent a significant source of stress and anxiety (Micali & Treasure, 2009). Adverse birth outcomes associated with related hormonal changes may represent secondary effects of sub optimal nutrition or sub clinical eating disorder symptoms (Bulik, 2005). The long-term reproductive or hormonal impacts of adolescent disordered eating are not yet clear and by implication represent an important area for future empirical investigation.

Low maternal weight and weight gain during pregnancy have been linked with restricted growth and development during gestation and a resultant increase in risk of low birth weight births (Franko & Walton, 1993; Katz & Vollenhoven, 2000; Morgan, 1999). Han et al. (2011) conducted a systematic review and meta-analysis of 78 observational studies investigating maternal underweight and risk of low birth weight and preterm births. They found that, for singleton pregnancies, women who were underweight were at an increased risk of low birth weight (RR 1.50, CI: 1.34–1.68) and preterm births (RR 1.21, CI: 1.14–1.28) compared to healthy weight women. Further to this, an association between disordered eating during pregnancy and risk of low birth weight, preterm and small for gestational age births has also been established (Bansil et al., 2008; Martos-Ordonez, 2005; Pasternak et al., 2012). This provides support for the premise that restricted eating and starvation contributes to
reproductive and hormonal changes associated with the development of adverse birth outcomes.

Morrill and Nickols-Richardson (2001) conducted a review of the literature that included study reports, case series, and retrospective studies of pregnancy and birth outcomes of women with BN. They found that women with BN during pregnancy were at an increased risk of low birth weight and preterm births. These findings suggest that disordered eating during pregnancy may be associated with harms for offspring. The large proportion of studies included in the review were retrospective in design and lacking in adequate control or comparison groups, thereby limiting the generalisability of results and increasing the potential for recall bias. Although current evidence tends to indicate greater risk of adverse birth outcomes to women with an eating disorder, some studies have reported conflicting findings or differences in the magnitude of effects (Franko & Walton, 1993; Micali & Treasure, 2009). For instance, Franko et al. (2001) reported that the majority of women with AN or BN, in their study, had infants of normal birth weight and gestational age. However, the absence of a control group meant that comparisons were unable to be made between women with and without an eating disorder. Micali and Treasure (2009) suggested that reported associations between maternal eating disorder and low birth weight births may, in part, be related to low maternal pre-pregnancy BMI or maternal smoking during pregnancy. This suggests that high quality replication studies, which utilise prospective longitudinal data and include a range of relevant covariates, are still required in order to adequately assess these relationships.

High comorbidity rates may also increase the potential for additional or secondary risks in pregnancy (Evans, Heron, Patel, & Wiles, 2007; Liu & Odouli, 2009). Comorbid conditions, such as depression, have been identified as independent predictors of low birth weight, preterm and small for gestational age births (Fransson et al., 2011; Grote et al., 2010; Kelly et al., 2002). There is the potential that up to 82% of women presenting with an eating disorder may be vulnerable to an accumulation of risk through comorbidities (Herzog et al., 1992). Psychological distress associated with either an eating disorder or comorbid condition, such as anxiety or depression, has been linked to deregulation of the HPA axis and increased stimulation of cortisol that in turn increases placental hypo fusion and the restriction
of oxygen to the foetus (Chamay-Weber et al., 2005; Dayan et al., 2006). Alternatively, comorbid depressive symptoms, such as amotivation and anhedonia, may increase the risk of poor maternal health practices through a decreased capacity for maternal self-care essential for healthy births (Grote et al., 2010). Disordered eating may incur direct risks during pregnancy but also predispose women to indirect or secondary risks through increased rates of comorbid diagnoses and maladaptive behaviours.

It has been suggested that recovery prior to conception may reduce risks of adverse birth outcomes (Blais et al., 2000; Fairburn, Stein & Jones, 1992). This premise in part explains observed discrepancies in study findings or comparable estimates of risk between eating disorder samples and the general population (Bansil et al., 2008; Conti, Abraham & Taylor, 1998; Franko et al., 2001). Inconsistencies in study findings may relate to variations in the timing of disordered eating behaviours, the length of behaviours and age of onset. For instance, a number of studies reporting significant effects examined both current and previous disordered eating (Abraham, King, & Llewellyn-Jones, 1994; Koubaa, Hallstrom, Hagenas, & Hirschlerg, 2013). As a result, distinctions between potential proximal and distal risks are limited. It is possible that a proportion of adverse birth outcomes are associated with early harms that contribute to permanent reproductive changes or risks. Research that examines risk of adverse birth outcomes in disordered eating populations at specified time points will help to address noted gaps in the literature.

4.6 The effects of preconception disordered eating on adverse birth outcomes

It is well recognised that maternal nutrition and weight during pregnancy is vital for optimal birth outcomes (Cnattingius et al., 1998). The effects of preconception diet and nutrition on the development of adverse birth outcomes represents a largely under-researched area of knowledge. This signifies an important area of future research, with eating disorders estimated to affect approximately 5% to 7% of women of childbearing age (Micali, Treasure et al., 2007). It is suggested that early maladaptive eating behaviours, occurring prior to conception, incur long-term effects that may alter reproductive development and hormonal patterns (Hoffman et al., 2011; Mason et al., 2007). A longer course associated with early onset of AN has
been associated with greater risks throughout development and possible pregnancy (Hebebrand & Remschmidt, 2001).

Emerging evidence of the long-term impacts of weight and diet throughout development on birth outcomes provides some support for theories indicating the importance of preconception influences (Frederick, Williams, Sales, Martin, & Killien, 2008). Weisman and Misra et al. (2011) conducted a prospective longitudinal study investigating the influence of maternal preconception health predictors on birth weight in a cohort of women in the US. They found that preconception BMI (normal or underweight) ($p=0.016$) and vegetable consumption ($p=0.005$) significantly predicted low birth weight births after adjusting for maternal age, marital status, race and ethnicity. Limited frequencies of singleton births at two year follow up, resulting from a small baseline sample size ($n=115$), meant that reported findings might not be representative of the general population. Irrespective of this, these findings provide preliminary support for theories of preconception reproductive health.

Salihu et al. (2009) examined the association between maternal pre-pregnancy weight and the incidence of spontaneous and medically induced preterm births. Pre-pregnancy weight, assessed during the first pre-natal visit, was categorised as either healthy weight (BMI= 19.5-24.9), mildly underweight (BMI= 17.0-18.5), moderately thin (BMI= 16.0-16.9) and severely thin (BMI= <15.9). Infants of healthy weight mothers weighed, on average, 208g more than infants born to underweight mothers (Mean=3350.6). In addition, underweight mothers were at an increased risk of spontaneous preterm births. Risk of preterm births, with the exception of very preterm births, occurred in a dose response fashion, with decreasing maternal weight increasing risk of preterm births. They suggested that BMI might be an indication of chronic nutritional deficiency and an indicator of weight prior to pregnancy. Their findings suggest that there may be benefit in investigating preconception disordered eating in the development of low birth weight and preterm births.

A number of studies have indicated an increased risk of low birth weight, preterm or small for gestational age births for women with an eating disorder (Abraham et al., 1994; Kouba, Hallstrom, Lindholm, & Hirschberg, 2005; Koubaa et al., 2013; Linna, Raevuori, Haukka, Suokas, & Gissler, 2014). For example, Sollid,
Wisborg, Hjort, and Secher, (2004) reported a two fold increase in risk of low birth weight births for women with a previous eating disorder compared to controls (OR: 2.2, CI: 1.4-3.2). The risk of preterm delivery and small for gestational age births increased to 70% and 80% (OR: 1.7, CI: 1.1-2.6; OR: 1.8, CI: 1.3-2.4). Similarly, Micali and Simonoff et al. (2007) found that women with a history of AN had infants of significantly lower birth weight than the general population ($B=-75.1$, $\beta=-0.016$, $p=0.03$). In contrast, Conti et al. (1998) reported comparable rates of low birth weight births between women with an eating disorder, including AN and BN, and control groups. However, elevated eating disorder psychopathology, based on Bulimia scores on the Eating Disorder Inventory (EDI) was found to be associated with risk of small for gestational age births. This is indicative of early evidence of the effects of preconception disordered eating. Inconsistencies in study findings imply that replication using prospective longitudinal data is needed.

One of the key limitations of the literature relates to how and when pre-pregnancy risks are defined and measured. To date, only one prospective study, conducted by Wentz, Gillberg, Anckarsater, Gillberg, and Rastam (2009), has examined birth outcomes in women with adolescent onset AN at 15 years of age. They found that, at 18 years following their initial assessment, women with adolescent onset AN had offspring of significantly lower birth weight compared to controls. Risk of preterm and small for gestational age births were comparable between women with adolescent onset AN and controls. Only three women in their sample reported active AN during pregnancy, suggesting that disordered eating behaviours in adolescence have consequences for birth outcomes. Nevertheless, a relatively small sample indicates that further clarification and replication is required to generalise from these conclusions. A more detailed systematic review of current evidence examining the effects of preconception disordered eating, including AN and BN, will be presented in the next chapter of this thesis.

A recent systematic review and meta-analysis conducted by Solmi, Sallis, Stahl, Treasure, and Micali (2014) investigated the risk of low birth weight births in women with a history of AN. Fourteen articles were included in their review, with nine selected for meta-analyses. Results from meta-analyses showed a standardised mean difference of -0.19kg (CI: -0.25-0.15, $p=.01$) in birth weight of infants born to
women with past or active AN compared to controls. Their review indicated that women with a history of AN were at an increased risk of low birth weight births. However, low statistical power to detect significant findings, due to the limited number of studies, means that results should be interpreted with caution. It is anticipated that further research exploring the underlying mechanisms or mediators of risk will help to clarify or confirm their findings. Furthermore, synthesis of the literature examining the effects of BN on birth outcomes, such as low birth weight, preterm and small for gestational age births will assist in unearthing greater insight into potential differences between clinical subtypes and pathways of risk.

Increasing prevalence rates of disordered eating and dieting behaviours within young female populations draws a need for further high quality empirical studies (Jones et al., 2001). Examination of adolescent disordered eating signifies an important area of future research. This may allow for opportunities for the development of preventive interventions that aim to target early adolescent risks. The next chapter represents the first study in which the objective is to systematically review the evidence base examining a link between preconception disordered eating and adverse pregnancy outcomes; low birth weight, preterm and small for gestational age births. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and methodology are used to assess overall study quality and study findings in relation to pregnancy and infant risks associated with disordered eating, including AN and BN, occurring prior to pregnancy.

CHAPTER 5: SYSTEMATIC LITERATURE REVIEW

5.1 Chapter overview

This chapter represents the first study of this thesis, which is a systematic review of the current literature examining risk of low birth weight, preterm or small for gestational age births for women with a history disordered eating, including AN or BN. This chapter outlines the procedures and protocols used to guide a systematic search of the literature as well as a discussion of the quality of presented literature and key findings.
5.2 Objectives

The purpose of this systematic review is to examine what is currently known about preconception disordered eating and the risk of low birth weight, preterm and small for gestational age births. Careful examination of the quality of evidence may further outline the need for specific and appropriate research directions. It is proposed that preconception care presents as a logical extension from typical notions of prenatal care, with preventative preconception interventions potentially increasing reproductive health awareness and health behaviour (Bhutta et al., 2011). Potential risks can then be addressed prior to pregnancy and appropriate time can be given for positive behavioural changes to occur (Bhutta et al., 2011). This may decrease the occurrence of preventable adverse birth outcomes and reduce costs and ongoing psychological morbidity associated with the trauma of low birth weight, preterm or small for gestational age births. This systematic review aims to synthesise the current evidence examining the relationship between adolescent disordered eating and later pregnancy outcomes; low birth weight, preterm and small for gestational age births. This review will evaluate research in the context of the proposition that preconception disordered eating behaviour increases the risk of experiencing low birth weight, preterm or small for gestational age birth.

5.3 Methods

Methods used in the current review were based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher, Liberati, Tetzlaff, & Altman, 2009). This is an evidence-based set of items for reporting that aim to help guide and improve the reporting of systematic reviews and meta-analyses.

5.3.1 Criteria for considering studies for this review

Studies were included in the review if they were published in a peer-reviewed journal, were obtainable without cost and were written in English. Inclusion criteria were based on study methodology, with observational designs such as cohort and case-control studies included within the current review. It is anticipated that relatively few prospective longitudinal designs would be available, therefore, case control
studies nested as part of a cohort study and retrospective designs were also included within the review. Studies including retrospective and prospective measurement were included if measuring disordered eating behaviour at some time point prior to conception. All other study designs, such as randomized controlled trials, case reports and reviews were excluded from the review so that the temporal direction of effects could be considered. Given that the research question was quantitative in nature, qualitative studies were also excluded from the review. Studies were deemed appropriate for inclusion in the review if they examined birth outcomes; birth weight or gestational age; of women with a reported eating disorder occurring prior to pregnancy. Studies examining or measuring disordered eating only during or after pregnancy were excluded from the review. Studies that did not include comparison groups, or participants without disordered eating symptoms, were also excluded from the review because they did not allow for comparative effects to be considered.

5.3.2 Search methods for identification of studies

A comprehensive and systematic search of the following electronic databases was conducted with all relevant studies published prior to these dates included within the review:

- Psych Info (searched on 19/07/14)
- Medline (searched on 19/07/14)
- PubMed (searched on 19/07/14)
- CINAHL Complete (searched on 19/07/14)

Refer to Table 1 for a complete list of search terms and databases searched or Appendix B. Studies were retrieved and then screened for duplicates before undertaking a title/abstract screening of articles. Articles, at this point, were excluded based on topic relevance. A full text screen was then conducted to further exclude articles based on study design, timing of disordered eating behaviour occurring during or prior to pregnancy, outcomes of interest, and exposure variables included within studies. For instance, five studies each were excluded as disordered eating was not measured prior to conception or because low birth weight, preterm or small for gestational age births were not included as study outcomes. Furthermore, six studies
were excluded due to the methodological approach used, being qualitative, rather than quantitative in nature. Reference lists of obtained articles retrieved at this stage of the search were cross checked in order to check for any new relevant studies not identified within the systematic search of chosen databases. A final pool of studies was consequentially retrieved for review. Refer to Figure 1: PRISMA diagram for a full description of inclusion criteria used and number of articles selected for review.

5.3.3 Data extraction and quality assessment

Data were extracted and organised in tables to permit comparison between included studies. Relevant information regarding the sample, design, analytic methodology, exposure variables, outcomes and key findings were extracted from these articles and combined into Table 2 and 3 for comparison and analysis. A number of quality indicators were evaluated and a discussion of limitations in relation to the quality of included studies is presented throughout the review. Quality indicators assessed in relation to reviewed studies included degree of bias and generalizability (sample characteristics), study design and methodology, timing of measurement in relation to predictors and outcomes, adequacy of included covariates and transparency in reporting of methodology and results.

5.4 Results

A systematic review of the literature retrieved 14 articles meeting criteria for inclusion. This number was attained from an initial pool of 507 articles obtained from the systematic search. Analysis and comparison of the included articles within the current systematic review are presented in two tables below. Table 2 and 3 outline study populations, design and sample characteristics of included studies as well as exposure and outcome measures, analytic methods and major findings. Refer to Appendix C for technical summaries of study characteristics and results.
Table 1  Search strategy and search terms

<table>
<thead>
<tr>
<th>Psych INFO</th>
<th>Medline complete</th>
<th>Pubmed</th>
<th>CINAHL Complete</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Subject terms=eating disorders or anorexia nervosa or bulimia or Free text=bulimi* or anorexi* or disordered eating</td>
<td>1 Subject terms=eating disorders or anorexia or anorexia nervosa or bulimia or bulimia nervosa or Free text=bulimi* or anorexi* or disordered eating</td>
<td>1 Subject terms=eating disorders or anorexia or anorexia nervosa or bulimia or bulimia nervosa or Free text=anorexi* or bulimi* or disordered eating</td>
<td>1 Subject terms= Eating disorders or Bulimia nervosa or Bulimia or Anorexia Nervosa or Anorexia or Free text=disordered eating or anorexi* or Bulimi*</td>
</tr>
<tr>
<td>2 Subject terms=pregnancy outcomes or premature birth or obstetrical complications or birth weight or Free text= low birth weight or gestational age</td>
<td>2 Subject terms=pregnant birth or birth weight or infant, low birth weight or pregnancy outcome or gestational age or infant, small for gestational age or Free text= obstetric outcome* or birth outcome*</td>
<td>2 Subject terms=infant, low birth weight or infant, very low birth weight or infant extremely low birth weight or gestational age or infant, small for gestational age or infant, premature or infant, extremely premature or Free text= pregnancy outcomes or pregnancy outcomes or low birth weight or preterm birth</td>
<td>2 Subject terms=pregnancy outcomes or Birth weight or childbirth, premature or Infant, low birth weight or Infant, very low birth weight or gestational age or Infant, small for gestational age or Free text=pregnancy outcomes or low birth weight or preterm birth</td>
</tr>
<tr>
<td>3 (1 and 2)</td>
<td>3 (1 and 2)</td>
<td>3 (1 and 2)</td>
<td>3 (1 and 2)</td>
</tr>
</tbody>
</table>
Figure 1: Prisma diagram outlining exclusion criteria and process for inclusion of articles in this review.

# Records retrieved through systematic search: (n = 507 articles)

Phase 1: Removal of duplicates, number of articles removed (n = 186)

Phase 2: Abstract screening, number of studies excluded based on relevance (n = 287)
- Eating disorder measured as outcome (n = 28)
- Exposure/outcome variable irrelevant (n = 180)
- Study design: Literature reviews/RCT’s/case studies (n = 37)
- Consequences of birth outcomes (n = 12)
- Studies did not measure relationship between exposure and outcome (n = 30)

Phase 2: Abstract screening (n = 323)

Phase 3: Full text screening (n = 35)

Phase 3: Full text screen, number of studies excluded (n = 22)
- Variables not measured in preconception (n = 5)
- Outcomes/exposures not relevant or clearly defined (n = 5)
- Lack of comparison group (n = 6)
- Analytic approach used: Qualitative research (n = 6)

Final articles included in systematic review (n = 14)
5.4.1 Country

The majority of included studies were conducted in Scandinavia, with four studies conducted in Sweden and one in Denmark, Norway and Finland respectively. The remaining study samples were obtained from the Netherlands ($n=1$), Scotland ($n=1$), UK ($n=1$), Australia ($n=2$) and New Zealand ($n=2$). Samples were based on Westernised countries, which may limit the generalizability of provided results to non-western countries. In particular, results may not be generalizable to populations within developing countries, with significant differences observed between reported incidences of low birth weight and preterm births for such countries (Kramer, 2003).

5.4.2 Sample size

Five of the 14 included studies obtained study samples over 1,000 participants, representing reasonably large-scale cohort samples. Sample sizes, however, varied considerably between included studies, with five studies including small samples ($n<150$). Some inconsistencies observed between study findings may be explained through differences in obtained sample sizes, with some studies potentially having low power and thus less likely to detect potential study effects.

5.4.3 Design

The majority ($n=11$) of included studies ($n=14$) reported using longitudinal study designs, although eight of the eleven studies that reported using longitudinal designs included data that were retrospectively obtained post pregnancy. Furthermore, few of these studies presented true prospective data with nine of the included studies measuring preconception disordered eating behaviours retrospectively during or after pregnancy. For this reason, there is the potential for a degree of report bias in relation to disordered eating symptoms and an under or over estimations of potential risk. Six of the fourteen studies included in the review used retrospective case control designs or population cohort studies with nested case control samples. One of the fourteen studies reported using a cross sectional design. This limits the nature of any causal interpretations and increases the potential for participant bias and error (Mann, 2003; Schulz & Grimes, 2002).
5.4.4 Measures

5.4.4.1 Exposure measure

The exposure variables of interest for the current review were AN, BN or reported disordered eating behaviours prior to conception. Thirteen of the fourteen included studies examined AN, and nine examined BN prior to conception. Nine of the fourteen studies measured past eating disorders based on diagnostic codes and criteria consistent with the Diagnostic and Statistical Manual of Mental Disorders (DSM) (American Psychiatric Association, 2013) and International Classification of Diseases (ICD) (World Health Organisation, 1992). Three of the fourteen included studies used self-report questionnaires and two studies used the Eating Disorders Inventory (EDI) (Garner, Olmstead, & Polivy, 1983). Four out of fourteen studies did not differentiate between AN or BN subtypes within their sample, resulting in consequent problems of generalizability to specific disordered eating populations. Six of the fourteen studies measured and compared AN and BN clinical subtypes, whilst four of the fourteen studies examined risk of birth outcomes in women with AN.

5.4.4.2 Time of measurement (exposure)

The length of exposure prior to conception varied quite significantly between studies, ranging from three months prior to conception to measures of disordered eating during adolescence. Three of the fourteen studies measured the presence of AN or BN behaviours occurring within the year prior to conception, with one of these only examining AN and BN in the three months prior to pregnancy. Eleven of the fourteen studies did not specify the length and all but one study did not report the mean age of onset of disordered eating behaviours, with any reported or identified history of disordered eating included within the sample. Wentz et al. (2009) represented the only study that specifically examined the impact of teenage onset AN, at 15 years, on later pregnancy outcomes. They reported that the average time between onset of AN and participation in the study was 18.1 years (range: 14.6-21.5 years). Six women (12%) were reported to have experienced AN symptoms during pregnancy.
Although all included studies measured disordered eating behaviours prior to conception, many \((n=7)\) of the studies measured disordered eating prior to and during pregnancy, with previous and current symptoms not differentiated within the analysis. A number of studies reported relapse of disordered eating during pregnancy. For example, Kouba et al. (2005) reported that 22\% \((n=11)\) of women in their study with a history of AN or BN relapsed during pregnancy. Findings from Waugh and Bulik’s (1999) study revealed that 40\% \((n=4)\) of women with a history of AN or BN relapsed during pregnancy. Koubaa et al. (2013) reported that the mean duration of eating disorder was nine years (range: 3 to 15 years) but that the average duration of remission prior to the study was 3.2 years (SD: 3.0 years). Yet, rates of potential relapse for women with an eating disorder during pregnancy were not apparent. Ekeus, Lindberg, Lindblad, and Hjern, (2006) reported that data on AN behaviours occurring during pregnancy were not available in their study, meaning that potential differences between active or remittent AN behaviours could not be assessed.

### 5.4.4.3 Outcome measures

The outcomes of interest were birth weight, low birth weight, gestational age, preterm births and small for gestational age births. Thirteen out of fourteen studies measured infant birth weight as an outcome; however, only six of those studies examined the risk of clearly defined low birth weight, <2500g or below the 25th percentile. The remaining studies examined continuous measures of infant birth weight or mean birth weight; either in grams or kilograms; from women with and without an eating disorder. All of the included studies measured infant gestational age, with the majority of these examining the risk of preterm delivery as defined as <37 weeks. Eight out of fourteen studies reported data in relation to small for gestational age (SGA) births. Small for gestational age was generally measured in Standard Deviations (SD’s) using Z-scores. Small for gestational age infants were generally defined as 2 standard deviations below the mean in relation to birth weight for their gestational age.
5.4.4.4 Covariates

A number of different covariates were measured in each of the studies. Maternal age, maternal BMI, tobacco smoking, and infant sex were commonly included although a number of studies also measured parity and other maternal behaviours or exposures such as weight gain during pregnancy, alcohol use and comorbid mental health diagnoses, including depression during or prior to pregnancy. Seven of the fourteen studies included BMI as a covariate, although only two of the seven studies adjusted for pre-pregnancy BMI (Bulik et al., 2009; Micali, Simonoff et al., 2007). Eight out of fourteen studies included maternal age, nine assessed maternal tobacco smoking and three included parity as covariate in their study. Nine of the fourteen studies reported adjusted analyses that accounted for the potential effects of confounding variables.

5.4.5 Analytic methodology

Most of the studies used logistic or linear regression to examine the relationship between current or previous disordered eating and the likelihood of adverse pregnancy outcomes. Odds Ratios (OR) or Relative Risk (RR) with 95% Confidence Intervals (CI) were reported in the majority of studies. The remaining five studies measured mean group differences and group frequencies, using T-Tests, Chi Square analyses or Fisher’s exact test, to determine potential differences in frequencies in low birth weight, preterm and small for gestational age births between disordered eating and control groups.

5.4.6 Relevant findings

5.4.6.1 Birth weight

All of the included studies examined mean birth weight or low birth weight as an outcome. Of the nine studies that analysed population risk, three reported a significant increase in risk of low birth weight births to women with a previous eating disorder (Eagles, Lee, Raja, Millar, & Bhattacharya, 2012; Linna et al., 2014; Sollid et al., 2004). All of those studies utilised clinical samples comprising of women with a
history of AN or a diagnosed eating disorder. Eagles et al. (2012) reported a significant increase in risk of low birth weight births to women with a history of AN (OR: 1.89, CI: 1.10–3.23), although found that this was no longer significant after adjusting for BMI (1.61, CI: 0.89–2.90). Two large studies reported significant effects after adjusting for potential covariates, including maternal age, smoking and BMI (Sollid et al., 2004; Linna et al., 2014). They reported a two-fold increase in risk of low birth weight births after adjusting for potential covariates (OR: 2.2, CI: 1.4-3.2; OR: 2.05, CI: 1.23-3.40); although, both studies did not include maternal BMI as a potential confounding variable in their analyses. Only one of two those studies (Linna et al., 2014) differentiated between AN and BN, reporting non-significant effects for women with a history of BN. Two community, and three clinical studies reported non-significant increases in risk of low birth weight births to women with a history of disordered eating.

Of the thirteen studies that analysed group mean differences in birth weight, nine reported significantly lower birth weight for women with a history of disordered eating compared to controls. Eight studies reported significantly lower infant mean birth weight for women with AN compared to women without an eating disorder. Two out of eight studies, however, reported non-significant findings when adjusting for maternal BMI (Eagles et al., 2012; Micali, Simonoff et al., 2007). Two out of thirteen studies reported non-significant differences in mean birth weight for women with a history of AN (Bulik et al., 2009; Micali et al., 2012). Both of these studies utilised retrospective data from large community samples. Four of the thirteen studies specifically examined differences in mean birth weight in women with and without a history of BN, of which, three reported non-significant effects. Linna et al. (2014) reported a significantly lower mean birth weight in women with a history of BN compared to women without an eating disorder (mean: 3464g; adjusted $p = .037$) in their prospective clinical sample. Overall, the current literature suggests that women with a history of AN are at an increased risk of giving birth to a child with lower mean birth weight. Yet, conflicting findings mean that conclusions remain inconclusive, particularly in relation to sub clinical or community samples.
<table>
<thead>
<tr>
<th>Study #</th>
<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>Sample size</th>
<th>Sample</th>
<th>Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Abraham et al.</td>
<td>1994</td>
<td>Australia</td>
<td><em>n</em>=100 (ED=24)</td>
<td>Community</td>
<td>Cross sectional</td>
</tr>
<tr>
<td>2</td>
<td>Bulik et al.</td>
<td>1999</td>
<td>New Zealand</td>
<td>AN <em>n</em>=66, controls <em>n</em>=98</td>
<td>Clinical</td>
<td>Historical observation cohort paired with a case control study</td>
</tr>
<tr>
<td>3</td>
<td>Bulik et al.</td>
<td>2009</td>
<td>Norway</td>
<td><em>n</em>=35929 (AN=35, BN=304)</td>
<td>Community</td>
<td>Prospective cohort</td>
</tr>
<tr>
<td>4</td>
<td>Conti et al.</td>
<td>1998</td>
<td>Australia</td>
<td>ED <em>n</em>=88, controls <em>n</em>=86</td>
<td>Community</td>
<td>Case control</td>
</tr>
<tr>
<td>5</td>
<td>Eagles et al.</td>
<td>2012</td>
<td>Scotland</td>
<td><em>n</em>=804 (ED=134)</td>
<td>Clinical</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>6</td>
<td>Ekeus et al.</td>
<td>2006</td>
<td>Sweden</td>
<td><em>n</em>=828582 (ED=1000)</td>
<td>Clinical</td>
<td>Prospective cohort</td>
</tr>
<tr>
<td>7</td>
<td>Kouba et al.</td>
<td>2005</td>
<td>Sweden</td>
<td>ED <em>n</em>=49, controls <em>n</em>=68</td>
<td>Community</td>
<td>Case control</td>
</tr>
<tr>
<td>8</td>
<td>Koubaa et al.</td>
<td>2013</td>
<td>Sweden</td>
<td>ED <em>n</em>=47, controls <em>n</em>=65</td>
<td>Community</td>
<td>Longitudinal cohort with nested case control</td>
</tr>
<tr>
<td>9</td>
<td>Linna et al.</td>
<td>2014</td>
<td>Finland</td>
<td><em>n</em>=7397 (AN=302, BN=724)</td>
<td>Clinical</td>
<td>Prospective longitudinal</td>
</tr>
<tr>
<td>10</td>
<td>Micali, Simonoff et al.</td>
<td>2007</td>
<td>UK</td>
<td><em>n</em>=12, 254 (AN=171, BN=199)</td>
<td>Community</td>
<td>Prospective cohort</td>
</tr>
<tr>
<td>11</td>
<td>Micali et al.</td>
<td>2012</td>
<td>Netherlands</td>
<td><em>n</em>=5256 (AN=129, BN=209)</td>
<td>Community</td>
<td>Prospective cohort</td>
</tr>
<tr>
<td>12</td>
<td>Sollid et al.</td>
<td>2004</td>
<td>Denmark</td>
<td><em>n</em>=1202 (ED=302)</td>
<td>Clinical</td>
<td>Prospective follow up</td>
</tr>
<tr>
<td>13</td>
<td>Waugh &amp; Bulik</td>
<td>1999</td>
<td>New Zealand</td>
<td>ED <em>n</em>=10, controls <em>n</em>=10</td>
<td>Clinical</td>
<td>Case Control</td>
</tr>
<tr>
<td>14</td>
<td>Wentz et al.</td>
<td>2009</td>
<td>Sweden</td>
<td>AN <em>n</em>=51, controls <em>n</em>=51</td>
<td>Community</td>
<td>Case control</td>
</tr>
</tbody>
</table>

Note: Study design reflects the overall design of the included study. The timing of data collection (prospective/retrospective) for each predictor and outcome variable was reported to differ from the overall study design in some studies.
5.4.6.2 Preterm births

All of the studies included a measure of gestational age or preterm birth. Three out of fourteen studies reported an increased risk of preterm births in women with an eating disorder (Bulik et al., 1999; Linna et al., 2014; Sollid et al., 2004). All three of those studies utilised clinical samples of women with AN or BN and two of those including large samples of \( n > 1000 \). Linna et al. (2014) reported a relatively moderate effect size (OR: 3.51, CI: 1.02-12.09), based on guidelines described by Chen, Cohen and Chen (2010), which was reported to increase when adjusting for relevant covariates (OR: 4.59, CI: 1.25-16.87). Sollid et al. (2004) reported smaller effects (OR: 1.7, CI: 1.1-2.6) that remained relatively unchanged when adjusting for covariates in their analyses. Bulik et al. (1999) reported significantly more preterm births in women with AN compared to controls (chi square: 3.48, \( p < 0.05 \)). All of the remaining studies (\( n=11 \)) reported non-significant differences in the risk of preterm births for women with a history of disordered eating compared to controls. Eagles et al. (2012) reported an increased although non-significant risk of preterm births for women with a history of AN. Two studies (Bulik et al., 2009; Ekeus et al., 2006) reported a reduced risk of preterm births to women with a history of AN (RR: 0.83, CI: 0.12-5.9; OR: 0.8, CI: 0.4–1.5). None of the included studies reported a significant increase in risk of preterm births for women with diagnosed with BN.

5.4.6.3 Small for gestational age births

Nine of the fourteen studies measured risk of small for gestational age births. Four of the nine studies reported an increase in risk of small for gestational age births to women with a history of disordered eating, although two of those studies did not differentiate between AN and BN sub types. Two of the four studies revealing significant results reported an increased risk of small for gestational age births in women with AN, whilst the remaining two studies did not differentiate between AN and BN subtypes. Two of the four studies that reported significant findings in women with AN used large prospective clinical samples (Linna et al., 2014; Sollid et al., 2004). The remaining two studies represented retrospective community based designs (Conti et al., 1998; Koubaa et al., 2013). Effect sizes varied among studies although larger effects were reported by Linna et al. (2014) and Sollid et al. (2004) which both...
utilised clinical samples (OR: 2.20, CI: 1.23-3.93; OR: 1.8, CI: 1.3-2.4). These effects remained significant when adjusting for potential covariates such as maternal age, smoking status and parity. Conti et al. (1998) reported a significant, although smaller, increase in risk of small for gestational age births for women reporting higher psychopathology based on Bulimia scores of the EDI (OR: 1.69, CI: 1.22-2.35). Six of the nine studies reported no association between preconception disordered eating, either AN or BN, and small for gestational age births. None studies that specifically examined risk of small for gestational age births in women with a history of BN (n=3) reported significant effects.

5.4.6.4 Birth outcomes in AN and BN subtypes

All of the studies (n=14) assessed AN as a predictor of adverse birth outcomes in women, although only ten studies included both AN and BN subtypes. Four out of ten of those studies did not differentiate between women with AN and BN in their analyses. Only one out of the four studies that differentiated AN and BN in their analyses reported significantly lower infant mean birth weight in women with a history of BN compared to women without an eating disorder (mean: 3464g; adjusted p=.037) (Linna et al. 2014). In contrast, only one out of ten studies reported non-significant differences in mean infant birth weight to women with a history of AN. Only one community case-control study, conducted by Conti et al. (1998), reported a significant increase in risk of small for gestational age births in women with a history of BN (OR: 1.69, CI: 1.22-2.35). However, these effects, which were relatively small in magnitude, were based on scores on the Bulimia subscale of the Eating Disorder Inventory (EDI) that represents only an indicator of population-based disordered eating characteristics and is not indicative of a diagnosis of BN (Garner et al., 1983). Three out of four studies reported non-significant estimates of risk of small for gestational age births to women with a history of BN. Two studies reported a significant increase in small for gestational age births to women with a history of AN (Koubaa et al., 2013; Linna et al., 2014) compared to four studies that reported comparable estimates of risk.
None of the studies that examined risk associated with BN reported a significant increase in risk of low birth weight or preterm births. None of the included studies examined risk of adverse birth outcomes in a sample of only BN. Two out of four clinical studies that examined risk of low birth weight in women with a history of AN reported significant increases in risk (Eagles et al. 2012; Linna et al. 2014). Eagles et al. (2012) and Micali, Simonoff et al. (2007) reported that the risk of low birth weight births was no longer significant when accounting for BMI. Four out of five studies reported non-significant increases in risk of low birth weight births in women with AN. Linna et al. (2014) reported significant increases in risk of preterm births to women with AN (adjusted OR: 4.59, CI: 1.25-16.87), whilst Bulik et al. (1999) reported significantly more preterm births for women with AN compared to those without an eating disorder (chi square: 3.48, p< 0.05). Eight of the ten studies reported non-significant effects.

5.5 Discussion

The purpose of this review was to examine the available evidence on the effects of preconception disordered eating on risk of adverse pregnancy outcomes. A systematic search of the literature revealed 14 studies meeting criteria for inclusion within the review. While a number of studies provided evidence of an increased risk of delivering a low birth weight infant in women with a history of disordered eating, overall results were mixed. Comparison of study findings provided some evidence of an increase in risk of preterm births for women with a history of disordered eating, yet further research is required to clarify and confirm these results. Examination of findings suggested that the risk of low birth weight and preterm births is associated with AN, compared to BN subtypes, although few studies specifically examined risk within bulimic populations. One out of three studies reported an increase in risk of small for gestational age births based on Bulimia scores on the EDI (Conti et al., 1998), although when measured discretely, BN was not associated with an increased risk of low birth weight, preterm or small for gestational age births. Significant differences were not observed in studies examining outcomes in active versus remitting disordered eating samples.
Overall, findings suggest some preliminary evidence of possible long-term pregnancy risk for women with a history of disordered eating. However, the potential for type I error, or incorrectly reporting significant effects, needs to be considered when interpreting these findings. It is possible that confounding variables, such as parity, multiple births, maternal stress or comorbid substance use, may account for reported findings or reported increases in risk. Pre-pregnancy BMI has been identified as an independent predictor of low birth weight and preterm births (Frederick et al., 2008; Goldenberg & Culhane, 2007). Significant increases in low birth weight and preterm births reported by Linna et al. (2014) and Solliid et al. (2004) may be explained by inadequate adjustment of BMI. Micali and Simonoff et al. (2007) and Eagles et al. (2012) both reported significantly lower mean infant birth weight to women with a history of AN, yet, this effect was no longer non-significant when adjusting for BMI. In contrast, Abraham et al. (1994), Bulik et al. (1999), Kouba et al. (2005) and Koubaa et al. (2013) all reported significant differences in mean birth weight when adjusting for maternal BMI.

Adequate adjustment for confounding variables was not consistent across all included studies with some accounting for some but not all of these factors. For instance, Waugh and Bulik (1999) used a small sample ($n=20$) and did not adjust for potential confounders, providing a likely explanation for significant differences in birth weight in women with a previous eating disorder compared to controls. In contrast, Solliid et al. (2004, $n=1202$) reported a smaller difference in birth weight after adjusting for gestational age. Significant findings reported in other studies may have resulted from inadequate adjustment of these factors. Significant findings reported within studies that have accounted for a number of potential covariates, such as Solliid et al. (2004), provide more convincing evidence of risk of low birth weight, preterm and small for gestational age births. There is the potential that for some studies, inadequate adjustment of covariates such as parity or maternal smoking may have led to incorrect rejection of the null hypothesis. Parity has been shown to alter risk of preterm births, whilst factors such as tobacco smoking and substance use have been linked to incidences of low birth, preterm and small for gestational age births (Ananth, Misra, Demissie, & Smulian, 2001; Astolfi & Zonta, 1999; Kelly et al., 2002). Significant increases in risk of preterm births reported by Bulik et al. (1999), for example, may have resulted from inadequate adjustment of these variables.
Explanations in relation to potential pathways or mechanisms of risk were rarely explored within included studies. It may be that low birth weight, preterm or small for gestational age births are mediated by other antenatal factors, such as body weight or BMI, or through antenatal disordered eating. It may be that adverse outcomes occur as a result of chronic early onset AN (Hebebrand & Remschmidt, 2001). Alternatively, it may be that preconception disordered eating, such as AN, contributes a partial direct contribution to later pregnancy risk, occurring as a result of early changes or damage to the reproductive system (Finfgeld, 2002). These findings support the rationale for the development of preventative interventions targeting eating behaviours prior to conception. So far, little research has specifically examined the impact of adolescent disordered eating on later pregnancy outcomes.

In fact, only one study included in the review measured teenage onset AN (Wentz et al., 2009). 12% of participants within the study reported ongoing AN during pregnancy. Despite use of prospective data, this study had a small sample \( n=102 \) and limited information regarding confounding variables. Remaining studies in the review were non-specific with regard to the timeframe of history of disordered eating behaviour, ranging from over ten years to three months prior to pregnancy. Further analysis of adolescent onset disordered eating using prospective longitudinal data are needed to provide a more accurate picture in relation to ongoing risk and thereby help to inform noted gaps within preventative interventions. This represents an area requiring further research to clarify the influence of adolescent disordered on later pregnancy and birth outcomes.

One of the main strengths of the current review is the inclusion of studies examining both individuals with AN and/or BN. This has allowed for greater comparison of differences between AN and BN subtypes in the development of adverse infant outcomes. A number of literature reviews have compared these outcomes in women with AN (Solmi et al., 2014) or BN (Morrill & Nickols-Richardson, 2001) although none so far have compared potential differences in outcomes between clinical subtypes. Similar etiological paths of risk may exist in some cases, with some behaviour such a restrictive eating and purging commonly experienced by women with AN and BN (Tozzi et al., 2005). Despite this, significant
differences between clinical classifications and associated features, with women with BN more likely to be within the healthy weight range, means that different reproductive outcomes may also occur (Garner et al., 1985). For this reason comparison of such findings between clinical subtypes within the literature is a real strength.

5.5.1 Substantive limitations in the studies reviewed

A limitation of the current evidence base relates to the timing of measurement in relation to disordered eating and length of exposure. Many studies measured disordered eating immediately prior to pregnancy or did not specify whether individuals were currently engaging in disordered eating behaviour or had ceased prior to pregnancy. Bulik et al. (2009), for instance, measured AN and BN during pregnancy and the six months prior to pregnancy. Waugh and Bulik (1999) reported than four women with a previous eating disorder (40%) relapsed during pregnancy, whilst Kouba et al. (2005) reported that 11 (22.45%) women with a previous eating disorder relapsed. Associated findings are unlikely to accurately capture preconception risks or differentiate between risks occurring in preconception from those associated with antenatal behaviours. Different pathways or mechanisms of risk exist for those engaging in disordered eating during pregnancy compared to those that cease such behaviours prior to conception.
<table>
<thead>
<tr>
<th>Study #</th>
<th>Study</th>
<th>Exposure variable &amp; measure</th>
<th>Time of measurement (exposure)</th>
<th>Outcome measure</th>
<th>Covariates</th>
<th>Analytic methodology</th>
<th>Relevant Findings</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Abraham et al. (1994)</td>
<td>Disordered eating, body weight and eating behaviour before and during pregnancy (Self-report)</td>
<td>Retrospective: Questionnaires completed 3 days after birth. &quot;Do you think you have or have had problems with disordered eating?&quot; (NST &amp; NSD)</td>
<td>Birth weight (kg) &amp; Low birth Weight (below the 25th percentile) (Hospital records)</td>
<td>Maternal BMI, attitudes to weight gain and weight gain during pregnancy</td>
<td>Chi squared analysis</td>
<td>Disordered eating and low birth weight births (chi square: 6.33; p &lt; 0.02)</td>
<td>Retrospective. Small sample size. Lack of validated measures of disordered eating. Did not differentiate between AN and BN subtypes.</td>
</tr>
<tr>
<td>2</td>
<td>Bulik et al. (1999)</td>
<td>History of AN (DSM criteria)</td>
<td>Retrospective: Cases obtained from records from eating disorder service between 1981-1984 (NST &amp; NSD)</td>
<td>Gestational weight (grams), preterm birth and SGA (self-report)</td>
<td>BMI, fertility treatment, maternal age</td>
<td>Comparison between groups using chi-square or fisher exact test</td>
<td>AN and preterm births (chi square: 3.48, p&lt; 0.05) and lower average birth weight (t value: 6.4, p&lt;0.01). No significant differences in risk of SGA births. No differences between active versus remitted groups</td>
<td>Retrospective. Small sample size. Limited statistical power</td>
</tr>
<tr>
<td>3</td>
<td>Bulik et al. (2009)</td>
<td>AN, BN, binge eating disorder and EDNOS (DSM criteria)</td>
<td>Retrospective: Recruited at 18 weeks gestation. Data on ED occurring 6 months prior to pregnancy (NST &amp; NSD)</td>
<td>Birth weight, low Birth Weight, preterm births (&lt;37 weeks) &amp; SGA (Medical birth registry)</td>
<td>Smoking, household income, education, parity, maternal age, maternal pre-pregnancy BMI, gestational weight gain</td>
<td>A Poisson Regression (Relative risk)</td>
<td>No significant differences. AN and preterm birth (RR: 0.83, CI: 0.12-5-9) &amp; SGA (RR: 0.87, CI: 0.3-2-5). BN and LBW (RR: 1.5, CI: 0.85-2.8), preterm birth (RR: 0.86, CI: 0.47-1.6) &amp; SGA (RR: 1.1, CI: 0.73-1.6)</td>
<td>Retrospective. Low participation rate (42%). Limited statistical power. Timing of measurement</td>
</tr>
<tr>
<td>4</td>
<td>Conti et al. (1998)</td>
<td>AN, BN and EDNOS (EDI and EDE)</td>
<td>Retrospective: ED data obtained one week post partum in relation to ED behaviour occurring 12 months prior to pregnancy (NST &amp; NSD)</td>
<td>Low Birth Weight (~2500g), preterm birth &amp; SGA (Birth register)</td>
<td>Maternal smoking, alcohol use and caffeine use.</td>
<td>Logistic Regression</td>
<td>ED not associated with significant risk of low birth weight or preterm births. ED (based on Bulimia scores on EDI) and SGA (OR: 1.69, CI: 1.22-2.35)</td>
<td>Retrospective. Small sample size. Attrition rates higher among women delivering SGA infants. Timing of measurement</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Case inclusion criteria</td>
<td>Follow-up</td>
<td>Outcomes</td>
<td>Statistical methods</td>
<td>Logistic or Multiple Regression</td>
<td>Comments</td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td>--------</td>
<td>-------------------------</td>
<td>-----------</td>
<td>----------</td>
<td>---------------------</td>
<td>---------------------------------</td>
<td>----------</td>
<td></td>
</tr>
<tr>
<td>Eagles et al. (2012)</td>
<td>Prospective</td>
<td>ED presenting from 1965 until 2007. Further ED data obtained from females &lt;13 presenting in psychiatric services from 200-2007 (NST &amp; NSD)</td>
<td>Preterm delivery (&lt;37 weeks) and Low Birth Weight (&lt;2500g) (Aberdeen Maternity and Neonatal Databank- AMND)</td>
<td>BMI, smoking, social class, marital status and pregnancy related events</td>
<td>Univariate conditional Logistic Regression</td>
<td>AN and LBW (unadjusted OR: 1.89, CI: 1.10–3.23 and adjusted RR: 1.61, CI: 0.89–2.90). No significant difference in risk of preterm births (RR: 1.30, CI: 0.71–2.39)</td>
<td>Attrition rates (65% of the original sample). Timing of measurement</td>
<td></td>
</tr>
<tr>
<td>Ekeus et al. (2006)</td>
<td>Prospective</td>
<td>Diagnosis of AN between 1973-1996 for women aged 10 years or over who gave birth during 1983-2002. (NST &amp; NSD)</td>
<td>Birth weight (grams), gestational age, SGA (SDs according to birth weight curve) (Swedish medical birth register)</td>
<td>Year of birth of child, maternal age and cigarette smoking</td>
<td>Logistic Regression and Multiple Regression</td>
<td>AN and Preterm births (OR: 0.8, CI: 0.4–1.5), SGA (OR: 1.0, CI: 0.7–1.4) &amp; Perinatal death (OR: 0.7, CI: 0.2–2.7). Significantly lower mean birth weight for AN group (3387g) compared to controls (3431g)</td>
<td>Bias and sample characteristics. Timing of measurement</td>
<td></td>
</tr>
<tr>
<td>Kouba et al. (2005)</td>
<td>Retrospective</td>
<td>Past or current AN, BN and EDNOS (DSM criteria)</td>
<td>Birth weight (grams), preterm births (Medical records) and SGA births</td>
<td>Maternal BMI and cigarette smoking</td>
<td>1-way analysis of variance of chi squared test</td>
<td>Past or current eating disorders and mean infant birth weight (P&lt;0.01) and SGA (P&lt;0.05). No significant differences in preterm births (p&lt;0.33)</td>
<td>Retrospective. Small sample size. Timing of measurement</td>
<td></td>
</tr>
<tr>
<td>Koubaa et al. (2013)</td>
<td>Past or current eating disorder (AN, BN or EDNOS) (DSM criteria and medical records)</td>
<td>Retrospective: Past ED identified during screening interviews at 10 weeks gestation. Length of ED (mean: 9yrs, range: 3-15 yrs.) n=11 ED relapse during pregnancy (NST)</td>
<td>Birth weight (kg), gestational age &amp; SGA (Medical records)</td>
<td>BMI, child's sex and maternal age</td>
<td>General linear model</td>
<td>AN and mean birth weight (SD: -0.66, CI: -1.25 -0.06) and SGA. BN not associated with significant differences in birth weight (SD: -0.2, CI: -1.24-0.6). Gestational age similar between groups</td>
<td>Retrospective. Small sample size. Timing of measurement</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Title</td>
<td>Study Design</td>
<td>Time Period</td>
<td>Maternal Characteristics</td>
<td>Outcome</td>
<td>Method</td>
<td>Results</td>
<td>Notes</td>
</tr>
<tr>
<td>-------</td>
<td>-------</td>
<td>--------------</td>
<td>-------------</td>
<td>--------------------------</td>
<td>---------</td>
<td>--------</td>
<td>---------</td>
<td>-------</td>
</tr>
<tr>
<td>9</td>
<td>Linna et al. (2014)</td>
<td>Lifetime eating disorders; AN, BN and binge eating disorder (ICD-10)</td>
<td>Prospective: Individuals attending ED clinic from 1995-2010 (NST &amp; NSD)</td>
<td>Gestational age, premature and very premature births (&lt;37 weeks, &lt;28 weeks). Birth weight and very low birth weight (&lt;2500g, &lt;1500g), &amp; SGA (Medical birth register)</td>
<td>Maternal age, parity, marital status &amp; smoking status</td>
<td>Linear Regression and Logistic Regression</td>
<td>AN and SGA (unadjusted OR: 2.09, CI: 1.17-3.73 and adjusted OR: 2.20, CI: 1.23-3.93)<em>, very preterm birth (unadjusted OR: 3.51, CI: 1.02-12.09 and adjusted OR: 4.59, CI: 1.25-16.87)</em>, and LBW (unadjusted OR: 2.05, CI: 1.23-3.40 and adjusted OR: 2.16, CI: 1.3-3.58)*. BN and SGA (OR: 1.51, CI: 0.92-2.48), Preterm birth (OR: 1.28, CI: 0.85-1.91) and LBW (OR: 1.37 CI: 0.90-2.07)</td>
<td>Bias and sample characteristics. Inadequate adjustment of confounding variables</td>
</tr>
<tr>
<td>10</td>
<td>Micali, Simonoff et al. (2007)</td>
<td>Current or past anorexia nervosa and bulimia nervosa (Self-report)</td>
<td>Retrospective: ED Measured at 12 weeks gestation (current or past history) (NST &amp; NSD)</td>
<td>Birth weight (grams), gestational age (&lt;37 weeks) (Obstetric records)</td>
<td>Psychiatric history (depression/schizophrenia), alcohol and smoking, parity, maternal age, employment and relationship status, Pre-pregnancy BMI</td>
<td>Bivariate Linear Regression</td>
<td>AN and average birth weight (adjusted OR: -75.1, CI: -143.6--6.5). No significant difference in SGA and preterm births.</td>
<td>Retrospective. Lack of statistical power. Measurement of ED symptoms</td>
</tr>
<tr>
<td>11</td>
<td>Micali et al. (2012)</td>
<td>Lifetime anorexia, lifetime bulimia, lifetime anorexia and bulimia (Self-report)</td>
<td>Retrospective: ED measured at 20 weeks gestation. Data on ED ever or in the past year obtained (NST &amp; NSD)</td>
<td>Birth weight (grams), premature birth (&lt;37 weeks) &amp; SGA (Obtained prospectively from midwife and hospital registers)</td>
<td>Depression, anxiety, psychosis &amp; mania, maternal age, education, ethnicity, pregnancy weight/height, maternal smoking &amp; alcohol use</td>
<td>Logistic Regression</td>
<td>No significant differences in mean birth weight, preterm or small for gestational age births</td>
<td>Retrospective. Large proportion of missing data. Lack of statistical power. Did not differentiate between AN and BN subtypes</td>
</tr>
<tr>
<td>Study</td>
<td>Authors</td>
<td>Design</td>
<td>Exposure</td>
<td>Outcome</td>
<td>Method</td>
<td>Results</td>
<td>Limitations</td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td>---------</td>
<td>--------</td>
<td>----------</td>
<td>---------</td>
<td>--------</td>
<td>---------</td>
<td>-------------</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Sollid et al. (2004)</td>
<td>Prospective: ED data obtained from Danish Psychiatric Central Register from 1969 to women giving birth from 1973 to 1993. Participants hospitalised for an ED within 8 years prior to conception (NST &amp; NSD)</td>
<td>Low birth weight (&lt;2500g), preterm birth (&lt;37 weeks) &amp; SGA (Medical birth register)</td>
<td>Maternal age, parity and marital status, sex of child, smoking status</td>
<td>Multiple Linear Regression</td>
<td>ED and LBW (OR: 2.2, CI: 1.4-3.2), preterm (OR: 1.7, CI: 1.1-2.6) and SGA births (OR: 1.8, CI: 1.3-2.4). No difference reported in findings after adjusting for covariates</td>
<td>Inadequate adjustment of confounding variables. Did not differentiate between AN and BN subtypes</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Waugh &amp; Bulik (1999)</td>
<td>Retrospective: Measured during May and August 1995 (NST &amp; NSD)</td>
<td>Birth weight (grams) and gestational age (&lt;39 weeks)</td>
<td>Smoking and alcohol</td>
<td>Comparison of means: chi square analyses</td>
<td>ED infants were 13% (523.5g) lighter in weight than controls. No difference in birth weight of infants born to mothers with active ED versus non symptomatic. No differences in preterm births</td>
<td>Retrospective. Small sample size. Inadequate adjustment for confounding variables. Did not differentiate between AN and BN subtypes</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Wentz et al. (2009)</td>
<td>Prospective: Individuals born in 1970 and living in Sweden in 1985 up to 1989. Participants followed at 21, 24 and 32 years of age. Mean time between ED onset and study 18.1 years (range: 14.6-21.5yrs)</td>
<td>Birth weight (grams), preterm birth (&lt;37 weeks) (Self-report)</td>
<td></td>
<td>Comparison of group frequencies: chi-square/Fisher’ s exact test and Mann Whitney test</td>
<td>AN and average birth weight (AN: 3,347.9g; median: 3,400; SD: 548.4, p&lt; .03). No significant differences in preterm births</td>
<td>Small sample size. Inadequate adjustment for confounding variables</td>
<td></td>
</tr>
</tbody>
</table>

Note: Results reported in bold represent significant findings

Note: NST= Timing, or age of onset of disordered eating behaviour, was not specified. NSD= The duration of disordered eating behaviour was not specified.

Note: Exposure measures were Eating Disorders Inventory (EDI), Diagnostic and Statistical Manual of Mental Disorders (DSM) and World Health Organisation Classification of Diseases (ICD)
Moreover, only one of the fourteen studies included in the review (Wentz et al., 2009) specifically assessed the effects of adolescent onset AN on later pregnancy outcomes. Whilst some studies, such as Eagles et al. (2012) and Ekeus et al. (2006), collected data during adolescence, analysis of preconception AN were not limited to the adolescent period. The specific impacts of adolescent onset disordered eating on pregnancy outcomes thereby remains a largely under-research area of knowledge. Adolescent onset AN has been associated with a longer course compared to adult onset, potentially incurring greater risks or an accumulation of risk through extended nutritional deprivation and increased vulnerabilities to comorbid conditions such as anxiety or depression (Hebebrand & Remschmidt, 2001; Swanson et al., 2011). Further examination of clearly defined adolescent onset disordered eating may provide additional information in relation to developmental risks and later pregnancy outcomes. This study attempts to address noted limitations related to the timing of measurement of disordered eating by utilising longitudinal data obtained at specified time points across development so as to examine the specific effects of adolescent disordered on pregnancy outcomes in young adulthood.

Transparency in reporting of methodology and results is an important indicator of the quality of presented research (Needleman et al., 2008). This varied across reviewed studies, with the severity of disordered eating symptoms not clearly reported in each study. This may be particularly relevant when comparing findings obtained from clinical verse community populations, where the severity of symptoms is likely to vary. There may be an underestimation of symptoms within population-based samples, with the inclusion of more sub clinical cases potentially diluting reported findings (Micali, Simonoff, et al., 2007). This may explain non-significant findings reported within some community-based samples (Bulik et al., 2009; Wentz et al., 2009). Differences in samples and symptom severity might also explain results in relation to low birth weight and preterm births, with significant increases in risk observed only in studies utilising clinical samples. Clinical samples may be more likely to include more severe cases, increasing the likelihood of obtaining significant findings. It may also be that the likelihood of preterm births increases with the severity of disordered eating. Given that significant increases in small for gestational age births were observed in both community and clinical studies, it may be suggested that even sub clinical symptoms pose a risk to later pregnancies.
Transparency in the reporting of study procedures and samples, particularly in relation to parity or twin births, appeared to be lacking in some studies. A number of studies obtained data from multiple pregnancies, with birth order and parity not clearly reported within some studies. Findings may be influenced by primiparity and multiparity, with birth outcomes generally more favourable for multiparae compared to primiparae women, or those who are giving birth for the first time (Kramer, 1987). Previous births have been shown to impact on following pregnancies, which may result in altered pathways of risk (Goldenberg et al., 2008). An increased risk of low birth weight, reduced birth weight or small for gestational age births have been observed in nulliparous, compared to multiparous, women (Kramer, 1987; Shah, 2010). Increased risk for nulliparous women has been associated with poorer overall health and nutritional status, higher rates of smoking, low pre-pregnancy weight and inadequate prenatal care (Shah, 2010). It may be that findings from studies including women of mixed parities are not generalizable to the general population, or those women pregnant for the first time.

Although most of the studies included only singleton births within their samples, many of the studies did not clearly report on multiple or twin births. In such cases, it is unclear whether these infants were included within study samples. The occurrence of multiple or twin births is likely to have influenced reported results, with multiple gestations shown to independently increase the likelihood of low birth weight and preterm infants (Blondel et al., 2002; Blondel et al., 2006). Greater transparency in relation to the methods and analyses undertaken in included studies may help to clarify the quality or credibility of reported findings (Simmons, Nelson & Simonsohn, 2011). Further clarification of the influence of these factors within future samples may help to provide a greater understanding of risk associated with disordered eating and low birth weight and preterm births.

A large number of the included studies examined the impact of AN on obstetric outcomes; however, the potential consequences of BN on risk of low birth weight, preterm and small for gestational age births appears to have received less attention. Half of the included studies did not examine, specifically, the impact of BN on low birth weight and preterm births, or did not differentiate between AN and BN
subtypes. In contrast, all of the included studies examined the impact of AN. This may provide a point of further research in examining the potential risks, or differences in risk, in birth weight and gestational age for women with a history of BN.

5.5.2 Methodological limitations

Study design is a strong indicator of overall study quality, particularly in relation to measurement of long-term risk. Prospective longitudinal designs are often considered most desirable in assessing the development trajectories of risk within epidemiological research (Anstey & Hofer, 2004). Although longitudinal designs do not provide definitive proof of causality, they do provide evidence of a temporal link between exposure variables and outcomes, which is a vital step in developing causal inference (Austin, Hill, Flanders, & Greenberg, 1994; Collins, 2006). For this reason, significant findings obtained from studies utilising prospective longitudinal data (Linna et al., 2014) may hold greater weight compared to cross sectional or case control studies (Conti et al., 1998).

Limitations in the number of available longitudinal designs required inclusion of studies using less rigorous methodological designs, including case control designs (Bulik et al., 2009; Conti et al., 1998). Case control studies have been shown to be more susceptible to various forms of self-report and selection bias that act to diminish interpretations of causal inference with respect to exposure and outcomes (Austin et al., 1994). Case control designs have also received criticism for being less effective in detecting small or weak associations (Austin et al., 1994). The use of case control designs may be problematic in the examination of preconception disordered eating, where the long-term associations may be expected to be small. Eagles et al. (2012), for example, reported only a small magnitude of risk, suggesting that small effects of this type may have been undetected within other case control designs.

Although the majority ($n=11$) of included studies reported utilising longitudinal designs, nine studies obtained retrospective reports of disordered eating behaviours. Issues of bias may arise in relation to use of retrospective data, with participants required to report back on events in an objective fashion. Subjective bias is often a problem with individual’s perceptions of events changing over time or
developing as a function of different standpoints and experiences (Bertrand & Mullainathan, 2001). There can also be a tendency to minimise or exaggerate behaviours that may, in retrospect, be considered ‘risk factors’ (Mann, 2003). Report bias may occur due to sensitivities or concerns about being judged or perceived negatively or as an attempt to minimise perceived blame or guilt in relation to consequent pregnancy outcomes (Mann, 2003). This may be particularly problematic within eating disorder populations, with such women characteristically secretive about their eating habits (Morrill & Nickols-Richardson, 2001). One of the strengths of the current study is that it aims to address problems of report bias, associated with retrospective data collection, by using prospective longitudinal data.

Case identification of those with a diagnosis of disordered eating disorder varied among some the studies. Whilst most utilised criteria consistent with the Diagnostic and Statistical Manual (DSM) or International Classification of Diseases (ICD), a small number of studies ($n=4$) used self-report measures to assess disordered eating behaviour. Some inconsistencies or misclassification may occur in relation to disordered eating diagnoses and behaviour. Self-report measures, compared to clinician rated, have been shown to result in lower scores on items which inquire about binges, compensatory behaviour, attitudes towards food and social interactions although higher scores for psychopathology or atypical bingeing (Fichter & Quadflieg, 2000). Self-report measures can influence reporting of symptom severity or the under or over reporting of symptoms (Wolk, Loeb, & Walsh, 2005).

Alternatively, some evidence has suggested that use of self-report measures can improve accuracy or disclosure of symptom reporting, with some individuals observed to deny symptoms during face-to-face interviews (Mond, Hay, Rodgers, & Owen, 2007). A sense of anonymity may help reduce feelings of shame or secrecy in relation to reporting of symptoms, yet, for clinical samples may facilitate symptom denial. Koubaa et al. (2013) and Waugh and Bulik (1999) reporting using both self-report measures and clinical diagnostic tools which means that interpretations in relation to the effects of AN and BN are likely to be more persuasive and valid. Accurate measurement of disordered eating behaviours may be more problematic within community samples, where individuals are less likely to have undergone formal assessment or where assessments of such behaviours are entirely self-report.
Given this, findings obtained by Micali et al. (2012), Abraham et al. (1994), and Conti et al. (1998) should be interpreted with some caution.

5.5.3. Sampling and demographic limitations

Sample sizes included within the review varied considerably, with some too small, between 20 and 49 participants, to draw conclusions that could be generalised. Sample size requirement for case-control studies depend on the prevalence of variable exposure and relative risk of a given outcome (Schlesselman, 2006). If adhering to such statistical methods, sample sizes across studies would be similar; however, this is not the case. Samples for cohort studies, on the other hand, depend on the incidence of disease among comparison groups and relative risk of outcome (Schlesselman, 2006). Problems arise with smaller samples and a lack of power, with possible increases in the chance of type II error (Cohen, 1992). Non-significant findings in relation to mean birth weight reported by Bulik et al. (1999) may be explained by small frequencies of anorexic cases (n=35) and a lack of power to detect findings. Although some smaller community based samples, such as those described in Kouba et al. (2005), Koubaa et al. (2013) and Wentz et al. (2009), reported significant findings, all of these studies utilised case control designs which increase the likelihood of detecting significant results within small samples (Mann, 2003).

Small samples meant that some included studies were likely to be underpowered and thus unable to differentiate or compare AN and BN subtypes. Furthermore, relatively low prevalence rates of AN and BN, cited at between 0.3% and 0.7% and 1% to 2% for AN and BN respectively, may mean that identification and comparison of AN and BN subtypes was limited (Hoek, 2006, Swanson et al., 2011). This may be particularly relevant for community, compared to clinical, based samples. For example, Micali et al. (2012) reported that their community sample was lacking in power to detect differences in rare outcomes between disordered eating groups. They attributed a lack of power to weak associations reported between exposure and infant outcomes. Interpretations from findings of studies that grouped eating disorder sub types (Abraham et al., 1994; Sollid et al., 2004; Waugh & Bulik, 1999) may be limited, with actual risks for clinical eating disorder sub types potentially different from those reported. Neither Sollid et al. (2004) or Waugh and
Bulik (1999) reported significant increases in risk of low birth weight, preterm or small for gestational age births.

Attrition rates represent another important indicator of the quality of presented research and should be considered when interpreting results. For cohort studies, attrition rates not exceeding 20% at follow up is generally acceptable (Song & Chung, 2010). Conti et al. (1998) indicated that only 76% of women within the small for gestational group completed the EDI following the first interview. Issues of selectivity and attrition may result in systematic differences between participants who remain and those who drop out of the study (Little, Lindenberger, & Maier, 2000). Women experiencing more severe symptoms may be susceptible to greater issues of study salience, with studies perceived to be concerned with potentially stigmatizing risk behaviours vulnerable to decreasing overall participation within disordered eating populations (Galea & Tracy, 2007). Bulik et al (2009) reported that women who decided not to participate had higher rates of low birth weight and preterm births and were less educated than those within the study. They reported that participating individuals reflected the healthier end of the eating disorder spectrum, which may have explained why significant findings were not observed. Self-selection bias in community samples may mean that individuals with less severe symptoms are more likely to participate, potentially diluting overall findings (Bulik et al., 2009).

Epidemiological studies of disordered eating are thought to be more susceptible to non-response bias, with eating disorder populations over represented among non-respondents in general population studies (Beglin & Fairburn, 1992). Micali et al. (2012) reported large estimates of missing data, resulting in the exclusion of 1176 women from the sample. This raises the question of whether significant participant qualities influenced participation and consequent results. Non-significant findings may be influenced by a degree of response bias and so may not be applicable to the general population. Analyses in relation to missing data were not reported in most studies and so it is not clear whether differences existed between groups. Despite this, some findings have suggested that for two-phase epidemiological studies, little differences are observed between women with and without disordered eating behaviours who declined participation in subsequent waves of data collection (Mond, Rodgers, Hay, Owen, & Beumont, 2004). This indicates that once involved
within the initial phase of participation, the effects of non-response bias may be reduced.

5.5.4 Review limitations

It should be noted that there is a potential for incomplete retrieval of some articles relevant to the review. Regardless of comprehensive search strategies employed, a number of databases were not included within the search, limiting the chances of retrieving relevant articles. Bias may also have occurred at a review level with overall publication and language bias observed within most peer-reviewed journals (Dwan et al., 2008). This may result in an increased number of articles published that report positive findings and are written in English. This bias should be taken into consideration when interpreting reported findings.

5.5.5 Future directions

Overall findings have provided preliminary evidence of preconception disordered eating risk on later pregnancy outcomes. Review of the current literature revealed a large degree of variation between study methodologies. This limits interpretations made from overall findings as few studies provided comparable designs, samples and statistical approaches. A trend in significant increases in risk of low birth weight, preterm and small for gestational age births appears to exist within large prospective clinical samples. Only five of the fourteen studies reviewed utilised prospective data, which represents a clear gap within the literature. Small sample size and issues of type I error, associated with inadequate adjustment of confounding variables, means these even those studies presenting prospective longitudinal data were unable to meet all quality indicators of epidemiological research.

Although providing insight into preconception risks, little is currently known about the long-term impacts of adolescent disordered eating. Only one study included in the review specifically examined the impact of adolescent AN (Wentz et al., 2009). This study is also the only prospective community study examining the influence of preconception AN on birth outcomes. A small sample in a case-control design, however, limits the quality of presented findings. Ekeus et al. (2006) also included
participants from 10 years of age, although did not specifically examine or differentiate adolescent AN or the duration of AN behaviours. Large prospective studies that measure disordered eating during clearly defined preconception periods and account for a range of relevant covariates, such as parity, maternal age and BMI, are required to ascertain more accurate measures of overall risk of low birth weight, preterm and small for gestational age births. This study aims to address noted limitations of previous research described in this review by prospectively examining the effects of preconception disordered eating, occurring during the adolescent period, on birth outcomes in young adulthood. Investigation of adolescent disordered eating may help to identify targets for early intervention to reduce adverse birth outcomes.

5.6 Aims and hypotheses for empirical analyses in this thesis

The empirical study to follow aims to extend on previous research, as documented in this chapter, by examining the effects of preconception disordered eating, between 15 and 16 years, on risk of low birth weight, preterm and small for gestational age births. Analyses to be presented in the upcoming chapters of this thesis are based on Drive for Thinness and Bulimia scores of the EDI. These subscales of the EDI assess eating disorder symptoms, rather than full diagnoses, representing useful indicators of disordered eating behaviours in population-based groups. Assessment of criterion related validity through one way analysis of variance has indicated that bulimic subtypes score higher on the Bulimia subscale, compared to restricting anorexic groups (Garner et al., 1983; Milos, Spindler, & Schnyder, 2004). Furthermore, discriminant analyses has indicated that 85% of individuals were correctly classified into restricting or purging subgroups based on scores on the Bulimia subscale (Garner et al., 1983). Differences between sub groups for other EDI subscales, however, have not been detected (Milos et al., 2004).

As detailed in Chapter four, disordered eating behaviours have been associated with poorer birth outcomes through biological and hormonal changes that negatively affect the quality of reproductive functioning and infant growth (Wadhwa et al., 2004). Specifically, these risks have been associated with maternal under-nutrition and physical starvation associated with a diagnosis of AN. Drive for Thinness items are indicative of excess concern with dieting and weight, which are described as
cardinal features of AN. For this reason, it is hypothesised that Drive for Thinness scores on the Eating Disorders Inventory (EDI) will significantly predict risk of low birth weight, preterm or small for gestational age births.

On the other hand, women in a more healthy weight range or engaging in purging behaviours, as is often the case in BN, are thought to experience different pathways of risk. Research examining reproductive risk for women with a history of BN has predominantly indicated that these women are not at a significantly increased risk or low birth weight, preterm or small for gestational age births (Conti et al., 1998; Linna et al., 2014). Yet, as evident in the review reported in this chapter, this finding is not consistent across the literature, with a number of clinical samples inferring significant increases in risk of low birth weight, preterm or small for gestational age births. Further still, few studies have specifically examined the effects of BN prior to pregnancy on birth outcomes. Despite the expectation of non-significant findings, this represents an important area of further investigation. Therefore hypotheses related to BN risk and birth outcomes are not presented in relation to risk of low birth weight, preterm or small for gestational age births.

Whilst a number of studies have included BMI as a covariate within their analyses, some current findings have conceptualised BMI as being embedded within ongoing disordered eating risk and predictive of disordered eating behaviour (Jones et al., 2001; Keel, Fulkerson, & Leon, 1997). Measures of disordered eating ‘Risk’, which incorporate EDI and BMI scores, are included in this study to reflect the importance of BMI in the development of reproductive risk (Garner, 2004). Measures of disordered eating ‘Risk’ may also be more likely to tap into biological pathways of risk and biological effects, associated with physical starvation, through identification of women who are underweight or have low BMI’s. Therefore, it is hypothesised that being ‘At Risk’ of an eating disorder will increase the risk of low birth weight, preterm or small for gestational age births. Operationalisation of the relevant variables is detailed in the following chapter.
6.1 The current study: The Australian Temperament Project- Generation 3 Study (ATPG3)

The current study aims to expand upon previous conceptualisations of maternal and reproductive health through examination of psychosocial predictors of pregnancy outcomes occurring during the pre-conception timeframe. Despite some emerging research investigating the preconception period and impact of psychosocial exposures occurring during this period (Strutz, Richardson, & Hussey, 2012; Weisman, Misra et al., 2011) the quantity of research remains quite limited. Use of a relatively large prospective longitudinal sample and design, in the current study, may also help to address issues of bias observed in previous retrospective designs and provide a basis for longer-term prediction of risk. A prospective longitudinal research design may also result in more accurate and ongoing data collection throughout the adolescent preconception period and into young adulthood.

Assessment of disordered eating behaviour during adolescence allows for prediction of later pregnancy outcomes within a more developmental and lifespan approach to maternal health and foetal outcomes. This potentially informs a preventative approach to reproductive health, targeting possible risks before women even become pregnant (Atrash et al., 2008). Preconception interventions that target adolescent risks will provide women adequate time in which to engage in positive behavioural change so that women enter pregnancy with optimal health (Bhutta et al., 2011). This may help to reduce the occurrence of preventable outcomes and alleviate some of the psychological and financial consequences associated with adverse birth outcomes such as low birth weight, preterm and small for gestational age births. Otherwise, improved awareness and identification of preconception risks may inform and guide obstetric and reproductive care for women who are identified as being at risk, during and post pregnancy.
6.2 Participants and procedure

Participant data were obtained from a large-scale longitudinal and intergenerational study, the Australian Temperament Project (ATP) and the ATP Generation 3 (ATP G3) Study. The ATP has followed the psychosocial development of a community sample from infancy to adulthood. Participants in the ATP were recruited in 1983 from 67 Local Government Authority areas (LGA’s) selected by the Australian Bureau of Statistics in order to provide a representative sample of individuals in Victoria from infancy to adulthood. Of the LGA’s selected in Victoria, twenty were urban (1,604 children) and 47 were rural (839 children). The original cohort consisted of 2443 participants, of which 52% were male and 48% female. Participants in the analysis presented here were all female.

Generation One (G1) participants and families were recruited through Maternal and Child Health Centres within selected areas. Generation Two (G2) participants were the infants of Generation One (G1) adult participants recruited during the initial waves of data collection 1983. Generation Two (G2) infant data were provided by G1 mothers when infants were aged between 4 and 8 months. Mothers attended identified centres between the 22nd April and 6th May and were provided with an ATP questionnaire to complete. Since initial recruitment in 1983, 15 waves of data have been collected. Pregnancy and birth information on G2 participants was obtained from maternal and child health nurses during wave 1 of the study when participants were between 4 and 8 months of age. G2 data was also obtained from primary school teachers when participants were 5, 7 and 11 years of age. Self-report data were obtained from individual G2 participants from wave 11 onwards when participants were 11 years of age and above. Questionnaires used in the study covered a range of psychosocial and demographic information and were delivered by mail to participants with reply paid envelopes. One round of postal reminder letters were sent followed by a second mail-out of questionnaires to participants who did not respond. If no response was received from these individuals a final telephone follow up reminder was conducted to encourage participants to return their questionnaires. Ethics was approved by the Human Research Ethics Committee at the Australian Institute of Family Studies. F
Attrition occurred on average at a rate of less than 1% per year. Currently, 76% of the original G2 cohort remains registered with the study. Table 4 indicates that, compared with the retained sample, non-participating families were more likely to be from a lower socio-economic background or contain a parent born outside of Australia. Although comprising of fewer families of lower socio economic status during later waves of data collection, the study sample was generally representative of families from a wide range of backgrounds and circumstances. The following attrition table was sourced from Letcher, Smart, Sanson, and Toumbourou, (2009) published in ‘Psychosocial precursors and correlates of differing internalising trajectories from 3-15 years’.

Table 4 Comparison of retained sample at Wave 11 and the original cohort on characteristics at recruitment in 1983

<table>
<thead>
<tr>
<th>Domain</th>
<th>Original cohort</th>
<th>Retained sample 2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>SES Quartile in 1983</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Highest</td>
<td>26.7%</td>
<td>32.3%</td>
</tr>
<tr>
<td>Medium-High</td>
<td>29.2%</td>
<td>30.4%</td>
</tr>
<tr>
<td>Medium-Low</td>
<td>24.4%</td>
<td>23.1%</td>
</tr>
<tr>
<td>Lowest</td>
<td>19.8%</td>
<td>14.2%</td>
</tr>
<tr>
<td>Mothers country of birth</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australian</td>
<td>79.9%</td>
<td>83.6%</td>
</tr>
<tr>
<td>UK</td>
<td>6.0%</td>
<td>5.6%</td>
</tr>
<tr>
<td>Other</td>
<td>14.1%</td>
<td>10.8%</td>
</tr>
<tr>
<td>Father’s country of birth</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australian</td>
<td>73.3%</td>
<td>77.0%</td>
</tr>
<tr>
<td>UK</td>
<td>7.3%</td>
<td>7.0%</td>
</tr>
<tr>
<td>Other</td>
<td>19.4%</td>
<td>16.0%</td>
</tr>
</tbody>
</table>
6.2.1 Generation 1 (G1) and Generation 2 (G2)

Generation One (G1) adult participants were the parents of Generation Two (G2) infants recruited during the initial waves of data collection 1983. Data in relation to G2 birth weight, gestational age and small for gestational age births were obtained during the initial wave of data collection in 1983. G2 infant data were collected from maternal health nurses during infancy. G2 adolescent data were then obtained prospectively, during wave 11 of data collection, at 15 and 16 years of age using self-report questionnaires.

6.2.2 Generation 3 (G3)

Recruitment into the Australian Temperament Project Generation Three (ATP G3) Study began in November of 2011 and is currently ongoing as G2 parents are identified and invited into the study. Generation Three (G3) assessments of infant and pregnancy data were obtained from adult ATP G2 participants from the age of 28 years and above. Pregnancies and offspring of the G2 cohort are detected through a six monthly contact process in which all ATP participants are emailed or telephoned and asked to confirm or update contact details and whether they or their partner are expecting a child. Recruitment is ongoing with a current response rate of 86% of all identified eligible offspring. G3 infant data were obtained during the third trimester of pregnancy and at 8 weeks and 12 months postpartum using Computer Assisted Telephone Interviews (CATI) and online surveys. In this study, the G3 sample comprised of the available pregnancy and infant data collected to date. Generation Two (G2) and Generation Three (G3) participants and study waves are presented in Figure 2 below.

6.3 The current sample

The current study used G2 participant data obtained during initial waves of data collection in 1983 as well as G2 data obtained at 15 and 16 years during 1998 (wave 11). G3 infant data were obtained at 12 months of age from parent report. The current sample comprised only the female participants with offspring up to the age of 18 months after the start of the Generation Three study in November 2011. This
resulted in a total of 248 female G2 participants and offspring. All of the participants within the sample reported being the biological parent of the included G3 offspring. The sample was also restricted to include only one infant from each G2 participant to ensure independence in associations. A total of 60 participants were identified as having multiple children within the study, with four of these infants representing two sets of twins. The oldest participating ATP sibling was included within the sample. Data from one infant, of those who were identified as being a twin, was randomly removed from the sample. The sample for analysis comprised 188 female G2 participants, who were mothers to 83 male (44.1%) and 105 female (55.9%) infants. The mean age of female participants in 1998 was 15.73 years and ranged between 15.42 years and 16.17 years (SD=1.479). Maternal age at the time of G3 12 month interviews, ranged from 26 to 32 years, with the mean age 28.54 years (SD= 1.375).

6.4 Materials

6.4.1 Predictor and outcome variables

Disordered eating measure. Disordered eating behaviour was measured at the age of 15 and 16 years using an adapted version of the Eating Disorder Inventory (EDI). The EDI is a 64-item, self-report, multi-scale measure designed to assess the psychological and behavioural traits consistent with AN and BN (Garner et al., 1983). The EDI is comprised of eight subscales; Drive for Thinness, Bulimia, Body Dissatisfaction, Ineffectiveness, Perfectionism, Interpersonal Distrust, Interoceptive Awareness and Maturity and Satiety. Nineteen items from the EDI were administered in the ATP questionnaires. These represented three of the eight core EDI subscales; Drive for Thinness, Bulimia and Body Dissatisfaction. The subscales of the EDI have been shown to significantly differentiate between individuals with an eating disorder and non-clinical controls (Clausen, Rosenvinge, Friborg, & Rokkedal, 2011; Nevonen & Broberg, 2001). Although included within the overall ATP study, scores from the Body Dissatisfaction subscale of the EDI were not included within current analyses. Some evidence has suggested that the Drive for Thinness and Bulimia subscales of the EDI are better at discriminating between clinical and non-clinical samples, compared to the Body Dissatisfaction scale (Garner, 2004). Klemchuck, Hutchinson and Frank (1990) reported, for example, that although
young females within their sample scored highly on the Body Dissatisfaction subscale, in general, they were not more likely engaging in bulimic behaviours or report psychological disturbances at levels characteristic of an eating disorder. Furthermore, the Body Dissatisfaction scale of the EDI tends to also identify those individuals at the higher end of the weight spectrum (Garner, 2004).

In the current study, total summed scores for the Drive for Thinness and Bulimia subscales of the EDI (Garner et al., 1983) were used to measure disordered eating behaviour at age 15 years. Seven items comprise the Drive for Thinness subscale of the EDI. These items relate to excessive concern with dieting, preoccupation with weight and entrenchment in an extreme pursuit of thinness. Seven items relating to a tendency towards episodes of uncontrollable eating as well as potential impulses to engage in purging following these episodes make up the Bulimia subscale. Items were rated on a six-point scale from “never” to “always”. Example items include “I am terrified of gaining weight” and “I think about bingeing: overeating”. The internal reliability and validity indices for all EDI subscales have been established (Jones et al., 2001). The reliability of the Drive for Thinness and Bulimia subscales within the current study was high, demonstrating a Cronbach’s alpha of $\alpha=0.90$ and $\alpha=0.71$ respectively. Prospective studies have indicated that the Drive for Thinness scale is a good predictor of binge eating and the development of formal eating disorders (Garner, 2004). Both the Drive for Thinness and Bulimia subscales of the EDI have shown high temporal stability (Joiner, Heatherton, & Keel, 1997). A full description of this measure and included items are described in Appendix A.

Given that the ATP study is a community sample, as recommended by Shoemaker et al. (1994), the untransformed method of response coding was used. Responses were scored on a six-point scale of 6, 5, 4, 3, 2 and 1 with higher scores indicative of greater disordered eating psychopathology (Shoemaker, Van Strien, & Van Der Staak, 1994). The use of untransformed responses has shown to increase the psychometric properties of the scale within nonclinical populations and reduce problems associated with skewed data (Shoemaker et al., 1994).
### Figure 2: Generation Two (G2) and Generation Three (G3) Participants and ATP and ATP-G3 Study Waves

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (G2 Participant)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>9</td>
<td>11</td>
<td>13</td>
<td>15</td>
<td>29</td>
<td>30</td>
<td>31</td>
<td>32</td>
</tr>
<tr>
<td>Wave</td>
<td>W1</td>
<td>W2</td>
<td>W3</td>
<td>W4</td>
<td>W5</td>
<td>W6</td>
<td>W7</td>
<td>W8</td>
<td>W9</td>
<td>W10</td>
<td>W11</td>
<td>W15</td>
<td>W16</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Generation Two (G2) Participants - Preconception period**

**Generation Three (G3) Observations**
A binary ‘At Risk’ disordered eating variable was also created within the current study with the purpose of identifying those individual who may be at risk of an eating disorder. The disordered eating ‘At Risk’ variable was developed using total summed scores from Drive for Thinness and Bulimia subscales of the EDI in addition to reported Body Mass Index (BMI) at age 15 and 16 years. This measure was based on the EDI-3 referral form (Garner, 2004) which is a brief self-report measure designed to assess eating disorder risk. Within clinical populations the EDI is commonly scored by transforming responses from a six-point scale; Always, Usually, Often, Sometimes, Rarely, and Never, to a three point scale. Scores are then summed for each subscale to obtain a clinical classification. In such cases, response items are scored as 3, 2, 1, 0, 0 and 0 points respectively. In order to identify more clinical presentations within the current sample, using the categorical ‘At Risk’ variable, scores were recoded so that responses for items on the Drive for Thinness and Bulimia subscales of the EDI were coded in a 4, 3, 2, 1, 0 and 0, point format. This helped to account for low prevalence rates of disordered eating and noted problems with sensitivity in screening of disordered eating within non-clinical populations (Raciti & Norcross, 1987; Shoemaker et al., 1994).

Critical scores were used to identify individuals who may be at risk of an eating disorder and were based on published guidelines by Garner (2004). Participants classified as high risk of disordered eating behaviour were those reporting both a BMI less than 15.5 and a raw score of 9 or 4, based on recoded Drive for Thinness or Bulimia subscales of the EDI as described above. EDI critical scores were derived from a sample of 302 adolescents, ranging in age from 13 to 17 years, who had been diagnosed with AN-restricting type, AN-binge purge type, or an eating disorder not otherwise specified (EDNOS) as well as a nonclinical control sample of 538 adolescents (Garner, 2004). The critical values were set to a value to identify approximately 85% to 90% of individuals with an eating disorder, which meant that 85% to 90% of individuals diagnosed with an eating disorder in the sample would receive a Drive for Thinness or Bulimia total raw score of 9 or 4 or above (Garner, 2004).
In order to develop a disordered eating ‘At Risk’ variable using the EDI-3 referral form, a prorated eighth item for the Bulimia subscale of the EDI was developed in order to account for an additional item that was included in the EDI-3 (Garner, 2004). This item, “When I am upset I worry that I will start eating”, was not administered to ATP participants, as it was not part of the Bulimia subscale of the EDI-2 on which the ATP questionnaire was based. The purposes of creating an ‘At Risk’ disordered eating variable using both EDI and BMI data were to develop a measure which may more accurately identify participants who may be actively engaging in disordered eating behaviours and experiencing symptoms of physical starvation. Whilst some individuals may report similar EDI scores on some subscales to the general population, those with an eating disorder are on average 30% thinner (Garner, 2004). The inclusion of an ‘At Risk’ variable meant that potential biological effects, associated with underweight status, may be assessed in addition to more psychological indicators of risk, as measured using the Drive for Thinness and Bulimia summed scores on the EDI.

**Body Mass Index:** Data on height and weight were obtained at 15 and 16 years of age through self-report. A measure of Body Mass Index (BMI) was developed by means of dividing self-reported weight (kg) by height (cm). Cut-off points to identify participants who were underweight were based on age specific norms or cut-points (Cole, Flegal, Nicholls, & Jackson, 2007). Recommendations from the World Health Organisation indicate that a BMI of 17 or below is used to determine individuals who are underweight (Cole et al., 2007).

**Generation Two (G2) and Generation Three (G3) Birth weight.** Data in relation to G2 birth weight were obtained from maternal health nurses during the initial wave of data collection in 1983. Data in relation to G3 birth weight were obtained through parent report in telephone interviews in the ATPG3 study when infants were 12 months of age. G2 and G3 birth weight data were used to create both continuous and binary variables. A binary low birth weight variable was developed based on low birth weight classifications defined by Tucker and McGuire (2004). Women reporting infant birth weight between 1.36 and 2.50kgs were classified as having a low birth weight infant. Infants weighing above 2.5kgs were defined as being within the normal weight range. Low frequencies of more severe low birth
weight infants necessitated inclusion of these participants in the overall low birth weight category. A continuous measure of birth weight variable was also used, which was coded in kilograms and rounded to the nearest 10 grams. This allowed for further information to be obtained in relation to the overall relationship between disordered eating and birth weight, given that frequencies of low birth weight infants were small within the current sample.

*Generation Two (G2) and Generation Three (G3) Gestational age.* Data on G2 gestational age were obtained from maternal health nurses during the initial wave of data collection in 1983. Data on G3 gestational age were obtained through parent report in telephone interviews with parents when infants were 12 months of age. Both continuous and binary variables were derived to measure average gestational age and preterm births. Preterm births were coded dichotomously based on classifications defined by Moutquin (2003). Preterm births were defined as births less than 37 weeks gestation. Births occurring after 37 weeks gestation were defined as near or full term births. Low frequencies meant that moderate (32-33 weeks gestation) and mild (34-36 weeks gestation) categories of preterm births, defined by Goldenberg et al. (2008), were collapsed into one low birth weight group. This may have implications for the predictive power in relation to this outcome, with data less sensitive to potential differences categories of preterm births within this group. A continuous measure of gestational age was also used, which was coded in terms of number of week’s gestation. This aimed to increase the amount of available information and account for smaller frequencies of preterm births observed within the current sample.

*Generation Two (G2) and Generation Three (G3) small for gestational age.* G2 small for gestational age status was derived from G2 birth weight and gestational data obtained their maternal health nurse during the initial wave of recruitment in 1983. G3 Small for gestational age status was based on G3 birth weight and gestational age data when infants were 12 months of age. G3 Small for gestational age status was determined based on Australian infant birth weight for gestational age percentile norms (Dobbins, Sullivan, Roberts, & Simpson, 2012). G2 small for gestational age status was determined based on Australian population norms obtained during 1999 (Roberts & Lancaster, 1999). Comparison of classifications of small for gestational age births based on population norms obtained during 2012 and 1999
revealed one G2 mother who was differently classified. This G2 participant was included in the sample and classified as not being small for gestational age based on 1999 norms. Infants classified as being small for gestational age were those with birth weight falling below the 10th percentile, or two standard deviations below the mean, for gestational age (Tucker & McGuire, 2004). Small for gestational age births were coded dichotomously, with infants falling below the 10th percentile of gestational age for weight, defined as being born small for gestational age and those above the 10th percentile classified as not being small for gestational age.

6.4.2 Covariates

Socioeconomic Status (SES). A strong association has been observed between low birth weight and socio economic status (Hughes & Simpson, 1995). Socioeconomic Status (SES) was measured during the first wave of data collection in 1983 and then reported in each subsequent wave. In the current study, SES was assessed during wave 11 of the study when participants were 15 and 16 years of age. SES was measured by calculating the mean of both parents’ reported level of education, rated on an eight point scale ranging from unskilled to professional, and occupation, rated on an eight point scale ranging from elementary school to postgraduate degree. Scores for SES ranged from 1 to 8 with higher scores indicating lower SES.

In Vitro Fertilisation (IVF). The use of assisted reproductive technology has been strongly associated with increased rates of twin and multiple births, preterm and low birth weight births. Schieve et al. (2002) cited low birth weight outcomes to be 2.6 times more likely for women in the study using assisted reproductive technology compared to the general population. In Vitro Fertilisation (IVF) was recorded in the G3 12 month interview when adult G2 participants were asked “Was IVF used to conceive (name)?”. Responses were coded as either “yes” or “no”.

Multiple Births. There is an inherent increase in risk of preterm and low birth weight births for women experiencing twin or multiple births (Goldenberg et al., 2008; Kogan et al., 2000). Findings from an international sample spanning from 1995 to 1997 indicated that the relative risk of preterm delivery in twins, compared to
single births, ranged from 5.4 to 9.5 (Blondel et al., 2002). In the current study, multiple births were assessed by self-report through one item that asked G2 participants whether their child was a twin, triplet or multiple birth. Responses were coded as “0” for single births, “1” for twin births, “2” for triplets or “3” for multiple births of 4 or more infants.

Parity. Birth order, being the first-born infant, was determined through responses to ATP devised branched questions in relation to the presence of younger or older siblings. A binary variable in relation to birth order was developed based on these responses, with individuals classified as being the first-born child or not.

Depression measures. An ATP adapted version of the Short Mood and Feelings Questionnaire (SMFQ; Angold, Costello, & Messer, 1995) was used to measure depressive symptoms at 15 and 16 years of age. The SMFQ is a brief 13 item self-report scale designed to detect clinical depression in children and adolescents. Twelve of these items were administered to ATP participants. One item from the SMFQ was removed from ATP questionnaires as it was deemed inappropriate for the sample based on negative participant feedback. This scale is comprised of a 3-point Likert-type response format where 0=rarely or never, 1=sometimes and 2=very often. Items measure affective and cognitive symptoms of depression, including some somatic and behavioural symptoms including feeling miserable, low energy, loneliness, self-hatred and anhedonia. Example items include “I hate myself”, “I feel lonely” and “I think nobody really loves me”. Total summed scores, ranging from 0 to 24, were used to assess the presence and severity of depressive symptoms, with higher scores indicating greater levels of depressive symptoms.

The SMFQ is based on DSM-III-R criteria and has been clinically validated, revealing substantial correlations between other validated measures, including the Children’s Depression Inventory and the Diagnostic Interview Schedule for Children (DISC) depression scale (Angold et al., 1995). The SMFQ has demonstrated good internal construct validity in clinical and community samples (Sharp, Goodyer, & Croudace, 2006). The SMFQ has good test-retest reliability, with higher scores associated with children and adolescents meeting diagnostic criteria for clinical depression (Angold et al., 1995). Sensitivity and specificity for the SMFQ have been
reported at 0.75 and 0.73 for an ICD-10 diagnosis of depression and at 0.86 and 0.87 for DSM-III-R depression (Thapar & McGuffin, 1998). The SMFQ demonstrated high reliability ($\alpha = 0.87$) within the overall ATP sample.

Substance use measure. ATP devised items were used to measure substance use in adolescents aged 15 and 16 years. The presence and frequency of any substance use, alcohol, tobacco or marijuana, was assessed using self-report branched questioning. If responding ‘yes’ to any previous alcohol or substance use, participants completed additional questions assessing the frequency of use, in days, over the previous month; 30 days. Example questions include “Have you smoked more than 2 cigarettes in your life?” “On how many days?” “And on average, how many per day?” Substance use risk variables were recoded, with level of risk based on frequency of use over the previous month.

6.5 Analytic approach

6.5.1 Statistical assumption testing

Statistical assumption testing was conducted to ascertain whether assumptions of the data were met and analyses were appropriate. Power analyses were conducted, using statistical software G Power 3.1 (Faul, Erdfelder, Buchner, & Lang, 2009), to determine the minimum sample size required for logistic regression analyses. These findings are presented in Figure 3. Analyses revealed that a minimum of 163 participants would be required, at an 80% probability level, to detect a significant effect. At a 90% probability level 223 participants would be required to detect a significant effect. This indicates that the current sample met minimum size requirements to complete logistic regression analyses but that there is the potential for analyses to be underpowered. Sample size requirements indicate that the minimum number of cases per predictor variable is $n=10$ for logistic regression analyses (Hosmer & Lemeshow, 2004). Assessment of adequacy of risk cases for each predictor variable (Drive for Thinness, Bulimia subscales and disordered eating ‘Risk’) revealed a sufficient number of cases for each predictor variable. The minimum number of cases for multiple births and IVF use ($n=2, n=8$ respectively) were not obtained so these variables were excluded from main analyses. The sample
size required to detect significant mediation effects, as recommended by Fritz and Mackinnon (2007), using a bias-corrected bootstrap method, based on effect sizes ranging from .2 to .3 is \( n=71 \). Hence, the sample used in this study \( (n=188) \) was adequately powered to detect significant results.

![Sample size requirements for logistic regression analyses based on power analyses using G Power 3.1](image)

Figure 3 *Sample size requirements for logistic regression analyses based on power analyses using G Power 3.1*

Although assumptions of normality do not need to be met in logistic regression, non-normally distributed data does violate assumptions of analyses used to assess potential mediation effects. Preliminary assessment of the overall distribution of the data was conducted through visual inspection of histograms and box plots. Kolmogorov-Smirnov, skew and kurtosis statistics were used to test assumptions of normality within the data. The Kolmogorov-Smirnov is a non-parametric test that assess whether a continuous sample distribution is significantly different from theoretical expectations (Mehmet & Akin, 2003). The null hypothesis infers that the sample represents a normal distribution, with a significant result \( (p<.05) \) indicating that this assumption has been violated and the data are not normally distributed. Regression analyses were bootstrapped using 1000 bootstraps to account for non-normally distributed data (Afifi, Kotlerman, Ettner, & Cowan, 2007).
The presence of univariate outliers was assessed through visual inspection of stem and leaf plots, box plots and histograms. Further assessment of standardised residual values was conducted to identify cases falling farthest from the predicted value or range. Typically, a $z$ score above 2.58 is used as a cut-off to identify cases that may be univariate outliers (Daszykowski, Kaczmarek, Vander Heyden, & Walczak, 2007). This cut-off is based on the assumption that $z$-scores are normally distributed, with 99.4% and 99.9% of centered cases expected to lie within two and a half and three standard deviations (Daszykowski et al., 2007). Post-Hoc analysis of potential multivariate outliers was conducted using logistic regression. Multivariate outliers were identified based on Cook’s distance values (Hosmer & Lemeshow, 2004). Cook’s distance values reflect the influence of a given case on the fitted data, with scores greater than 1.0 indicating that a data point is potentially having an undue effect on the overall data (Cousineau & Chartier, 2010). Removal of outliers can reduce the probability of Type I and II error and improve the accuracy of estimates, although can also reduce the validity of reported findings (Osborne & Waters, 2002). Multivariate outliers were reviewed and analyses were run with and without identified outliers to check if these cases were having an undue influence on the data.

Chi square and Fisher’s Exact Tests were conducted to assess independence of potential covariates and pregnancy outcomes. Lower frequencies of IVF and multiple births indicated use of Fisher’s exact test to assess statistical significance due to greater cited validity within small samples (Routledge, 2005). Multicollinearity of birth outcomes, including low birth weight, preterm and small for gestational age births, was assessed given that these outcomes are known to be related (Kramer, 1987; Tucker & McGuire, 2004). Considering that measures of low birth weight and preterm births were derived from data on overall birth weight and gestational age, these variables were regressed separately to address potential issues of multicollinearity. Similarly, classification within the disordered eating ‘At Risk’ group was based on scores on the Drive for Thinness and Bulimia subscales. For this reason, these variables were entered as predictors into separate analyses. Collinearity statistics, in the form of tolerance and Variance Inflation Factor (VIF) values, were used to identify and quantify collinearity within the model. Tolerance values less than .1 and or VIF values above 5 were used as criteria to assess whether assumptions of multicollinearity had been violated (Craney & Surles, 2002).
Missing data analyses, using Little’s Missing Completely at Random (MCAR) test, was conducted to determine whether missing data were missing at random, missing completely at random or not missing at random. A non-significant result indicated that missing data were likely to be missing completely at random. For data to be MCAR the missingness needs to be unrelated to the observed data (Enders, 2006). Although potentially resulting in a decrease in statistical power, data that are missing completely at random yield unbiased parameter estimates (Graham, 2009). Missing data were imputed in SPSS using the expectation maximisation algorithm given that this method is valid for data where the missingness mechanism is MCAR (Scheffer, 2002). This method has been shown to be a valid way of reducing bias associated with missing data in epidemiological research (Abraham & Russell, 2004).

6.5.2 ATP Study 2-Effects of preconception disordered eating on low birth weight, preterm and small for gestational age births

Preliminary unadjusted analyses were conducted using zero order correlations to investigate potential relationships between continuous predictors, outcomes and covariates. Chi square tests of independence and independent samples t-tests were conducted to assess the relationships between categorical predictors, outcomes and covariates. Main analyses, in the form of logistic regression analyses, were conducted using the statistical software program IBM SPSS Statistics Version 20 (Nie, Hull, & Bent, 2011). Logistic regression was used to assess the risk of low birth weight, preterm and small for gestational age births in women reporting preconception disordered eating at 15 and 16 years of age. Analyses were completed in two phases, with both unadjusted and adjusted analyses conducted that included potential covariates.

Unadjusted logistic regression models were conducted initially, regressing each adolescent disordered eating predictor variable separately onto each binary infant outcome; low birth weight, preterm and small for gestational age births. Adjusted analyses were then conducted to determine whether observed effects remain after accounting for potential covariates, including maternal age, socio-economic status, infant gender, birth order, BMI and substance use (alcohol, tobacco and cannabis use) and depressive symptoms at the age of 15 and 16 years.
6.5.3 ATP Study 3-Intergenerational birth risk and mediating effects of adolescent disordered eating

Bivariate correlations were conducted to assess hypotheses predicting continuity between continuous G2 and G3 birth outcomes. Furthermore, logistic regression analyses were conducted to assess whether G2 maternal low birth weight, preterm or small for gestational age births predicted low birth weight, preterm or small for gestational age births in G3 infants. Mediation analyses were conducted using the statistical software program Mplus version 7.2 (Muthén & Muthén, 1998-2012). Traditionally, it has been argued that a direct effect needs to be established between predictor and outcome variable before assessing mediation effects. This has since been disputed, with the effect of the predictor variable on the outcome variables equivalent to the total effect of these variables or the sum of the indirect and direct paths (Zhao, Lynch & Chen, 2010). Current evidence suggests that the only requirement for demonstration of a mediation relationship is that a strong association exist between the predictor variable and the mediator, and the mediator variable and the outcome variable (Kazdin, 2007).

Mediation analyses conducted in final study assessed the mediating effects of adolescent disordered eating on the relationship between G2 maternal birth outcomes and G3 infant outcomes. Hypotheses are detailed fully in Chapter eight. The bias-corrected bootstrap method was used to assess potential mediated effects, with this method shown to be a powerful test recommended for assessment of mediation effects (Fritz & Mackinnon, 2007). This method corrects for skewed data and contains a correction for the bias created by central tendency of the estimate (Fritz & Mackinnon, 2007). The mediation estimator used was WLSMV, which uses a weighted least squares probit regression. Bootstrapping methods, using 5000 bootstraps, were used to account for non-normally distributed data and improve issues of reliability associated with smaller sample sizes (Mallinckrodt, Abraham, Wei, & Russell, 2006; Zhao et al., 2010). Mediation effects are considered significant if falling within 95% confidence intervals, or if Upper Confidence Intervals (CIU) and Lower Confidence Intervals (CIL) do not include 0.
CHAPTER 7: RESULTS AND DISCUSSION OF THE EFFECTS OF ADOLESCENT DISORDERED EATING ON RISK OF LOW BIRTH WEIGHT, PRETERM AND SMALL FOR GESTATIONAL AGE BIRTHS

7.1 Chapter overview

This chapter presents the results from the second study of this thesis, which examined the effects of preconception disordered eating, during adolescence, on risk of low birth weight, preterm or small for gestational age births. The chapter begins with a brief review of the rationale for this study and the associated research question and hypotheses. Results are then presented from statistical assumption testing, preliminary analyses and main analyses, using logistic regression. Included in this chapter is a discussion of the study findings in the context of previous research outlined in the systematic literature review. Key findings are reviewed, drawing on DOHaD theory, and implications and recommendations for future directions will be discussed.

7.2 Rationale and research aims

Low birth weight, preterm and small for gestational age births contribute to large proportions of overall neonatal morbidity and mortality (Lumley, 2003; Petrou, 2003). Despite advances in reproductive technology and maternal health, the problem of low birth weight, preterm and small for gestational age births remains pertinent. The DOHaD framework has drawn attention to the importance of maternal nutrition and diet in optimising infant health through generational studies examining birth outcomes to women facing poor nutritional conditions (Schulz, 2010). Although providing a strong basis for maternal nutrition and weight during gestation, continued concern regarding the problem of low birth weight, preterm and small for gestational age births has called for a new perspective on how such risk develops. Examination of risk occurring prior to gestation and during adolescence may provide targets for early intervention aimed at circumventing preventable instances of low birth weight, preterm or small for gestational age births.
This study extends on traditional DOHaD theory by examining the impact of adolescent disordered eating behaviour, measured between 15 and 16 years of age, on pregnancy and birth outcomes in young adulthood. Disordered eating has been linked to significant medical complications that negatively impacts on reproductive functioning and birth outcomes (Sidiropoulos, 2007). In particular, anorexic individuals are thought to be at a greater risk of adverse birth outcomes, including low birth weight births, due to endocrine abnormalities associated with physical starvation (Hoffman et al., 2011; Mason et al., 2007). Accordingly, it was hypothesised that adolescent disordered eating behaviour, measured using summed scores on the Drive for Thinness scale of the EDI and classification within the disordered eating ‘At Risk’ group, would significantly increase the risk of low birth weight, preterm or small for gestational age births.

Few studies have specifically examined the effects of BN, occurring prior to pregnancy, on birth outcomes. Overall, it may be suggested that bulimic symptoms incur different pathways of risk, with the majority of available findings indicating non-significant estimates of risk of low birth weight, preterm and small for gestational age births (Bulik et al., 2009; Linna et al., 2014). Regardless, inconsistencies between findings warrant further examination to explore and clarify the long-term effects of these behaviours, therefore a hypothesis was not put forward regarding an association between risk of low birth weight, preterm or small for gestational age births.

7.3 Statistical assumption testing

Assessment of normality, using the Kolmogorov-Smirnov statistic, indicated that the distribution of scores across birth weight and gestational age were not normally distributed. Analysis of skew and kurtosis indicated that data for outcome and predictor variables were negatively and positively skewed respectively. Data on birth weight and gestational age were found to be leptokurtic with the distribution of scores peaked and more extreme scores occurring less frequently than in the normal distribution. The distribution of birth weight and gestational age were negatively skewed, with higher incidences of scores occurring within the upper ranges. Data distribution in relation to disordered eating predictor variables appeared platykurtic. Findings regarding assessment of normality are presented in Table 5. Assessment of
normality for potential covariates including maternal age, birth order, Body Mass Index (BMI) and depressive symptoms indicated that a number of these variables were not normally distributed. These findings are presented in Table 6. Despite non-normality, as previously mentioned, data were not transformed given that correlations were bootstrapped. Post-hoc assessment of multicollinearity of disordered eating predictor variables revealed high tolerance values (above .1) and low VIF values (below 5). These findings indicate that observed variability of one predictor variable was not explained by the other predictor variable and that assumptions of multicollinearity had been met. Assumptions of homogeneity in relation to independent samples t-tests were assessed using Levene’s test for equality of variances. Significant results indicated that, for all but one t-test, assumptions of homogeneity were met and so equal variances among groups were assumed. For t-tests were assumptions of homogeneity were violated, equal variances among groups were not assumed.

Table 5 Analysis of normality for predictor and outcome variables; Kolmogorov-Smirnov, Skew and Kurtosis

<table>
<thead>
<tr>
<th></th>
<th>Birth weight</th>
<th>Gestational age</th>
<th>Bulimia</th>
<th>Drive for Thinness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kolmogorov-Smirnov</td>
<td>0.095*</td>
<td>0.212*</td>
<td>0.139*</td>
<td>0.111*</td>
</tr>
<tr>
<td>Skew</td>
<td>-0.877</td>
<td>-1.373</td>
<td>1.052</td>
<td>0.423</td>
</tr>
<tr>
<td>Kurtosis</td>
<td>1.445</td>
<td>3.393</td>
<td>1.209</td>
<td>-0.656</td>
</tr>
</tbody>
</table>

*Sig p < .05

Note: Predictor variables; Bulimia and Drive for Thinness; represent summed scores from subscales of the EDI

Table 6 Analysis of normality for covariates; Kolmogorov-Smirnov, Skew and Kurtosis

<table>
<thead>
<tr>
<th></th>
<th>Maternal age</th>
<th>First born</th>
<th>BMI</th>
<th>Depressive symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kolmogorov-Smirnov</td>
<td>0.166*</td>
<td>0.445*</td>
<td>0.120*</td>
<td>0.118*</td>
</tr>
<tr>
<td>Skew</td>
<td>0.011</td>
<td>0.903</td>
<td>2.900</td>
<td>0.649</td>
</tr>
<tr>
<td>Kurtosis</td>
<td>-0.733</td>
<td>-1.200</td>
<td>16.000</td>
<td>-0.0303</td>
</tr>
</tbody>
</table>

*Sig p < .05

Note: Covariates included were those identified as having a significant relationship with either predictor or outcome variable
Assessment of univariate outliers revealed a small number of potential outliers in relation to birth weight, gestational age and disordered eating data. Further examination of standardised residual values identified four outliers each for data on birth weight and gestational age. No outliers were identified for data in relation to Drive for Thinness scores. Based on standardised residuals, ten outliers were identified for data based on Bulimia scores. All of these cases were placed at the higher end of the scale. Analysis of 5% trimmed mean scores indicated that observed outliers were not significantly different from the remaining distribution, suggesting that they were not having a strong influence on the data. Extreme cases for birth weight and gestational age were all within plausible or expected ranges. Furthermore, outcomes of interest in the current study, low birth weight and preterm births, are those that fall below optimal ranges. In this sense, more extreme cases observed are those that were sought within the sample. In the absence of any coding or data entry errors, it was decided that these cases were all valid and therefore deemed appropriate to remain within the data set and to be included in final analyses.

Assessment of multivariate outliers, using Cook’s Distance values, revealed one case that was potentially having an undue influence of the data. This case was removed from the sample and analyses were rerun with a total of 187 cases to check whether this case was having an undue effect on the overall model. Removal of this case resulted in an increase in the effect size and statistical significance for adolescent disordered eating predictor variables. Review of accuracy of classification of cases within the model, when including and excluding this case, revealed little difference between models suggesting that it was appropriate for this case to remain within final analyses. For this reason, this case was included within the final analyses.

Missing data for outcomes included in the study were relatively low, with missing data on birth weight (n=1) and gestational age (n=0) accounting for 1.2% and 0% of data obtained for each outcome respectively. No missing data were revealed in relation to small for gestational age births. Analysis of missing data in relation to disordered eating predictor variables; Drive for Thinness and Bulimia scores; revealed n=33 cases of missing data for each predictor, which accounted for 17.6% of the sample. The disordered eating ‘At Risk’ variable was found to have a relatively large
amount of missing data \((n=74, 39.4\% \text{ of the sample})\) given that data imputation occurred at the derived rather than item level. This meant that a number of participants had missing data on one or more of the items comprising the ‘At Risk’ variable, including BMI, Drive for Thinness or Bulimia scores. Missing data for predictors, outcomes and covariates are presented in Table 7. A non-significant result obtained from Little’s Missing Completely at Random (MCAR) test \((\text{Chi-Square}=875.907, \text{df}=888, p=0.607)\) indicated that missing data for disordered eating predictor variables is likely to be missing completely at random. Missing data were imputed in SPSS using the expectation maximisation method, which has been shown to be a valid method of reducing bias associated with missing data (Abraham & Russell, 2004). The final analyses included the whole sample of 188 cases.

Table 7 Missing data, percentage missing in the sample and mean scores

<table>
<thead>
<tr>
<th>Missing</th>
<th>% in sample</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>G3 Sex</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Age (months)</td>
<td>4</td>
<td>2.1</td>
</tr>
<tr>
<td>SES</td>
<td>28</td>
<td>14.9</td>
</tr>
</tbody>
</table>

*Predictor Variables*

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Drive For Thinness</td>
<td>33</td>
<td>17.6</td>
</tr>
<tr>
<td>Bulimia</td>
<td>33</td>
<td>17.6</td>
</tr>
<tr>
<td>ED At Risk</td>
<td>74</td>
<td>39.4</td>
</tr>
<tr>
<td>BMI</td>
<td>74</td>
<td>39.4</td>
</tr>
<tr>
<td>Depressive symptoms</td>
<td>33</td>
<td>17.6</td>
</tr>
<tr>
<td>Alcohol</td>
<td>36</td>
<td>19.7</td>
</tr>
<tr>
<td>Tobacco</td>
<td>37</td>
<td>18.5</td>
</tr>
<tr>
<td>Marijuana</td>
<td>35</td>
<td>18.6</td>
</tr>
</tbody>
</table>

*Outcome variables*

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Age</td>
<td>2</td>
<td>1.1</td>
</tr>
<tr>
<td>Infant sex</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>DOB</td>
<td>2</td>
<td>0.4</td>
</tr>
<tr>
<td>Gestational age</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>Birth weight</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>IVF use</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>First born</td>
<td>19</td>
<td>10.1</td>
</tr>
<tr>
<td>Multiple births</td>
<td>1</td>
<td>0.5</td>
</tr>
</tbody>
</table>
7.4 Descriptive statistics: Disordered eating and adverse birth outcomes

In the current sample, infant birth weight ranged from 1.36kgs to 4.8kgs, with the mean birth weight in offspring 3.42 kilograms (SD= .54). Eleven women reported having a low birth weight birth, which represented 5.9% of the sample. Gestational age ranged from 32 to 44 weeks gestation, with the average length of gestation 39.48 weeks (SD= 1.85). Ten women reported having a preterm birth, which accounted for approximately 5.3% of the current sample. Nineteen infants, 10.1% of the sample, were classified as being small for gestational age based on Australian population norms of gestational age by weight (Dobbins et al., 2012). Table 8 presents frequencies of low birth weight, preterm and small for gestational age births observed within the current sample. Incidence rates of low birth weight, preterm and small for gestational age births in the current sample are relatively consistent with rates cited in previous epidemiological studies (Blencowe et al., 2012; Goldenberg et al., 2008).

<table>
<thead>
<tr>
<th>Table 8 Frequencies of birth outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Birth weight</strong></td>
</tr>
<tr>
<td>Normal birth weight</td>
</tr>
<tr>
<td>Low birth weight</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td><strong>Gestational age</strong></td>
</tr>
<tr>
<td>Near term</td>
</tr>
<tr>
<td>Preterm birth</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td><strong>SGA</strong></td>
</tr>
<tr>
<td>Not SGA</td>
</tr>
<tr>
<td>SGA</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Infants included in the current sample were identified as being the oldest participating child in the ATPG3 study. 135 (71.8%) infants were identified as being the first-born child in the family. Of the 188 participants, 8 responded ‘yes’ to having used IVF to conceive, representing approximately 4.30% of the sample. None of the women who conceived using IVF reported having a low birth weight, preterm or small for gestational age birth. Despite research indicating a higher risk of multiple births for individuals conceiving using IVF (Kulkarni et al., 2013), none of the women who conceived via IVF (n=8) reported having a multiple birth. Approximately
1% of cases were twin or multiple births (n=2). Both twin births were also low birth weight births and one of these was also being born preterm. The gender distribution across birth outcomes appeared quite equal. Of the reported cases of low birth weight births, five were male and six were female. Similarly, half of the reported preterm births were male and half were female. Of those infants born small for gestational age, 12 were male and 7 were female.

The incidence of low birth weight, preterm and small for gestational age births was higher in women classified as being ‘At Risk’ of an eating disorder, compared to those classified as not being at risk. 7.27% of individuals ‘At Risk’ of an eating disorder reported having a low birth weight birth, compared to 5.26% in women classified as not being at risk. 5.45% of women ‘At Risk’ of an eating disorder reported having a premature birth compared to 5.26% of women who were not at risk of an eating disorder. 18.18% (n=10) of women ‘At Risk’ of an eating disorder reported having a small for gestational age birth in contrast to 6.76% (n=9) of women who were not at risk of an eating disorder. Frequencies of low birth weight, preterm and small for gestational age births are presented in Table 9, as well as frequencies of adverse birth outcomes for women identified as being ‘At Risk’ of an eating disorder. Table 9 also outlines frequencies of multiple births, IVF use, birth order and rates of low birth weight, preterm and small for gestational age births observed in these cases.

Table 9 Frequencies of IVF use, multiple births, first births, disordered eating ‘Risk’ and low birth weight, preterm and small for gestational age births

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>% in sample</th>
<th>Low birth weight</th>
<th>Preterm birth</th>
<th>SGA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low birth weight</td>
<td>11</td>
<td>5.9</td>
<td>-</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Preterm Birth</td>
<td>10</td>
<td>5.3</td>
<td>6</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>SGA</td>
<td>19</td>
<td>10.1</td>
<td>7</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>IVF</td>
<td>8</td>
<td>4.3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Multiple Birth</td>
<td>2</td>
<td>1.1</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>G3 Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>83</td>
<td>44.0</td>
<td>5</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>First Born</td>
<td>135</td>
<td>71.0</td>
<td>6</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>ED Risk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at risk</td>
<td>133</td>
<td>70.7</td>
<td>7</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>At Risk</td>
<td>55</td>
<td>29.3</td>
<td>4</td>
<td>3</td>
<td>10</td>
</tr>
</tbody>
</table>
Demographics and descriptive information, including disordered eating, socioeconomic status and BMI of G2 participants at 15 and 16 years of age, is presented in Table 10. Summed scores of the Drive for Thinness and Bulimia subscales of the EDI ranged from 7 to 38 and 7 to 28 respectively, with higher scores indicating greater levels of disordered eating psychopathology. 55 individuals in the sample were classified as being ‘At Risk’ of an eating disorder. 9.57% of the sample ($n=18$) reported a BMI within the underweight range, BMI < 17.

Table 10 Demographics of adolescent sample at 15 and 16 years of age

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean (SD)</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>188</td>
<td>188.85 (1.479)</td>
<td>185</td>
<td>195</td>
</tr>
<tr>
<td><strong>SES</strong></td>
<td>188</td>
<td>4.02 (1.277)</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>188</td>
<td>21.31 (3.621)</td>
<td>13</td>
<td>49</td>
</tr>
<tr>
<td><strong>Drive for Thinness</strong></td>
<td>188</td>
<td>18.87 (7.215)</td>
<td>7</td>
<td>38</td>
</tr>
<tr>
<td><strong>Bulimia</strong></td>
<td>188</td>
<td>12.93 (3.832)</td>
<td>7</td>
<td>28</td>
</tr>
</tbody>
</table>

7.5 Preliminary analysis of continuous variables: Correlations

Bivariate correlations were conducted to explore the relationships between continuous predictors, outcomes and potential covariates. Zero order correlations for all continuous predictors, outcomes and covariates were bootstrapped, using 1000 bootstraps, to account for non-normally distributed data. These are presented in Table 11. Both Drive for Thinness and Bulimia scores were positively correlated with each other ($r=.253, p<.01$). Drive for Thinness and Bulimia scores were found to have a significant positive correlation with total summed depression scores ($r=.293, p<.01; r=.481, p<.01$) as well as BMI at 15 years of age ($r=.370, p<.01, r=.189, p<.01$). Bulimia scores were found to have a significant positive correlation with adolescent alcohol use ($r=.144, p<.05$). Birth weight was not significantly correlated with Drive for Thinness or Bulimia scores on the EDI ($r=.008, r=.033$). Similarly, gestational age was not significantly correlated with Drive for Thinness or Bulimia scores ($r=.133, r=.020$).
<table>
<thead>
<tr>
<th></th>
<th>Birth weight</th>
<th>Gestational age</th>
<th>EDI DFT</th>
<th>EDI BUL</th>
<th>BMI</th>
<th>Maternal Age</th>
<th>SES</th>
<th>Depressive symptoms</th>
<th>Tobacco</th>
<th>Alcohol</th>
<th>Marijuana</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>0.622**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational age</td>
<td>1</td>
<td>0.133</td>
<td>0.020</td>
<td>0.118</td>
<td>-0.014</td>
<td>-0.102</td>
<td>0.094</td>
<td>0.041</td>
<td>-0.040</td>
<td>0.140</td>
<td></td>
</tr>
<tr>
<td>EDI DFT</td>
<td>1</td>
<td>0.253**</td>
<td>0.370**</td>
<td>-0.063</td>
<td>-0.002</td>
<td>0.265**</td>
<td>0.055</td>
<td>0.076</td>
<td>-0.011</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDI BUL</td>
<td>1</td>
<td>0.189**</td>
<td>0.008</td>
<td>0.054</td>
<td>0.481**</td>
<td></td>
<td>0.092</td>
<td>0.144*</td>
<td>-0.037</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>1</td>
<td>0.021</td>
<td>0.125</td>
<td>0.209**</td>
<td>0.006</td>
<td></td>
<td>0.002</td>
<td>-0.058</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal Age</td>
<td>1</td>
<td>-0.053</td>
<td>0.005</td>
<td>0.192**</td>
<td>0.032</td>
<td></td>
<td>0.082</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SES</td>
<td>1</td>
<td>0.050</td>
<td>-0.112</td>
<td>-0.102</td>
<td>-0.027</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressive symptoms</td>
<td>1</td>
<td>0.189**</td>
<td>0.058</td>
<td>0.043</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobacco</td>
<td>1</td>
<td>0.295**</td>
<td>0.402**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>1</td>
<td>0.266**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marijuana</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

** Significant at p< .01 (2-tailed).
* Significant at the p< .05 (2-tailed).

Note: Correlations were bootstrapped using 1000 bootstraps to account for non-normally distributed data.
Note: Tobacco, alcohol and marijuana use was coded 0=none, 1=monthly, 2=weekly and so while not representing a continuous scale, were included here to provide a preliminary assessment of these relationships.
7.6 Preliminary analysis of categorical variables

Chi square and Fischer’s Exact Tests of independence were conducted to assess the relationships between categorical predictor and outcome variables and potential covariates. Results from chi square and Fischer’s Exact Tests of independence are presented in Table 12. Analyses revealed that low birth weight, preterm and small for gestational age births were all independent of gender, parity, IVF use, birth order or being the first-born infant, and substance use (alcohol, tobacco and marijuana) in adolescence. Findings indicated that low birth weight births were not independent of multiple or twin births. Despite revealing a significant relationship with low birth weight births, data on multiple births were not included in final analyses due to low frequencies of these outcomes. Low birth weight and preterm births were not independent of each other and small for gestational age births were not independent of low birth weight or preterm births. This is not unexpected given that, as noted in Chapter two, these outcomes are known to not be independent of one another (Kramer, 1987; Tucker & McGuire, 2004). Disordered eating ‘Risk’ in adolescence was found to be independent of low birth weight and preterm births but not small for gestational age births.

Table 12 Chi Square Analyses and Fischer’s Exact Test

<table>
<thead>
<tr>
<th></th>
<th>Gender</th>
<th>First Born</th>
<th>IVF</th>
<th>ED ‘At Risk’</th>
<th>Multiple births</th>
<th>LBW</th>
<th>Preterm</th>
<th>SGA</th>
<th>Alcohol</th>
<th>Tobacco</th>
<th>Marijuana</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBW</td>
<td>1</td>
<td>0.297</td>
<td>1</td>
<td>0.733</td>
<td>0.003*</td>
<td>-</td>
<td>0.000*</td>
<td>0.000*</td>
<td>0.390</td>
<td>0.177</td>
<td>0.392</td>
</tr>
<tr>
<td>Preterm</td>
<td>0.752</td>
<td>0.472</td>
<td>1</td>
<td>1</td>
<td>0.104</td>
<td>0.000*</td>
<td>-</td>
<td>1</td>
<td>0.519</td>
<td>0.664</td>
<td>0.428</td>
</tr>
<tr>
<td>SGA</td>
<td>0.092</td>
<td>0.781</td>
<td>1</td>
<td>0.030*</td>
<td>0.193</td>
<td>0.000*</td>
<td>1</td>
<td>-</td>
<td>0.457</td>
<td>0.481</td>
<td>0.542</td>
</tr>
</tbody>
</table>

*Significant at p< .05

Independent sample t-tests were conducted to compare mean differences in continuous measures of birth weight and gestational age between women at risk of an eating disorder at 15 and 16 years of age and normal comparisons, or those classified as not being at risk of an eating disorder. Findings revealed no significant difference
in mean offspring birth weight in women ‘At Risk’ (Mean=3.36kg, SD=.55) and not at risk (Mean=3.44, SD=.53) of an eating disorder ($t=.996$, $df=186$, $p=.321$, two tailed). Similarly, no significant differences in mean gestational age were observed between women at risk of and eating disorder (Mean=39.55, SD=1.65) compared to those classified as not at risk (Mean=39.45, SD=1.93) ($t=-.318$, $df=186$, $p=.751$, two tailed). Results are presented in Table 13 and 14.

Table 13 Independent samples T-Test comparing birth weight between disordered eating ‘Risk’ and not at risk groups

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>T</th>
<th>df</th>
<th>Sig (two tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At Risk</td>
<td>3.36</td>
<td>0.55</td>
<td>0.996</td>
<td>168</td>
<td>0.321</td>
</tr>
<tr>
<td>Not at risk</td>
<td>3.44</td>
<td>0.53</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 14 Independent samples T-test comparing gestational age between disordered eating ‘Risk’ and not at risk groups

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>T</th>
<th>df</th>
<th>Sig (two tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At Risk</td>
<td>39.55</td>
<td>1.65</td>
<td>-0.318</td>
<td>168</td>
<td>0.751</td>
</tr>
<tr>
<td>Not at risk</td>
<td>39.45</td>
<td>1.93</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Independent sample t-tests were also conducted to assess mean differences in Drive for Thinness and Bulimia scores in women reporting low birth weight, preterm or small for gestational age births compared to women reporting normal weight term births. Findings did not reveal any significant differences in Drive for Thinness or Bulimia scores in women reporting low birth weight or preterm births compared to normal weight term births. However, significant differences in mean Drive for Thinness scores were observed in women reporting small for gestational age births (Mean=22.4, SD=8.655) compared to women reporting appropriate weight for age births (Mean=18.47, SD=6.953) ($t=-2.275$, $df=186$, $p=.024$, two tailed). Significant differences in mean scores on the Bulimia subscale of the EDI were not observed between women reporting small for age and appropriate for age births. These results are presented in Tables 15, 16 and 17.
Table 15 *Independent samples T-test comparing Drive for Thinness and Bulimia scores between low birth weight and normal weight births*

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>T</th>
<th>df</th>
<th>Sig (two tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drive for Thinness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal weight</td>
<td>18.880</td>
<td>7.127</td>
<td>0.131</td>
<td>186</td>
<td>0.896</td>
</tr>
<tr>
<td>LBW</td>
<td>18.590</td>
<td>8.903</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bulimia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal weight</td>
<td>13.020</td>
<td>3.818</td>
<td>1.362</td>
<td>186</td>
<td>0.175</td>
</tr>
<tr>
<td>LBW</td>
<td>11.400</td>
<td>3.916</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 16 *Independent samples T-test comparing Drive for Thinness and Bulimia scores between preterm and term births*

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>T</th>
<th>df</th>
<th>Sig (two tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drive for Thinness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not preterm</td>
<td>18.880</td>
<td>7.248</td>
<td>0.088</td>
<td>186</td>
<td>0.930</td>
</tr>
<tr>
<td>Preterm births</td>
<td>18.670</td>
<td>6.958</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bulimia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not preterm</td>
<td>12.900</td>
<td>3.764</td>
<td>-0.381</td>
<td>186</td>
<td>0.704</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>13.380</td>
<td>5.125</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 17 *Independent samples T-test comparing Drive for Thinness and Bulimia scores between small for gestational age and appropriate weight for age births*

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>T</th>
<th>df</th>
<th>Sig (two tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drive for Thinness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not SGA</td>
<td>18.470</td>
<td>6.953</td>
<td>-2.275</td>
<td>186</td>
<td>0.024*</td>
</tr>
<tr>
<td>SGA</td>
<td>22.400</td>
<td>8.655</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bulimia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not SGA</td>
<td>12.960</td>
<td>3.829</td>
<td>0.381</td>
<td>186</td>
<td>0.704</td>
</tr>
<tr>
<td>SGA</td>
<td>12.610</td>
<td>3.950</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Significant at p< .05
Independent sample t-tests were then conducted to assess the potential relationships between continuous covariates and categorical outcome variables. These results are presented in Table 18. Results revealed significant mean differences in maternal age for infants born small for gestational age (mean=27.84, SD=1.385) compared to infants born appropriate weight for age (mean=28.62, SD=1.355) ($t=2.368$, $df=186$, $p=0.019$, two tailed). Significant differences in mean depression scores were also revealed for women identified as being ‘At Risk’ of an eating disorder (mean= 8.00, SD=4.036) compared to being classed as not being at risk (mean=5.72, SD=3.560) ($t=-3.846$, $df=186$, $p=.000$, two tailed).

Table 18 *Independent sample t-tests between continuous covariates and categorical predictor and outcome variables*

<table>
<thead>
<tr>
<th></th>
<th>Maternal age</th>
<th>SES</th>
<th>Depressive symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low birth weight</td>
<td>$t=1.809$</td>
<td>$t=0.127$</td>
<td>$t=1.538$</td>
</tr>
<tr>
<td></td>
<td>$p=0.072$</td>
<td>$p=0.906$</td>
<td>$p=0.126$</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>$t=-0.527$</td>
<td>$t=-1.262$</td>
<td>$t=0.283$</td>
</tr>
<tr>
<td></td>
<td>$p=0.609$</td>
<td>$p=0.208$</td>
<td>$p=0.777$</td>
</tr>
<tr>
<td>SGA</td>
<td>$t=2.368$</td>
<td>$t=-0.555$</td>
<td>$t=0.444$</td>
</tr>
<tr>
<td></td>
<td>$p=0.019^*$</td>
<td>$p=0.580$</td>
<td>$p=0.657$</td>
</tr>
<tr>
<td>ED 'At Risk'</td>
<td>$t=0.673$</td>
<td>$t=-1.159$</td>
<td>$t=-3.846$</td>
</tr>
<tr>
<td></td>
<td>$p=0.501$</td>
<td>$p=0.248$</td>
<td>$p=0.000^*$</td>
</tr>
</tbody>
</table>

Significant at $p < .05$

*Note: Levene’s test of equality, for models assessing mean differences in maternal age between women reporting preterm and full term births, revealed that the assumption of homogeneity had been violated. Given this, equal variances between groups were not assumed.*

7.7 Main analyses: Logistic regression

Unadjusted logistic regression analyses were conducted, using SPSS Version 20, regressing each disordered eating predictor variable separately onto low birth weight, preterm and small for gestational age births. These analyses aimed to test hypotheses predicting an increase in risk of low birth weight, preterm births and small for gestational age births to women experiencing disordered eating behaviour at 15 and 16 years of age. Drive for Thinness, Bulimia scores and disordered eating ‘Risk’ was assessed independent of one another to reduce potential issues associated with collinearity. Results from unadjusted logistic regressions are presented in Table 19.
7.7.1 Unadjusted analyses predicting low birth weight and preterm births

Findings from unadjusted logistic regression analyses confirmed results from preliminary analyses by revealing that Drive for Thinness and Bulimia scores did not significantly predict risk of low birth weight (OR: 0.994, CI: .913-1.083, OR: 0.867, CI: .706-1.065) or preterm births (OR: .996, CI: 911-1.089; OR: 1.031, CI: .881-1.206). Similarly, disordered eating ‘Risk’ did not significantly predict risk of low birth weight (OR: 1.412, CI: .396-5.031) or preterm births (OR: 1.038, CI: .259-4.172).

7.7.2 Unadjusted analyses predicting small for gestational age births

Risk of small for gestational age births was significantly increased in women scoring higher on the Drive for Thinness subscale of the EDI, and individuals ‘At Risk’ of an eating disorder in adolescence (OR: 1.074, CI: 1.08-1.145, p< .05, OR: 3.062, CI: 1.169-8.020, p< .05). Women who scored higher on the Drive for Thinness subscale of the EDI were 1.07 times more likely to have a small for gestational age birth. Individuals ‘At Risk’ of an eating disorder were approximately three times more likely to experience a small for gestational age birth, compared to women who were not at risk. Adolescent Bulimia scores did not significantly predict risk of small for gestational age births (OR: 0.975, CI: .856-1.110).

7.7.3 Adjusted analyses predicting risk of small for gestational age births

Adjusted logistic regression analyses were conducted to account for the potential effects of covariates. Covariates included within adjusted models were those that revealed a significant relationship with either small for gestational age births or disordered eating in adolescence. Logistic regression models were adjusted for maternal age, Body Mass Index (BMI) and depressive symptoms at 15 and 16 years of age. However, BMI was excluded from adjusted models that assessed disordered eating ‘Risk’ as this variable was comprised of data on BMI and therefore likely to be highly related. Covariates that did not reveal a significant relationship, based on
results from preliminary analyses, with either predictor or outcome variables were excluded from the final analyses. Findings from adjusted logistic regression analyses are presented in Table 20.

Drive for Thinness scores and disordered eating ‘Risk’ in adolescence remained the strongest predictors of small for gestational age births after adjusting for maternal age, BMI, and depressive symptoms (OR: 1.104, CI: 1.027-1.188, OR: 3.473, CI: 1.241-9.722). Reported effects, in relation to adolescent disordered eating, were observed to increase slightly when adjusting for potential covariates. However, confidence intervals were found to widen indicating a relative decrease in the precision of effects. Maternal age was the only other predictor making a unique contribution to the model. Increasing maternal age was found to result in a significant decrease in the likelihood of small for gestational age births when included in models regressing Drive for Thinness scores and disordered eating ‘Risk’ (OR: .672, CI: .453-.998; OR: 3.473, CI: 1.241-9.722). The overall adjusted models explained between 5.9% and 14% of the variance in small for gestational age births and correctly classified approximately 89.9% of cases. Examination of Omnibus tests of model coefficients indicated that both models were statistically significant, indicating that these models were likely able to adequately distinguish between individuals who did and did not report having a small for gestational age birth. These findings suggests that the disordered eating behaviour, at 15 and 16 years of age, independently contribute to the risk of small for gestational age births in adulthood.

7.8 Discussion of findings of the effects of adolescent disordered eating on next generation adverse birth outcomes

Hypotheses predicting an increased risk of low birth weight, preterm or small for gestational age births to women reporting higher scores on the Drive for Thinness scale, or those classified as being ‘At Risk’ of eating disorder in adolescence, were only partially supported. Drive for Thinness scores and being ‘At Risk’ of an eating disorder did not predict risk of low birth weight or preterm births. Yet, significant increases in risk of small for gestational age births were revealed after adjusting for maternal age, adolescent Body Mass Index (BMI) and depression. Bulimia scores were not significantly associated with risk of low birth weight, preterm or small for gestational age births.
Table 19 Unadjusted logistic regression analyses assessing the effects of adolescent disordered eating on low birth weight, preterm and small for gestational age births

<table>
<thead>
<tr>
<th></th>
<th>Low birth weight</th>
<th>Preterm Birth</th>
<th>Small for Gestational Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (CI)</td>
<td>B</td>
<td>Sig</td>
</tr>
<tr>
<td>Drive for Thinness</td>
<td>0.994 (0.913-1.083)</td>
<td>-0.006</td>
<td>0.896</td>
</tr>
<tr>
<td>Bulimia</td>
<td>0.867 (0.706-1.065)</td>
<td>-0.143</td>
<td>0.173</td>
</tr>
<tr>
<td>ED 'At Risk'</td>
<td>1.412 (1.396-5.031)</td>
<td>0.345</td>
<td>0.595</td>
</tr>
</tbody>
</table>

*Sig at p< .05

Note: Each disordered eating predictor variable and birth outcome was entered separately into logistic models to account for potential issues of multicollinearity

Table 20 Adjusted logistic regression analyses assessing the effects of adolescent disordered eating on risk of small for gestational age births

<table>
<thead>
<tr>
<th></th>
<th>Low birth weight</th>
<th>Preterm Birth</th>
<th>Small for Gestational Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (CI)</td>
<td>B</td>
<td>Sig</td>
</tr>
<tr>
<td>Drive for Thinness</td>
<td>1.104 (1.027-1.188)</td>
<td>0.099</td>
<td>0.008*</td>
</tr>
<tr>
<td>Maternal Age</td>
<td>0.672 (.453-.998)</td>
<td>-0.397</td>
<td>0.049*</td>
</tr>
<tr>
<td>Depressive symptoms</td>
<td>0.929 (.801-1.077)</td>
<td>-0.072</td>
<td>0.329</td>
</tr>
<tr>
<td>BMI</td>
<td>0.896 (.707-1.067)</td>
<td>-0.141</td>
<td>0.172</td>
</tr>
</tbody>
</table>

*Sig at p< .05

Note: Variables included within adjusted models (maternal age, depressive symptoms and BMI) were those revealing significant correlations with predictor or outcome variables. BMI was not included in models regressing ED Risk as BMI is embedded within the At Risk score.
Findings in this study are inconsistent with results reported by Sollid et al. (2004), Eagles et al. (2012) and Linna et al. (2014) who reported a significant increase in risk of low birth weight births to women reporting a history of AN or disordered eating behaviours. Findings from the current study, however, are not likely comparable with findings from Sollid et al. (2004), Eagles et al. (2012) and Linna et al. (2014) given that their samples consisted of clinical cases that included individuals diagnosed with AN or BN. The community sample used in the current study was less likely to include more clinical cases, which may explain inconsistencies between study findings. Results from this study revealed no significant differences in mean infant birth weight in women ‘At Risk’ of an eating disorder in adolescence compared to those who were not at risk. This finding is also inconsistent with the majority of reviewed studies which reported significantly lower mean infant birth weight in women with a history of disordered eating compared to women without. Yet, findings in this study are consistent with findings from two large community studies that reported non-significant differences in average infant birth weight (Bulik et al., 2009; Micali et al., 2012). Both of these studies, however, were retrospective rather than prospective in design. The only prospective study that examined differences in mean infant birth weight in women with and without a history of disordered eating, which utilised a community sample, reported significantly lower average infant birth weight for women with a history of disordered eating.

The finding that adolescent disordered eating is not associated with preterm births is also at odds with findings reported by Bulik et al. (1999), Linna et al. (2014) and Sollid et al. (2004). What made this study unique from those reporting significant findings was the use of a community, rather than clinical, sample. Linna et al. (2014) measured lifetime disordered eating in their study whilst Sollid et al. (2004) assessed disordered eating in the eight years prior to conception. Both studies utilised prospective data and provide persuasive evidence of long-term effects in clinical populations. This suggests that long-term risk may vary as a function of symptom severity, with reproductive complications dependent on the degree of weight loss, length of disorder and rate of weight loss (Herpertz-Dahlmann, 2008). The overall risk of low birth weight or preterm births may be reduced in the general population where fewer clinical or more severe cases are likely to be observed. This may explain non-significant findings revealed in this study. Increasing severity of disordered
eating may increase the risk of low birth weight and preterm births, whilst sub clinical symptoms may predispose women to small for age but normal weight infants. This may explain why, in the current community sample, significant findings were observed in relation to small for gestational age births but not low birth weight or preterm births despite being highly correlated outcomes.

Hypotheses predicting significant increases in risk of small for gestational age births were supported. Findings from this study indicated that adolescents ‘At Risk’ of an eating disorder were three times more likely to have a small for gestational age birth. Analyses revealed that 5.9% to 12.3% of the variance in risk of small for gestational age births was explained through these analyses, which provides a relatively new perspective on factors that contribute to such outcomes. This finding may have important implications given that poorer perinatal outcomes have been associated with infants born even marginally premature to full term or of a relatively normal birth weight, such as those identified as being small for gestational age (Saigal & Doyle, 2008). This may suggest that adolescent disordered eating incurs long-term risks by potentially predisposing women to small for gestational age births in adulthood. This provides preliminary support for developmental theories of risk which stress the influence of adolescent restrictive eating in altering hormonal activity, such as corticotrophin-releasing hormone (CRH), and consequent birth outcomes (Wadhwa et al., 2004). Chronic elevation of cortisol resulting from stress in early life, such as that associated with disordered eating, has been associated with long-term changes that in turn result in a hyper responsive or chronically activated physiologic stress response (Shonkoff et al., 2012). Furthermore, low folate and iron intake has been shown to increase the risk of small for gestational age births (Baker et al., 2009). Restricted eating patterns, during adolescence, may indicate poorer nutritional intake throughout development and pregnancy.

Risk associated with scores on the Drive for Thinness scale infers that as disordered eating psychopathology increases the risk of small for gestational age births in increased. When accounting for adolescent BMI to identify women ‘At Risk’ of an eating disorder, observed effects sizes were found to increase (OR: 3.473). This provides support for biological effects, beyond that associated with psychological factors alone. Interestingly, BMI alone did not significantly predict risk of small for
gestational age births (OR: 0.896, CI: .707-1.067), suggesting that other mechanisms associated with the psychological factors assessed play an important role. Inclusion of an ‘At Risk’ disordered eating variable represents a strength of this study in identifying individuals more likely to engage in restrictive eating or experience physical symptoms of starvation. This suggests that the risk of small for gestational age births is greater for women experiencing physical signs of starvation in addition to psychological pathology.

Significant findings in relation to small for gestational age births are consistent with results reported by Conti et al. (1998), Koubaa, et al., (2013), Linna et al. (2014) and Sollid et al. (2004) who also found that risk of small for gestational age births was higher in women with a history of disordered eating. Importantly, the current study may be one of the first to reveal significant increases in risk of small for gestational age births using prospective community based data. Only two studies, reporting significant findings, obtained data prospectively, though both of these comprised of clinical samples. This study was able to address limitations associated with use of retrospective reporting and recall bias through use of prospective longitudinal data (Little, 1986). Therein lies one of the main strengths of this study and the ATP. The only other prospective community study, examining the effects of preconception disordered eating (Wentz et al., 2009), reported a non-significant association between preconception disordered eating and risk of small for gestational age births. Non-significant findings in their study may be explained by a small sample (n=102) and low frequencies of small for gestational births (n=3). Higher frequencies of small for gestational age births in this study meant that more information was available in which to assess these relationships and detect potential effects.

Another important finding from this study is a significant decrease in risk of small for gestational age births associated with increasing maternal age. Increasing maternal age has been consistently associated with an increased risk of pregnancy complications and adverse birth outcomes, with mothers 35 years and above believed to be at the greatest risk (Jacobsson, Ladfors, & Milsom, 2004; Kenny et al., 2013). The relationship between birth risks and maternal age is U-shaped, with higher risks observed for the youngest and oldest mothers (Reichman & Pagnini, 1997). The sample in this study comprised of mothers aged between 26 to 32 years, which
represents a period of optimal biological reproductive health. Reductions in risk associated with increasing maternal age, in this sample, may reflect improvements in prenatal health behaviours associated with increasing maternal age and greater pregnancy intent (Keeton & Hayward, 2007). Decreases in risk may not apply for women above 32 years of age, where risk of adverse birth outcomes is likely to rise (Luke & Brown, 2007).

In line with most recent research, scores on the Bulimia subscale of the EDI did not significantly predict risk of low birth weight, preterm or small for gestational age births. This provides a positive prognosis for individuals presenting with bulimic symptoms though further investigation is required. This finding in consistent with studies reporting non-significant increases in risk of adverse birth outcomes in bulimic samples (Bulik et al., 2009; Linna et al., 2014) although is contradictory to results reported by Conti et al. (1998). They reported that elevated bulimia scores on the EDI significantly predicted risk of small for gestational age births. Significant findings reported by Conti et al. (1998) may be associated with use of a small case control sample and an increased risk of type I error. Limitations in available studies that specifically examine preconception risks for bulimic women meant that analyses in this study were largely exploratory in nature. These findings do not infer an absence of risk for women experiencing bulimic symptoms in adolescence but suggests that risks may differ from women presenting with symptoms characteristic of AN. Metabolic dysfunction, associated with BN, for instance, has been linked to cardiac abnormalities in infants and increased risk of miscarriage and foetal death (Micali, Simonoff et al., 2007; Micali & Treasure, 2009).

It is possible that non-significant findings, in relation to risk of low birth weight and preterm births, may be explained by a degree of heterogeneity within disordered eating and birth outcomes. Differential pathways of risk have been proposed based on subtypes of disordered eating or birth outcomes (Micali & Treasure, 2009; Wilcox, Skjaerven, & Lie, 2007). Yet, differences in birth outcomes, such as indicated verse spontaneous preterm births, were not able to be assessed. What is more, large amounts of symptom overlap for Drive for Thinness and Bulimia subscales means that clinical subtypes could not be clearly distinguished and differential pathways of risk could not be adequately explored (Garner et al., 1983; Le
Low prevalence rates of these birth outcomes and disordered eating subtypes means that even large population-based studies may have limited power to detect differences between exposure groups (Micali et al., 2012). The actual risk for sub-populations may be different from estimates of risk reported in this study.

Few studies, to date, have specifically examined the effects of adolescent disordered eating on birth outcomes. This study provided a point of difference from previous research in clearly measuring disordered eating behaviour between 15 and 16 years of age. Maternal age of ATP mothers ranged from 26 to 32 years, meaning that there was a gap of approximately 11 to 21 years between assessment in adolescence and birth outcomes in adulthood. Non-significant findings reported in this study, in relation to low birth weight and preterm births, may be associated with the timing of disordered eating, with patterns or pathways of risk different for individuals engaging in these behaviours during adolescence, adulthood or pregnancy. Only one other study (Wentz et al., 2009) specifically examined the effects of adolescent onset disordered eating, at 15 years of age, on birth outcomes. They reported that the mean time between onset of disordered eating behaviour and pregnancy was 18.1 years (range: 14.6-21.5 years). Similar to this study, they reported no significant increase in risk of preterm births, suggesting that risk of preterm births for women reporting teenage onset disordered eating is comparable to non-disordered eating women.

It may be suggested that the development of healthy eating habits prior to pregnancy may offset potential long-term effects of adolescent disordered eating (Abraham, 1998). However, Koubaa et al. (2005) reported that 22% of women with a history of disordered eating relapsed during pregnancy. If disordered eating behaviours continues during pregnancy or relapse occurs during pregnancy, risk of low birth weight or preterm births may increase (Pasternak et al., 2012). Disordered eating data were not obtained during generation three of the ATP study. Disordered eating during pregnancy may result in direct harms to offspring that differ from risks occurring through adolescent exposure. Despite this, reported reductions in disordered eating for some women once becoming pregnant suggests that the percentage of women engaging in disordered eating behaviour during pregnancy may be low (Blais et al., 2000). This may be particularly relevant for community samples where
symptoms may be less severe or entrenched. It has been suggested that pregnancy rates are reduced for women with active eating disorders due to decreased fertility rates and poorer social and emotional functioning (Herpertz-Dahlmann et al., 2001; Katz & Vollenhoven, 2000; Lowe et al., 2001). This may infer that women who become pregnant are more likely to represent those who have ceased such behaviours. Adolescent disordered eating may either result in long-term biological effects or predispose individuals to continuation of maladaptive behaviours during pregnancy.

The findings from this study remain preliminary in nature with the ATPG3 study still in the process of data collection and recruitment. It is acknowledged that a relatively small sample obtained in the current study may contribute to an overestimation or underestimation of effects and low reproducibility of current findings (Button et al., 2013). Furthermore, low frequencies of birth outcomes may have meant that these outcomes were not adequately represented in the sample and potential effects were unable to be detected (Johnson, 1999). The ATP project aims to recruit 1000 G3 infants within the coming years so that larger replication studies may be conducted. In conclusion, this study demonstrated early evidence of the long-term effects of adolescent disordered eating. Specifically, results from this study revealed a significantly increased risk of small for gestational age births to women reporting elevated scores on the Drive for Thinness subscale or those identified as being ‘At Risk’ of an eating disorder between 15 and 16 years of age. This has implications for the prevention and management of small for gestational age births, with adolescence potentially representing a critical period of early intervention.

CHAPTER 8: INTERGENERATIONAL RISK OF LOW BIRTH WEIGHT, PRETERM AND SMALL FOR GESTATIONAL AGE BIRTHS

8.1 Chapter overview

This chapter expands on findings obtained in the second study of this thesis by examining continuity of low birth weight, preterm and small for gestational births across generations. This chapter presents a review of intergenerational research and theory in the context of generational transmission of low birth weight, preterm and small for gestational age births. Also provided is a rationale for examining the role of
adolescent disordered eating in the transmission of adverse birth outcomes from mother to offspring. Aims and hypotheses for the final study of this thesis are presented in light of current literature.

8.2 Intergenerational risk of low birth weight, preterm and small for gestational age births

The Developmental Origins of Health and Disease (DOHaD) hypothesis proposes that early life experiences, particularly during neonatal development and infancy influence later development and wellbeing (Wadhwa et al., 2009). The DOHaD framework provides a foundation for examining the transmission of risk of disease from mother to child as a result of altered or suboptimal uterine conditions. Traditional models of developmental risk have focused on the examination of risk factors occurring during gestation, or the risks experienced by the developing infant (Chapman & Scott, 2001). It is proposed that an extended intergenerational approach, that directs the focus much earlier to consider risks occurring during maternal development and infancy, may provide a more comprehensive framework for understanding the transmission of risk from one generation to the next (Chapman & Scott, 2001). Intergenerational factors refer to conditions, exposures and environments experienced by one generation that in turn relate to the health growth and development of the next generation (Emanuel, 1986).

The prenatal period has been identified as playing a key role in the transmission of risk from mother to offspring, particularly in relation to low birth weight, preterm and small for gestational age births (Chapman & Scott, 2001). Maternal birth weight, or a mother's weight when she was born, is thought to be indicative of underlying conditions, such as substandard nutrition, experienced during in utero development. Restricted intrauterine growth in mothers has been linked to the intrauterine growth of offspring (Hackman, Emanuel, Van Belle, & Daling, 1983). It is argued that conditions experienced in utero result in permanent changes in maternal growth and development, which alter the in utero environment for foetal development in later pregnancies (Drake & Walker, 2004). In such cases, a self-perpetuating mechanism may occur, whereby risks that alter the uterine environment are passed
Building on this, findings from studies of the Dutch winter famine between 1944 and 1945 support theories of intergenerational associations between maternal and infant birth weight (Schulz, 2010; Stein & Lumey, 2000). Women exposed to famine during late pregnancy had offspring with significantly lower birth weight compared to women unexposed (Stein & Lumey, 2000). This is indicative of transmission of risk across generations and highlights the influence of environment during critical stages of development, not only for mothers but also for the next generation. In contrast to this, findings from recent studies, that used third generation data, suggest that patterns of birth weight are not necessarily passed from grandparent to grandchild (Painter et al., 2008; Veenendaal et al., 2013). Whilst these studies in principle support the theory of generational continuity of risk, a central finding to consider is that under some circumstances risk appears to dissipate across multiple generations. Although, evidence also supports the proposition that in certain contexts, risk may ‘skip’ a generation. For instance, studies have found that normal weight infants born to women exposed to the Dutch famine during early pregnancy had smaller babies in the next generation (Steing & Lumey, 2000). Intergenerational risk may reoccur in a delayed response to changing conditions, with favourable conditions potentially ameliorating risk in one generation only for this to return where conditions become unfavourable.

Empirical studies have demonstrated a strong association between maternal and infant birth weight (Emanuel, Filakti, Alberman, & Evans, 1992; Farina, Dini, Mattioli, Rosa & Rizzo, 2010; Godfrey, Barker, Robinson, & Osmond, 1997; Hackman et al., 1983; Klebanoff, Meirik, & Berendes, 1989). Magnus, Bakketeig and Skjaerven (1993) examined transmission of birth weight and age in a sample of 11092 Norwegian mothers born between 1967 and 1969 and offspring born between 1986 and 1989. Mothers born with low birth weight were at a significantly increased risk of low birth weight births, compared to mothers weighing 4kgs or above at birth (OR: 3.03, CI: 1.79-5.11). Interestingly, mothers born prematurely were not significantly more likely to have a premature birth (OR: 1.46, CI: .96-2.21). Whilst not discounting the importance of risk associated with premature births, the relative absence of
significant next generation effects suggests that intergenerational transmission of risk is associated with low birth weight rather than with gestational age. Farina et al. (2010) revealed that a total of 28.6% of infants to mothers who were born small for gestational age were also born small for gestational age compared with 8.6% of the children born to appropriate weight for age mothers ($p<0.01$). They inferred that intrauterine growth restriction in mothers presents as a risk for intrauterine growth restriction in their children.

Intergenerational patterns of low birth weight births appears to hold across studies examining ethnicity as a possible correlating factor. This was reported in a cohort of African American and Caucasian mothers born between 1989 and 1991 (Coutinho, David, & Collins, 1997). The incidence of low birth weight births for Caucasian mothers born with low birth weight was 8.5% compared to 4.8% for mothers who were born at a normal weight (RR=1.7, CI: 1.6-2.0). In addition, the rate of low birth weight births for African American mothers born low birth weight was 17.9%, compared to 10.8% for controls. Winkvist, Mogren, and Hogberg (1998) reported a 50% increase in risk of small for gestational age births for mothers born small for gestational age, yet this association was not statistically significant. They reported that this was likely due to a lack of power to detect potential effects. Overall, findings contribute to a body of evidence suggesting transmission of birth weight from mother to offspring (Selling, Cartensen, Finnstrom, & Sydsjo, 2006; Wang, Zuckerman, Coffman, & Corwin, 1995).

A review of the literature conducted by Ramakrishnan, Martorell, Schroeder, and Flores (1999) revealed that for every 100 grams increase in maternal birth weight, infant birth weight increased by 10 to 20 grams. They concluded that young women who experienced sub-optimal growth in early life became stunted as adults, and were then more likely to give birth to low birth weight infants. For these infants, the cycle is thought to repeat into adulthood and onto the next generation. Further to this, an inverse dose effect response association has been indicated between maternal birth weight and adverse birth outcomes, with the strongest association between maternal and infant birth weight (Emanuel et al., 1999). This pattern was observed across a number of ethnic groups including Caucasian, African-American, Native American
and Hispanic women, drawing attention to the potential influence of environmental factors, such as poverty and disadvantage, in transmission of risk of low birth weight.

Low birth weight has been identified as an indicator of similar outcomes in next generation offspring, including risk of small for gestational age births or those falling below the 10th percentile for gestational weight and age. Klebanoff, Schulsinger, Mednick, and Secher (1997) examined the transmission of preterm and small for gestational age births in 2596 Danish women born between 1959 and 1961. They found that women born small for gestational age were twice as likely (CI=1.4-3.0) to have a small for gestational age birth. However, preterm births were not significantly correlated between mothers and infants. In light of this, it was proposed that transmission of risk occurred as a result of similar environmental, social and behavioural conditions replicated across generations as well as genetic vulnerabilities. Jaquet et al. (2005) examined generational patterns of small for gestational age births, accounting for primiparity, parent education, pregnancy induced hypertension, maternal tobacco use and adequate prenatal care. Results from their study confirmed intergenerational patterns of small for gestational age births from mothers to offspring (OR: 4.7, CI: 2.36-9.38) offset by predisposing factors, such as maternal hypertension and substance use, as well as social conditions related to limited education and inadequate maternal care.

Collins, Rankin, and David (2011) examined whether economic environment, including neighbourhood, education, marital status, prenatal care utilisation, parity and maternal age, can be seen to underlie an association between maternal and infant low birth weight. They found a significant intergenerational effect independent of economic environment among Caucasian and African American women. They reported that only a small percentage of low birth weight, preterm and small for gestational age births could be attributed to maternal low birth weight. To explain this they proposed that other environmental or psychosocial variables, such as a lack of exercise, access to medical care and eating habits, underlie the association between maternal and infant low birth weight. Of course it can be claimed that access to medical care and adequate nutrition may be directly related to economic conditions. This study, nevertheless, indicates that further research is required to better
understanding the impact of environmental factors on the risks of transmission of low birth weight and small for gestational age births.

Studies undertaken so far have, in the main, indicated non-significant trans-generational effects in relation to preterm births. However, overall conclusions remain tentative due to inconsistencies between study findings (Alberman, Emanuel, Filakti, & Evans, 1992; Castrillio, Rankin, David & Collins, 2014; Klebanoff et al., 1989; Klebanoff et al., 1997; Magnus et al., 1993; Swamy, Ostbye, & Skaerven, 2008). Selling et al. (2006) conducted a large population based study in Sweden comprising a cohort of first-born children of 38,720 women born between 1973 and 1975. They found that the risk of preterm births was 30% higher in women who were born premature, although this effect was no longer significant when accounting for socio-economic status, maternal Body Mass Index (BMI) and smoking status (adjusted OR: 1.24, CI: 0.95-1.62). This may indicate that environmental influences play a greater role in the development of preterm births, compared to the transmission of birth weight to which independent associations remained after adjusting for socio economic conditions (Collins et al., 2011). This may also suggest that maternal weight, as opposed to gestational age, is a stronger predictor of adverse birth outcomes in infants (Emanuel et al., 1992).

Porter, Fraser, Hunter, Ward, and Varner (1997) examined maternal contributions to preterm births in a cohort of 4186 US women born between 1970 and 1992 and their offspring born between 1970 and 1992. In contrast to previous findings, they reported a significantly increased risk of preterm births in preterm mothers, compared to mothers born at term (OR: 1.18, CI: 1.02-1.37). Moreover, the risk of preterm births was found to increase as gestational age in mothers, at birth, decreased below 30 weeks gestation. The divergence in findings, compared to previous research suggesting non-significant correlations, was thought to be associated with the use of linked birth records that contribute to a reduction in potential self-report and recall bias associated with other samples (Little, 1986). Their findings were further strengthened by procedures to control for potential confounding variables such as parity and maternal age. Limitations noted within previous studies in terms of inadequately adjusting for these variables were addressed (Hennessy & Alberman, 1998). Extended timeframes between predictor and outcome variables,
associated with intergenerational designs, means that there is the potential for a significant range of exposures to contribute to the development of measured outcomes. Given this, examination of a range of confounding variables is important to reduce the likelihood of type 1 error.

A Meta-analysis, conducted by Shah and Shah (2009), examined the relationship between maternal and offspring birth outcomes. Their findings were consistent with theories of intergenerational patterns of birth weight, revealing a significant increase in the risk of low birth weight and small for gestational age births to women born low birth weight or small for gestational age (OR: 2.23, CI 2.11–2.35; OR: 2.64, CI: 2.28-3.05). Pooled data obtained from six studies indicated a significant increase in risk of preterm births for offspring of women born premature (OR: 1.41, CI: 1.26-1.59). Findings from this analysis help to clarify discrepancies amongst studies investigating patterns of preterm births to infer that intergenerational effects are more substantial than initially thought. In saying this, conclusions made from this review were based on unadjusted data only, in an attempt to reduce variability between studies. Considering that a number of studies reported a reduction in significant effects, after adjusting for confounding variables, it may be suggested that overall effects reported in this review are an over estimation of the true effects.

The current evidence base examining intergenerational continuity of birth outcomes particularly preterm births remains relatively underdeveloped. Issues of design and participant selection, missing data and chosen cut-offs for assessment of birth outcomes are proposed to explain contradictions between study findings (Farina et al., 2010; Klebanoff et al., 1989). Significant variations across study designs, including single institution based studies, national samples and case-control designs, may impact on the interpretation and generalizability of these findings (Klebanoff et al., 1989; Porter et al., 1997; Shah & Shah, 2010). Further to this, methods used to assess gestational age have changed over the years, with different criteria used to identify preterm births for mothers and offspring. This may have implications for findings presented so far, with the potential for an over or underestimation of effects within older cohorts (Selling et al., 2006). Increasing trends in the incidence of low birth weight, preterm and small for gestational age births over the past few decades means that more dated studies may no longer reflect the current problem in relation to
these adverse birth outcomes (Goldenberg et al., 2008; Tucker & McGuire, 2004). Replication studies using prospective intergenerational data are required in order to address noted limitations within current research and provide a more comprehensive picture of how risk develops from one generation to the next.

8.3 Mechanisms of intergenerational risk

Understandings of the mechanisms shaping intergenerational risk are at present speculative, although genetic factors are thought to play an important role (Johnstone & Inglis, 1974). Patterns of recurrent low birth weight and preterm births, across multiple pregnancies, have inferred potential genetic effects from mother to offspring (Bakketeig, Hoffman, & Harley, 1979; Goldenberg et al., 2008; Khoury, Berg, & Calle, 1990). Furthermore, transmission of risk from father to offspring has also been documented, as has patterns of risk among family members including siblings (Alberman et al., 1992; Coutinho et al., 199; Jaquet et al., 2005; La Batide-Alanore, Tregouet, Jaquet, Bouyer, & Tiret, 2002; Wang et al., 1995). Svensson, Pawitan, Cnattingius, Reilly, and Lichtenstein (2006) concluded that genetic factors accounted for almost half (47%) of the variance in small for gestational age births, with 37% attributed to foetal and 9% to maternal genetics. Findings provide persuasive evidence of genetic effects in transmission of risk from one generation to the next, particularly along the maternal line.

Other biological explanations have also been proposed to explain patterns of birth outcomes across generations. Intergenerational birth weight risk is theorised to occur through maternal regulating mechanisms influenced by conditions imposed on women during infancy (Jaquet et al., 2005). Ibanez, Potau, Enriquez and De Zegher (2000) reported that girls born small for small for gestational age had a smaller uterus (mean difference of 20%, $p < 0.006$) and a reduced ovarian volume (mean difference of 38%, $p < 0.0002$) compared to girls who were born at an appropriate weight. Reductions in the size of reproductive organs during maternal infancy may contribute to an increased likelihood of growth restriction during subsequent pregnancies and a resultant risk of small for gestational age births across generations. Regardless, there are a number of psychosocial factors that are recognized as known determinants of intrauterine growth restriction (Raisanen et al., 2013). Considering this,
Intergenerational patterns of restricted infant growth may represent an interaction of both genetic and environmental influences (Ramakrishnan et al., 1999).

Nonetheless, the period from infancy to adulthood and pregnancy cannot be overlooked. Environmental or psychological risks, underscored by nutrition and disordered eating, are now being debated as important determinants of intergenerational risk (De Stavola, Leon & Koupil, 2011; Wilcox et al., 2007). Continuity of risk outside of families, in the form of trans-generational health risks in socially disadvantaged and ethnic populations highlight the importance of social and psychological factors as underlying pathways of risk (Rutter & Madge, 1976; Rutter, 1998). Low birth weight may be a marker for later social and environmental risks or conditions that continue to operate during development thereby increasing risk of low birth weight births (Price & Coe, 2000). It has been argued that genetic risks passed from mother to offspring may be modified by environmental or psychosocial risks occurring throughout development.

**8.4 Mediating role of disordered eating on intergenerational patterns of low birth weight, preterm and small for gestational age births**

Intergenerational studies provide valuable insights into transmission of risk across generations. They also provide opportunities for examination of potential influences, occurring throughout the lifespan, that contribute to the development of specified risks. It is important to note that continuity of risk is not always reported and that inconsistencies across intergenerational patterns may infer the presence of protective factors that defer generational effects for offspring at risk (Serbin & Karp, 2004). This also emphasizes the importance of investigation of potential mediating factors that may indirectly contribute to the development of risk of low birth weight, preterm or small for gestational age births across generations. Thus, recognition of both distal and proximal causes of intergenerational risk and how these influences are associated, may allow for a more comprehensive picture of how these outcomes occur (Rutter, 1998). Research investigating factors that mediate risk will be important in breaking cycles of risk from one generation to the next.
Few studies have examined the influence of psychosocial mediators, such as maladaptive eating behaviours, on intergenerational patterns of low birth weight and preterm births. This is surprising given that the importance of nutrition and eating behaviour for optimal infant growth and development is well established (Cnattingius et al., 1998; Frederick et al., 2008; Wu, Bazer, Cudd, Meininger & Spencer, 2004). Adequate nutrition during pregnancy has been shown to influence the nutritional status of offspring during adulthood and appetite programming throughout life. This, in turn, has been linked to both the development of disordered eating throughout the lifespan and next generation low birth weight births (Favaro, Tenconi, & Santonastaso, 2006). Easter et al., (2014) reported that females born to women with a history of an eating disorder were shorter throughout development and had a lower BMI at 2 years of age compared to controls. These findings suggest that restricted growth patterns in children may be influenced by maternal eating behaviours or weight. Genetic or familial transmission has been proposed to explain disordered eating, with studies demonstrating that even women recovering from AN maintain lower body weights (Sullivan et al., 1998).

Longitudinal studies point to a link between factors in infancy including low birth weight, preterm and small for gestational age births and the subsequent development of disordered eating behaviour in adolescence and adulthood (Andrews & Brown, 1999; Cnattingius, Hultman, Dahl, & Sparen, 1999; Favaro et al., 2006). A recent study, for example, that utilised data obtained from the Australian Temperament Project indicated a correlation between early gestational age and the development of disordered eating behaviour in adolescence in a model that included multiple childhood predictors (Le Grange et al., 2014). A systematic review of the literature has indicated that current understandings are hindered by contradictory findings, with a number of studies reporting significant and non-significant associations between birth outcomes and disordered eating behaviours (Krug, Taborelli, Sallis, Treasure & Micali, 2013). Meta-analysis of data obtained from five studies included in their review revealed a non-significant correlation between premature births and the development of AN (OR: 1.17, CI: 0.91-1.52) (Krug et al., 2013). Few available studies meant that analysis of overall effects for low birth weight and small for gestational age births could not be conducted. Findings from a review of the literature, conducted by Raevuori, Linna, Keski and Rahkonen (2014),
are in contrast to those reported by Krug et al. (2013). They indicated that that the only birth outcome demonstrating replicable risks for later disordered eating was preterm births. A recent prospective study of 143 individuals born very preterm, or less than 33 weeks gestation, revealed high levels of disordered eating psychopathology at 21 years of age (Micali et al., 2015). Overall, further investigation of these associations is required.

Studies examining the risk of birth weight as an indicator for disordered eating have contributed to theories on cycles of risk for individuals with an eating disorder (Linna et al., 2014). This cycle is characterised by an increased risk of adverse birth outcomes that in turn increases the risk of disordered eating and then later adverse birth outcomes (Linna et al., 2014). Low pre-pregnancy body weight and inadequate nutrition, associated with disordered eating, has been shown to increase the risk of adverse birth outcomes (Katz & Vollenhoven, 2000; Morgan, 1999). Maternal weight and nutrition are also influenced by maternal genotypes and birth history, with a genetic predisposition potentially impacting on one’s ability to maintain adequate weight across the lifespan (Bulik, 2005; Bulik, Reba, Siega-Riz & Reichborn-Klennerud, 2005). The perpetuation of this cycle of risk is likely to be at least partially dependent on environmental factors occurring during development, such as inadequate nutrition or weight loss in adolescence (Bulik et al., 2005). Adolescent disordered eating may incur direct risks for the development of small for gestational age births. It may also indirectly influence or mediate the relationship between maternal and offspring to repeat similar adverse birth outcomes from one generation to the next.

The role of adolescent disordered eating on intergenerational patterns of adverse birth outcomes represents an under-researched area of knowledge, making it important to draw on available research potential. It is suggested that longitudinal studies examining sources of intergenerational risk may facilitate the development of preventive interventions aimed at breaking cycles of risk across generations (Serbin et al., 1998). Furthermore, identifying mediating influences may be crucial to redirecting developmental trajectories towards positive outcomes, particularly for women identified at risk. Preventative interventions intended to increase resilience or circumvent mediating risks will contribute to reducing the incidence of preventable
adverse birth outcomes and associated infant morbidity and mortality, not only for this generation but the next (Goldenberg et al., 2008; Lee et al., 1980).

### 8.5 Aims and hypotheses

The central objective in this study is to draw on findings obtained from the second study for this thesis by examining whether patterns of low birth weight, preterm and small for gestational age births occur across generations. A review of relevant literature revealed persuasive evidence of intergenerational patterns of birth weight from mother to offspring (Coutinho et al., 1997; Godfrey, et al., 1997; Magnus et al., 1993). Evidence in relation to generational patterns of preterm births appears to indicate trends of increasing risk from mother to infant, although overall findings remain contradictory (Klebanoff et al., 1997; Porter et al., 1997; Selling et al., 2006). Considering this, further exploratory investigation of these associations, using prospective intergenerational data, is warranted to clarify these effects. It is hypothesised that continuity of risk will be observed between maternal and infant low birth weight, preterm and small for gestational age births.

This study explores the potential mediating effect of adolescent disordered eating in the transmission of adverse birth outcomes from mother to infant. It draws on research proposing that a self-perpetuating cycle of risk exists between adverse birth outcomes and disordered eating (Linna et al., 2014; Bulik et al., 2005). Disordered eating may be situated on the pathway prior to and or between maternal and infant adverse birth outcomes. Current research suggests that the only requirement for demonstration of a mediation relationship is that a strong association exist between predictor variables and the mediator, and the mediator variable and the outcome (Kazdin, 2007). Findings from the study in Chapter seven of this thesis revealed that Drive for Thinness scores and being ‘At Risk’ of an eating disorder in adolescence significantly increased the risk of small for gestational age births but not low birth weight or preterm births. Bulimia scores did not significantly predict adverse birth outcomes. Considering that a significant relationship was not established between Bulimia scores and adverse birth outcomes, or adolescent disordered eating and low birth weight or preterm births, these variables were not included as mediators or outcomes for mediation analyses in this chapter. However, the risks of small for
gestational age births were seen to hold in relation to disordered eating. The findings of this thesis were helpful for establishing a relationship between adolescent disordered eating and small for gestational age births.

Empirical evidence has demonstrated a link between maternal birth weight and the development of disordered eating in adolescence (Cnattingius et al., 1999; Favaro et al., 2006). A review of the literature revealed some inconsistencies between study findings although indicated that the overall effect of preterm births on the development of disordered eating is non-significant (Krug et al., 2013). Yet, findings from a recent study that utilised data from the ATP reported a significant correlation between early gestational age and the development of disordered eating (Le Grange et al., 2014). The true impact of preterm births on the development of disordered eating behaviour appears relatively contentious and so is worthy of further investigation. Accordingly, it was hypothesised that adolescent disordered eating, measured using Drive for Thinness scores and being ‘At Risk’ of an eating disorder, would mediate an association between maternal low birth weight, preterm or small for gestational age births and infant small for gestational age births. Table 21 outlines the predicted mediated pathways from maternal to infant adverse birth outcome.

Table 21 Hypothesised mediated pathways

<table>
<thead>
<tr>
<th>G2 maternal birth outcome (Predictor Variable)</th>
<th>G2 adolescent disordered eating (Mediator)</th>
<th>G3 infant birth outcome (Outcome Variable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Maternal low birth weight Drive for Thinness</td>
<td>Infant SGA</td>
<td></td>
</tr>
<tr>
<td>2 Maternal low birth weight Disordered eating 'Risk'</td>
<td>Infant SGA</td>
<td></td>
</tr>
<tr>
<td>3 Maternal birth weight Drive for Thinness</td>
<td>Infant SGA</td>
<td></td>
</tr>
<tr>
<td>4 Maternal birth weight Disordered eating 'Risk'</td>
<td>Infant SGA</td>
<td></td>
</tr>
<tr>
<td>5 Maternal preterm births Drive for Thinness</td>
<td>Infant SGA</td>
<td></td>
</tr>
<tr>
<td>6 Maternal preterm births Disordered eating 'Risk'</td>
<td>Infant SGA</td>
<td></td>
</tr>
<tr>
<td>7 Maternal SGA Drive for Thinness</td>
<td>Infant SGA</td>
<td></td>
</tr>
<tr>
<td>8 Maternal SGA Disordered eating 'Risk'</td>
<td>Infant SGA</td>
<td></td>
</tr>
</tbody>
</table>
8.6 Methods: ATP G3 Study 3

Study methodology, including participants, procedures and analytic approach, utilised for the third study of this thesis were previously outlined in Chapter six.

CHAPTER 9: RESULTS AND DISCUSSION OF INTERGENERATIONAL BIRTH RISK AND MEDIATING EFFECTS OF ADOLESCENT DISORDERED EATING

9.1 Chapter overview

This chapter presents the results from the third study of this thesis, which examined continuity of birth outcomes from G2 mothers to G3 offspring and the influence of adolescent disordered eating on the development of these outcomes across generations. Results from statistical assumption testing, correlational analyses, logistic regression, and analyses assessing potential mediation effects are outlined. This chapter also includes a discussion of results, obtained from the third study of this thesis, in the context of theory on intergenerational transmission of risk.

9.2 Rationale and research aims

The third study of this thesis aimed to expand on findings revealed in the second study by examining the role of disordered eating on intergenerational patterns of low birth weight, preterm and small for gestational age births. Review of the literature revealed considerable evidence of intergenerational patterns of maternal and infant birth weight (Farina et al., 2010; Ramakrishnan et al., 1999). Growing evidence exists in relation to intergenerational patterns of preterm births, yet inconsistencies among findings infer some uncertainty in overall conclusions and a need for further clarification of these associations (Selling et al., 2006; Shah & Shah, 2009). Bivariate correlations were conducted to test the hypothesis that birth weight and gestational age would be significantly correlated across generations, between G2 mothers and G3 infants.
Furthermore, the potential mechanisms underlying trans-generational patterns of birth risk are yet to be adequately explored. Given this, the purpose of this study was to examine the role of disordered eating in potentially mediating the pathway from maternal to infant adverse birth outcomes. Findings identifying a link between adverse birth outcomes and the development of disordered eating (Andrews & Brown, 1999; Favaro et al., 2006) have contributed to preliminary theories around intergenerational cycles of risk in disordered eating populations (Linna et al., 2014; Bulik et al., 2005). Adverse birth outcomes, associated with disordered eating, may result in a genetic predisposition that impacts on one’s ability maintain adequate weight across the lifespan (Bulik, 2005; Bulik et al., 2005). It may be that disordered eating sits on the causal pathway from maternal birth outcomes to infant small for gestational age births, indirectly influencing the development of risk across generations. As such, analyses were conducted to investigate the hypothesis that risk of being small for gestational age would be transmitted from mother (G2) to infant (G3), mediated by adolescent disordered eating.

9.3 Statistical assumption testing

Statistical assumption testing was conducted using the statistical software program SPSS, Version 20. Examination of the distribution of maternal birth weight and gestational age data, based on Kolmogorov-Smirnov, skew and kurtosis statistics revealed that data were not normally distributed. These findings, as well as results from normality assessments of G2 disordered eating and G3 birth outcomes described in Chapter seven, are presented in Table 22. Visual inspection of box plots and histograms revealed that data in relation to maternal birth weight and gestational age were negatively skewed, with a greater number of cases occurring at higher ranges. Data on maternal birth weight and gestational age were found to be leptokurtic, with the distribution of scores peaked and clustered around the mean. Despite non-normality, as previously mentioned in Chapter seven, data were not transformed as correlational analyses were bootstrapped in SPSS using 1000 bootstraps to account for non-normal data. Mediation analyses were run using the bias-corrected bootstrap method, which corrects for skewed data. This bootstrapping method involves repeatedly sampling from the data set and estimating the indirect effect in each resampled data set (Preacher & Hayes, 2008). This bias-corrected bootstrap method
thereby corrects for issues of skew and multivariate outliers within the data to address assumptions of normality (Fritz & MacKinnon, 2007).

Table 22 Analysis of normality of G2 and G3 birth outcomes and G2 adolescent disordered eating based on the Kolmogorov-Smirnov statistic, Skew and Kurtosis

<table>
<thead>
<tr>
<th></th>
<th>G2 Birth weight</th>
<th>G2 Gestational age</th>
<th>Bulimia</th>
<th>Drive for Thinness</th>
<th>G3 Birth weight</th>
<th>G3 Gestational age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kolmogorov-Smirnov</td>
<td>0.073*</td>
<td>0.386*</td>
<td>0.139*</td>
<td>0.111*</td>
<td>0.095*</td>
<td>0.212*</td>
</tr>
<tr>
<td>Skew</td>
<td>-0.490</td>
<td>-3.357</td>
<td>1.052</td>
<td>0.423</td>
<td>-0.877</td>
<td>1.373</td>
</tr>
<tr>
<td>Kurtosis</td>
<td>2.563</td>
<td>14.116</td>
<td>1.209</td>
<td>-0.656</td>
<td>1.445</td>
<td>3.393</td>
</tr>
</tbody>
</table>

*Sig p< .05

Assessment of univariate outliers for data on maternal birth weight and gestational age, through examination of stem and leaf plots, boxplots and histograms revealed seven outliers for birth weight and 22 outliers for gestational age. All of the identified outliers for maternal birth weight and gestational age represented plausible data points, with more extreme cases observed at the lower end of the data representing those that were sought within the sample. Assessment of standardised residual values revealed five cases that fell farthest from the predicted range for maternal birth weight, and six cases for maternal gestational age. These cases represented those with a z score above or below 2.58. Examination of 5% trimmed mean and mean scores revealed little difference between observed values and the remaining distribution, indicating that identified outliers were unlikely to be having an undue effect on the data. Given this, these cases were deemed appropriate for inclusion in mediation analyses. Assessment results in relation to univariate outliers for adolescent disordered eating data and G3 infant data are presented in Chapter seven of this thesis, although indicate that it was appropriate for the complete data set to be included within analyses.

Assessment of multivariate outliers, using Cook’s Distance values, revealed two cases that were potentially having an undue influence of the data. These cases were removed from the sample and logistic regression analyses rerun with a total of
186 cases to check whether these cases were having an undue effect on the overall model. Removal of these cases resulted in an increase in the effect size and variance explained by the models, although no change in the statistical significance of models. Moreover, little differences were observed in the accuracy of classification of cases within logistic regression models when excluding identified outliers. Given this, it was deemed appropriate for these cases to remain within analyses.

Analysis of missing data for maternal birth outcomes revealed three cases with missing data on birth weight and fourteen cases with missing data on gestational age and small for gestational age each. Missing data is presented in Table 23. Analysis of missing data, using Little’s Missing Completely at Random (MCAR) test, revealed a non-significant result indicating that the data in relation to maternal birth weight, gestational age and small for gestational age are likely to be missing completely at random (Chi-Square= 232.238, $df=280$, $p= 0.983$). Missing data were imputed in SPSS using the expectation maximisation method. Correlational analyses were conducted in SPSS and then the full data set ($n=188$) was transferred to Mplus to assess for potential mediation effects.

Table 23 Missing data for G2 and G3 predictor and outcome variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Missing</th>
<th>% In sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>G2 Sex</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>G2 Birth weight</td>
<td>3</td>
<td>1.6</td>
</tr>
<tr>
<td>G2 Gestational age</td>
<td>14</td>
<td>7.4</td>
</tr>
<tr>
<td>G2 SGA</td>
<td>14</td>
<td>7.4</td>
</tr>
<tr>
<td>G2 Birth order</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Drive for Thinness</td>
<td>33</td>
<td>17.6</td>
</tr>
<tr>
<td>Bulimia</td>
<td>33</td>
<td>17.6</td>
</tr>
<tr>
<td>ED 'At Risk'</td>
<td>74</td>
<td>39.4</td>
</tr>
<tr>
<td>G3 SGA</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>G3 Birth weight</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>G3 Gestational age</td>
<td>0</td>
<td>0.0</td>
</tr>
</tbody>
</table>
9.4 Descriptive statistics: Maternal and infant adverse birth outcomes

In the current sample, G2 maternal birth weight ranged from 1.23 to 4.83kgs, with the average birth weight reported at 3.38kgs. Seven G2 participants were identified through maternal health nurse records as being low birth weight births, representing 3.7% of the sample. Maternal gestational age ranged from 28 to 44 weeks and averaged at 39.45 weeks. Ten G2 participants, 5.3%, were reported as being premature. Eighteen G2 participants were identified as being small for gestational age at birth, which represented 9.6% of the sample. Incidence rates of maternal low birth weight births were lower than those reported within previous studies, which were reported at 5% to 7% (Valero de Bernabe et al., 2004). The incidence of preterm births in G2 mothers was relatively consistent with rates cited in the literature (Goldenberg et al., 2008). Table 24 presents frequencies of G2 maternal low birth weight, preterm and small for gestational age births as well as frequencies of G3 infant low birth weight, preterm and small for gestational age births as described in Chapter seven. The incidence of low birth weight and small for gestational age births was observed to increase from one generation (G2 mothers) to the next (G3 infants). This is consistent with findings from the Victorian perinatal data collection unit, reporting a gradual increase in the incidence of these outcomes since 1985 (Department of Health, 2005). Rates of preterm births were comparable between mothers and offspring ($n=10$ each).
Table 24 Frequencies of maternal (G2) and infant (G3) birth outcomes

<table>
<thead>
<tr>
<th></th>
<th>Generation Two (G2)</th>
<th>Generation Three (G3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency</td>
<td>% In sample</td>
</tr>
<tr>
<td>Not LBW</td>
<td>181</td>
<td>96.3</td>
</tr>
<tr>
<td>LBW</td>
<td>7</td>
<td>3.7</td>
</tr>
<tr>
<td>Total</td>
<td>188</td>
<td>100.0</td>
</tr>
<tr>
<td>Near term</td>
<td>175</td>
<td>94.7</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>10</td>
<td>5.3</td>
</tr>
<tr>
<td>Total</td>
<td>188</td>
<td>100.0</td>
</tr>
<tr>
<td>Not SGA</td>
<td>157</td>
<td>90.4</td>
</tr>
<tr>
<td>SGA</td>
<td>18</td>
<td>9.6</td>
</tr>
<tr>
<td>Total</td>
<td>188</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Frequencies of infant low birth weight, preterm and small for gestational age births, to mothers also born low birth weight, preterm or small for gestational age are presented in Table 25. Rates of low birth weight and small for gestational age births were higher for G2 mothers experiencing similar outcomes at birth. 42.8% (n=3) of mothers identified as being low birth weight at birth (n=7) reported having a low birth weight infant compared to 4.4% of healthy weight mothers. None of the mothers, who were born with low birth weight, reported having a preterm infant. Ten G2 mothers were born preterm, however, none of these women reported experiencing a preterm birth. 5.6% (n=10) of healthy weight mothers reported giving birth to a preterm infant. 10% (n=1) of G3 infants born to preterm mothers were born low birth weight. 22.2% (n=4) of G3 small for gestational age births were born to mothers who were also small for gestational age compared to 8.8% (n=15) in healthy weight mothers. 16.6% (n=3) and 5.5% (n=1) of small for gestational age mothers reported having a low birth weight and preterm birth respectively.
Table 25 \textit{Frequencies of low birth weight, preterm and small for gestational age infants in mothers born low birth weight, preterm and small for gestational age}

<table>
<thead>
<tr>
<th></th>
<th>G3 Low birth weight (n=11)</th>
<th>G3 Preterm births (n=10)</th>
<th>G3 SGA (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G2 healthy weight (n=181)</td>
<td>8</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>G2 LBW (n=7)</td>
<td>3</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>G2 Term births (n=178)</td>
<td>10</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>G2 Preterm births (n=10)</td>
<td>1</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>G2 Not SGA (n=170)</td>
<td>8</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>G2 SGA (n=18)</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

\textbf{9.5 Preliminary analyses: Continuity of adverse birth outcomes between Generation Two mothers and Generation Three infants}

Bivariate correlations were conducted, using SPSS, to assess whether continuous birth outcomes would be correlated between mother and offspring. Correlations presented were bootstrapped using 1000 bootstraps to account for non-normally distributed data. These results are presented in Table 26. G2 maternal birth weight was significantly correlated with G3 birth weight ($r = .212, p < .01$) and G3 small for gestational age births ($r = -.289, p < .01$) but not significantly correlated with G3 gestational age ($r = .011$). G2 maternal gestational age, however, did not have a significant correlation with G3 gestational age or birth weight ($r = .080, r = .102$). G2 maternal birth weight and gestational age were not significantly correlated with adolescent Drive for Thinness or Bulimia scores.
Table 26 Pearson’s r correlations between maternal (G2) and infant (G3) birth outcomes

<table>
<thead>
<tr>
<th></th>
<th>G2 Birth weight</th>
<th>G2 Gestational age</th>
<th>DFT</th>
<th>Bulimia</th>
<th>BMI</th>
<th>G3 Birth weight</th>
<th>G3 Gestational age</th>
</tr>
</thead>
<tbody>
<tr>
<td>G2 Birth weight</td>
<td>1</td>
<td>0.419**</td>
<td>-0.110</td>
<td>-0.096</td>
<td>-0.016</td>
<td>0.212**</td>
<td>0.011</td>
</tr>
<tr>
<td>G2 Gestational age</td>
<td>1</td>
<td>-0.015</td>
<td>0.043</td>
<td>-0.014</td>
<td>0.102</td>
<td>0.080</td>
<td></td>
</tr>
<tr>
<td>DFT</td>
<td>1</td>
<td>0.253**</td>
<td>0.370**</td>
<td>0.008</td>
<td>0.133</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bulimia</td>
<td>1</td>
<td>0.189**</td>
<td>0.033</td>
<td>0.020</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>1</td>
<td>0.046</td>
<td>0.118</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G3 Birth weight</td>
<td></td>
<td></td>
<td>1</td>
<td>0.622**</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Significant at p< .01 (2-tailed).
*Significant at p< .05 (2-tailed).
Note: Correlations are bootstrapped, using 1000 bootstraps, to account for non-normally distributed data.

Logistic regression analyses were also conducted to assess continuity of categorical birth outcomes, including low birth weight, preterm and small for gestational age births, between G2 mothers and G3 infants. These results are presented in Table 27. Results from logistic regression analyses revealed that infants born to mothers who were born low birth weight are at a greater risk of also being born low birth weight (OR: 16.219, CI: 3.095-84.982). Extremely large effect sizes confidence intervals invite caution in relation to interpretation of results. Low frequencies of maternal low birth weight births (n=7) means that the precision of effects is likely to be reduced. Maternal (G2) preterm birth status did not significantly predict risk of preterm births in G3 infants. Similarly, maternal small for gestational age births did not significantly predict risk of infant small for gestational age births. However, G2 mothers who were born low birth weight or preterm were found to be at a significantly increased risk of having a small for gestational age birth (OR: 29.821, CI: 5.297-167.897; OR: 7.244, CI: 1.839-28.545).
Table 27 Logistic regression analyses assessing G2 maternal low birth weight, preterm and small for gestational age births on G3 low birth weight, preterm and small for gestational age births

<table>
<thead>
<tr>
<th>G2 Predictor Variable</th>
<th>G3 birth outcome</th>
<th>Odds Ratio (CI) B</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBW</td>
<td>LBW</td>
<td>16.219 (3.095-84.982) 2.786</td>
<td>0.001*</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>LBW</td>
<td>1.867 (.215-16.222) 0.624</td>
<td>0.572</td>
</tr>
<tr>
<td>SGA</td>
<td>LBW</td>
<td>4.050 (.971-16.898) 1.399</td>
<td>0.055</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>Preterm birth</td>
<td>0.000 (.000-.000) -18.382</td>
<td>0.999</td>
</tr>
<tr>
<td>LBW</td>
<td>Preterm Birth</td>
<td>0.000 (.000-.000) -18.364</td>
<td>0.999</td>
</tr>
<tr>
<td>SGA</td>
<td>Preterm birth</td>
<td>1.052 (.126-8.816) 0.051</td>
<td>0.963</td>
</tr>
<tr>
<td>SGA</td>
<td>SGA</td>
<td>0.339 (.099-1.160) -1.083</td>
<td>0.085</td>
</tr>
<tr>
<td>LBW</td>
<td>SGA</td>
<td>29.821 (5.297-167.897) 3.395</td>
<td>0.000*</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>SGA</td>
<td>7.244 (1.839-28.545) 1.980</td>
<td>0.005*</td>
</tr>
</tbody>
</table>

9.6 Mediational analyses

The empirical analyses in Chapter seven of this thesis revealed that adolescent disordered eating behaviours significantly increased the risk of small for gestational age births. Based on this finding eight mediation models were conducted, using Mplus version 7.2 (Muthén & Muthén, 1998-2012), that examined the mediating effects of adolescent disordered eating on the relationship between maternal birth outcomes and infant small for gestational age births. Standardised (β) and unstandardized (B) direct effects are reported as well as unstandardized standard error estimates and 90% and 95% confidence intervals. Bootstrapping methods, using 5000 bootstraps were used to account for non-normally distributed data. Maternal and infant adverse birth outcomes, including low birth weight, preterm and small for gestational age births, were coded dichotomously. A continuous measure of maternal birth weight was also included given that maternal birth weight was associated with adolescent disordered eating and small for gestational age births. The direct effects of maternal birth outcomes and adolescent disordered eating on infant small for gestational age births are presented in Table 28.
9.6.1 Direct effects of maternal birth outcomes and adolescent disordered eating on infant small for gestational age births

Results revealed a non-significant direct effect of maternal low birth weight, preterm and small for gestational age births on infant small for gestational age births. Yet, continuous measures of maternal birth weight had a significant direct effect on infant small for gestational age births ($B=-0.423, \beta=-0.877, p=.003; B=-0.396, \beta=-0.822, p=.006$). The direct effect of adolescent disordered eating on small for gestational age births was not significant. When applying less conservative error estimates (90% confidence intervals) adolescent disordered eating was a significant predictor of infant small for gestational age births, although this finding was not consistent across all models. Moreover, maternal preterm and low birth weight births were significant predictors of infant small for gestational age births.

9.6.2 Indirect effects of adolescent disordered eating on transmission of risk of adverse birth outcomes from mother to infant

Eight mediation pathways were conducted, assessing the indirect effects of adolescent Drive for Thinness scores and disordered eating ‘Risk’ on the relationship between maternal birth outcomes and infant small for gestational age births. Mediation models are considered significant if bootstrapped 95% Upper Confidence Intervals (CIU) and Lower Confidence Intervals (CIL) do not include 0. Findings are presented in Table 29. Results, using 5000 bootstraps, indicated that disordered eating did not mediate an association between maternal birth outcomes and infant small for gestational age births. When applying less conservative error estimates (90% CI’s) significant mediation effects were revealed. Specifically, significant indirect effects of Drive for Thinness scores and disordered eating ‘Risk’ on the relationship between maternal and infant small for gestational age births were observed (CIL= 0.004, CIU =0.384; CIL=0.014, CIU=0.548). Standardised model estimates, for models revealing significant indirect effects at 90% confidence intervals, are presented in Figure 4.
Table 28 Standardised and unstandardized direct effects of G2 birth outcomes and disordered eating risk on G3 small for gestational age births

<table>
<thead>
<tr>
<th>Generation Three SGA</th>
<th>Beta</th>
<th>B</th>
<th>S.E</th>
<th>P</th>
<th>CI (95%)</th>
<th>CI (90%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G2 Low birth weight</td>
<td>0.284</td>
<td>1.706</td>
<td>1.562</td>
<td>0.275</td>
<td>(-0.176-6.217)</td>
<td>(0.409-5.979)*</td>
</tr>
<tr>
<td>G2 ED Risk</td>
<td>0.233</td>
<td>0.242</td>
<td>0.176</td>
<td>0.170</td>
<td>(-0.132-0.554)</td>
<td>(-0.061-0.502)</td>
</tr>
<tr>
<td>G2 Birth weight</td>
<td>0.309</td>
<td>1.856</td>
<td>1.537</td>
<td>0.227</td>
<td>(0.746-6.241)**</td>
<td>(0.958-6.085)*</td>
</tr>
<tr>
<td>G2 Drive for Thinness</td>
<td>0.196</td>
<td>0.029</td>
<td>0.018</td>
<td>0.099</td>
<td>(-0.009-0.061)</td>
<td>(-0.001-0.056)</td>
</tr>
<tr>
<td>G2 Birth weight</td>
<td>-0.396</td>
<td>-0.822</td>
<td>0.301</td>
<td>0.006*</td>
<td>(-1.487--0.320)**</td>
<td>(-1.358--0.390)*</td>
</tr>
<tr>
<td>G2 ED Risk</td>
<td>0.240</td>
<td>0.263</td>
<td>0.170</td>
<td>0.122</td>
<td>(-0.096-0.565)</td>
<td>(-0.028-0.518)</td>
</tr>
<tr>
<td>G2 Preterm Births</td>
<td>0.223</td>
<td>1.020</td>
<td>0.708</td>
<td>0.149</td>
<td>(-0.114-1.847)</td>
<td>(0.215-1.702)*</td>
</tr>
<tr>
<td>G2 Ed Risk</td>
<td>0.319</td>
<td>0.328</td>
<td>0.160</td>
<td>0.040*</td>
<td>(-0.014-0.610)</td>
<td>(0.046-0.565)*</td>
</tr>
<tr>
<td>G2 Preterm Births</td>
<td>0.226</td>
<td>1.034</td>
<td>0.755</td>
<td>0.171</td>
<td>(-0.075-1.914)</td>
<td>(0.186-1.747)*</td>
</tr>
<tr>
<td>G2 Drive for Thinness</td>
<td>0.224</td>
<td>0.032</td>
<td>0.018</td>
<td>0.072</td>
<td>(-0.006-0.065)</td>
<td>(0.001-0.060)*</td>
</tr>
<tr>
<td>G2 SGA</td>
<td>0.113</td>
<td>0.387</td>
<td>0.732</td>
<td>0.596</td>
<td>(-0.718-1.131)</td>
<td>(-0.439-1.014)</td>
</tr>
<tr>
<td>G2 ED Risk</td>
<td>0.325</td>
<td>0.325</td>
<td>0.159</td>
<td>0.041*</td>
<td>(-0.026-0.601)</td>
<td>(0.031-0.556)*</td>
</tr>
<tr>
<td>G2 SGA</td>
<td>0.131</td>
<td>0.450</td>
<td>0.728</td>
<td>0.537</td>
<td>(-0.550-1.198)</td>
<td>(-0.335-1.071)</td>
</tr>
<tr>
<td>G2 Drive for Thinness</td>
<td>0.231</td>
<td>0.033</td>
<td>0.018</td>
<td>0.068</td>
<td>(-0.007-0.065)</td>
<td>(0.001-0.059)*</td>
</tr>
</tbody>
</table>

**Significant at p< .05  
*Significant at p< .1  
Note: Effects are bootstrapped, using 5000 bootstraps, to account for non-normally distributed data
Table 29 *Indirect effects of G2 disordered eating on G2 and G3 birth outcomes*

<table>
<thead>
<tr>
<th></th>
<th>Beta</th>
<th>B</th>
<th>S.E</th>
<th>CI (95%)</th>
<th>P</th>
<th>CI (90%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generation Three SGA on G2 ED Risk and G2 LBW</td>
<td>0.050</td>
<td>0.281</td>
<td>0.539</td>
<td>(-0.151-2.365)</td>
<td>0.602</td>
<td>(-0.051-1.892)</td>
</tr>
<tr>
<td>Generation Three SGA on G2 DFT and G2 LBW</td>
<td>0.024</td>
<td>0.133</td>
<td>0.161</td>
<td>(-0.070-0.582)</td>
<td>0.410</td>
<td>(-0.032-0.509)</td>
</tr>
<tr>
<td>Generation Three SGA on G2 ED Risk and G2 Birth weight</td>
<td>-0.048</td>
<td>-0.099</td>
<td>0.088</td>
<td>(-0.346-0.018)</td>
<td>0.265</td>
<td>(-0.302-0.000)</td>
</tr>
<tr>
<td>Generation Three SGA on G2 DFT and G2 Birth weight</td>
<td>-0.021</td>
<td>-0.043</td>
<td>0.043</td>
<td>(-0.170-0.009)</td>
<td>0.316</td>
<td>(-0.145-0.002)</td>
</tr>
<tr>
<td>Generation Three SGA on G2 ED Risk and G2 Preterm Births</td>
<td>0.022</td>
<td>0.102</td>
<td>0.245</td>
<td>(-0.159-0.581)</td>
<td>0.676</td>
<td>(-0.092-0.478)</td>
</tr>
<tr>
<td>Generation Three SGA on G2 DFT and G2 Preterm Births</td>
<td>0.020</td>
<td>0.089</td>
<td>0.114</td>
<td>(-0.048-0.447)</td>
<td>0.432</td>
<td>(-0.021-0.371)</td>
</tr>
<tr>
<td>Generation Three SGA on G2 ED Risk and G2 SGA</td>
<td>0.058</td>
<td>0.199</td>
<td>0.159</td>
<td>(-0.013-0.632)</td>
<td>0.212</td>
<td>(0.014-0.548)*</td>
</tr>
<tr>
<td>Generation Three SGA on G2 DFT and G2 SGA</td>
<td>0.040</td>
<td>0.137</td>
<td>0.114</td>
<td>(-0.010-0.443)</td>
<td>0.230</td>
<td>(0.004-0.384)*</td>
</tr>
</tbody>
</table>

**Significant at p< .05  
*Significant at p< .1  
Note: Effects are bootstrapped, using 5000 bootstraps, to account for non-normally distributed data**
Note: Pathways include standardised model estimates obtained from mediation models assessing the indirect effect of DFT and ED Risk on relationship between G2 and G3 SGA births.

Figure 4 Mediating effects of adolescent Drive for Thinness and eating disorder ‘Risk’ on transmission of risk of small for gestational age births from G2 to G3. Indirect models are significant within 90% confidence intervals.

9.7 Post-hoc analyses: Effects of preconception disordered eating and maternal birth outcomes on risk of small for gestational age births

Results from this study revealed a relationship between maternal birth outcomes and infant small for gestational age births at a 90% confidence interval level. Given this, post hoc analyses were conducted to examine whether findings obtained from the second study of this thesis in Chapter seven withstand after
controlling for maternal birth outcomes. Post hoc analyses aimed to examine whether observed increases in risk of G3 small for gestational age births, based on adolescent disordered eating predictors, are better accounted for by maternal birth characteristics such as birth weight and gestational age.

Initial logistic regression models were re-run to assess whether adolescent disordered eating predicted risk of small for gestational age births, when accounting for maternal birth weight (kilograms), gestational age (weeks), low birth weight, preterm and small for gestational age births. Drive for Thinness and disordered eating ‘Risk’ was assessed independent of one another to reduce potential issues associated with collinearity. Considering that low frequencies of maternal low birth weight, preterm and small for gestational age births were observed, continuous measures of maternal birth weight and gestational age were also included in analyses to allow for additional information to assess these relationships. Maternal birth weight and gestational age were assessed separately from maternal low birth weight, preterm and small for gestational age births, as these variables were derived from data on birth weight and age and thus likely to be highly related. Additional covariates included in each model were maternal age, adolescent depressive symptoms and Body Mass Index (BMI). BMI was not included in adjusted models regressing disordered eating ‘Risk’ as this variable was comprised of data from both EDI scores and BMI.

9.7.1 Statistical assumption testing

Statistical assumption testing, in relation to G2 maternal birth outcomes, was conducted using a statistical software program SPSS, Version 20. Chi square tests of independence for G2 maternal birth outcomes revealed that low birth weight births were not independent of preterm and small for gestational age births. Maternal preterm births were found to be independent of small for gestational age births. Results are presented in Table 30. Nevertheless, post hoc assessment of Tolerance and Variance Inflation Factor (VIF) values confirmed that maternal birth outcomes; low birth weight, preterm and small for gestational age births, were not too closely related and that assumptions of multicollinearity had been met. This suggests that it was appropriate for all three maternal (G2) birth outcomes to be included together within logistic regression models.
### Table 30 Chi Square analyses of independence for maternal birth outcomes

<table>
<thead>
<tr>
<th></th>
<th>G2 Low birth weight</th>
<th>G2 Preterm births</th>
<th>G2 SGA</th>
</tr>
</thead>
<tbody>
<tr>
<td>G2 Low birth weight</td>
<td>1</td>
<td>0.00*</td>
<td>.002*</td>
</tr>
<tr>
<td>G2 Preterm births</td>
<td>0.00*</td>
<td>1</td>
<td>0.29</td>
</tr>
<tr>
<td>G2 SGA</td>
<td>.002*</td>
<td>0.29</td>
<td>1</td>
</tr>
</tbody>
</table>

*Significant at p< .05

Assessment of multivariate outliers based on Cook’s Distance values revealed two cases that were potentially having an undue influence on the data. These cases were removed from the sample and regression models were rerun (n=186) to assess whether identified cases were having a significant impact on overall results. The percentage of cases correctly classified was observed to increase, although not significantly, as was the amount of variance explained by the model. Removal of these cases resulted in a change in the statistical significance of predictor variables included in the model, although only small differences in the size of effects, indicative of an overall improvement in the precision of estimated effects. Identified outliers were also removed separately from logistic regression models to assess the independent influence of each case. Both cases appeared to exert similar influence on overall results. Given that removal of these outliers resulted in changes in the statistical significance of effects and consequent interpretation of results, these cases were excluded from final analyses. A description of each outlier is included in Appendix D as well as results from post-hoc logistic regression models utilising the whole sample (n=188).

#### 9.7.2 Post hoc logistic regression results

Findings from adjusted logistic regression analyses revealed that Drive for Thinness scores significantly predicted risk of G3 small for gestational age births when adjusting for G2 maternal low birth weight, preterm and small for gestational age births (OR: 1.099, CI: 1.011-1.196) and birth weight and gestational age (OR: 1.104, CI: 1.020-1.196). This means that women reporting higher Drive for Thinness scores in adolescence were 1.09 and 1.10 times more likely to have a small for
gestational age birth. The models were statistically significant, indicating that they were able to adequately distinguish between mothers who did and did not report having a small for gestational age birth. The overall model explained between 15.4% and 36.9% of the variance in small for gestational age births and correctly classified approximately 93% of cases. Results from post hoc logistic regression analyses predicting risk of G3 small for gestational age births based on adolescent disordered eating and G2 maternal birth outcomes are presented in Table 31 and 32.

G2 adolescent disordered eating ‘Risk’ did not significantly predict risk of G3 small for gestational age births (OR: 3.332, CI: .974-11.400, \( p < .055 \)) when adjusting for G2 maternal low birth weight births (categorical measure). However, when adjusting for G2 maternal overall birth weight (continuous measure in kilograms) and G2 gestational age (weeks), adolescent disordered eating ‘Risk’ did remain a significant predictor of G3 small for gestational age births (OR: 3.852, CI: 1.159-12.801). The overall models were statistically significant and accounted for 14.8% and 35.5% the variance in risk of small for gestational age births. Approximately 92% of all cases were correctly identified within models.

G2 maternal low birth weight births (OR: 50.487, CI: 2.195-1161.422; OR: 30.770, CI: 1.478-640.466) and continuous measures of birth weight (OR: .191, CI: .050-.722) were found to contribute to a significant proportion of risk of G3 small for gestational age births. Extremely large effects and confidence intervals, in relation to estimates of risk based on maternal low birth weight births, suggests that this finding should be interpreted with caution. Low frequencies \( n = 7 \) of maternal low birth weight births are likely to have contributed to a significant decrease in the precision of estimated effects. Furthermore, results revealed that maternal age was a significant predictor of small for gestational age births, consistent with results revealed in the second study of this thesis.
Table 31 Logistic regression assessing G2 Drive for Thinness and disordered eating ‘Risk’ on G3 infant small for gestational age births adjusting for categorical indicators of G2 maternal low birth weight, preterm and small for gestational age births

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio (CI)</th>
<th>B</th>
<th>Sig</th>
<th>Odds Ratio (CI)</th>
<th>B</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drive for Thinness</td>
<td>1.099 (1.011-1.196)</td>
<td>0.095</td>
<td>0.027*</td>
<td>ED Risk</td>
<td>3.332 (.974-11.400)</td>
<td>1.204</td>
</tr>
<tr>
<td>Maternal Age</td>
<td>0.532 (.323-.876)</td>
<td>-0.630</td>
<td>0.013*</td>
<td>Maternal Age</td>
<td>0.534 (.330-.863)</td>
<td>-0.628</td>
</tr>
<tr>
<td>Depression</td>
<td>.859 (.706-1.044)</td>
<td>-0.152</td>
<td>0.127</td>
<td>Depression</td>
<td>.863 (.713-1.045)</td>
<td>-0.147</td>
</tr>
<tr>
<td>BMI</td>
<td>.902 (711-1.144)</td>
<td>0.103</td>
<td>0.395</td>
<td>G2 LBW</td>
<td>30.770 (1.478-640.466)</td>
<td>3.427</td>
</tr>
<tr>
<td>G2 LBW</td>
<td>50.487 (2.195-1161.422)</td>
<td>3.922</td>
<td>0.014*</td>
<td>G2 Preterm birth</td>
<td>1.964 (.185-20.840)</td>
<td>0.675</td>
</tr>
<tr>
<td>G2 Preterm birth</td>
<td>1.677 (.150-.18.696)</td>
<td>0.517</td>
<td>0.674</td>
<td>G2 SGA</td>
<td>3.530 (.678-18.369)</td>
<td>1.261</td>
</tr>
<tr>
<td>G2 SGA</td>
<td>3.026 (.553-16.553)</td>
<td>1.107</td>
<td>0.202</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Sig at p< .05
Note: Two identified outliers were removed from the regression models, with analyses including n=186

Table 32 Logistic regression analyses assessing G2 Drive for Thinness and disordered eating ‘Risk’ on G3 infant small for gestational age births adjusting for continuous indicators of G2 maternal birth weight in kilograms and gestational age in weeks

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio (CI)</th>
<th>B</th>
<th>Sig</th>
<th>Odds Ratio (CI)</th>
<th>B</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drive for Thinness</td>
<td>1.104 (1.020-1.196)</td>
<td>0.099</td>
<td>0.014*</td>
<td>ED Risk</td>
<td>3.852 (1.159-12.801)</td>
<td>1.349</td>
</tr>
<tr>
<td>Maternal Age</td>
<td>.567 (.355-.907)</td>
<td>-0.567</td>
<td>0.018*</td>
<td>Maternal Age</td>
<td>.580 (.371-.907)</td>
<td>-0.545</td>
</tr>
<tr>
<td>Depression</td>
<td>.827 (.681-1.004)</td>
<td>-0.19</td>
<td>0.054</td>
<td>Depression</td>
<td>.839 (.698-1.009)</td>
<td>-0.175</td>
</tr>
<tr>
<td>BMI</td>
<td>.933 (.764-1.139)</td>
<td>-0.069</td>
<td>0.495</td>
<td>G2 birth weight</td>
<td>.207 (.056-.767)</td>
<td>-1.576</td>
</tr>
<tr>
<td>G2 birth weight</td>
<td>.191 (.050-.722)</td>
<td>-1.657</td>
<td>0.015*</td>
<td>G2 Gestational age</td>
<td>.930 (.699-1.237)</td>
<td>-0.072</td>
</tr>
<tr>
<td>G2 Gestational age</td>
<td>.923 (.693-1.229)</td>
<td>-0.08</td>
<td>0.582</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Sig at p< .05
Note: One identified outlier was removed from regression models, with analyses including n=187
Note: G2 birth weight and gestational age were regressed separately from G2 low birth weight, preterm and small for gestational age births as these outcomes are derived from data on birth weight and gestational age
9.8 Discussion of findings regarding the mediating role of adolescent disordered eating on intergenerational transmission of adverse birth outcomes

9.8.1 Continuity of low birth weight, preterm and small for gestational age births

Hypotheses predicting continuity of low birth weight, preterm and small for gestational age births in G2 mothers and G3 infants were only partially supported. As hypothesised, G2 mothers born low birth weight were at a significantly increased risk of having a low birth weight birth. In fact, 42.8% of low birth weight mothers reported giving birth to a low birth weight infant compared to 4.4% of mothers born at a normal weight. Similarly, maternal birth weight was significantly positively correlated with and infant birth weight. Findings from this thesis did not support hypotheses predicting intergenerational patterns of preterm or small for gestational age births, revealing non-significant associations between mother and infant preterm and small for gestational age births. Likewise, maternal gestational age was not significantly correlated with infant gestational age. What is more, none of the preterm mothers ($n=10$) reported having a premature birth. Interestingly, G2 mothers born low birth weight or preterm were significantly more likely to have a small for gestational age births.

Continuity in maternal and infant low birth weight is consistent with current evidence indicating intergenerational patterns of low birth weight births (Godfrey, et al., 1997; Magnus et al., 1993; Wang et al., 1995). This finding may provide support for biological theories of risk that suggest that the gestational experience of a mother may impact on the intrauterine environment. The effects of which may in turn be passed from generation to the next. These results suggest that length of gestation carries fewer intergenerational risks. Rather, intergenerational effects may relate more to patterns of restricted in utero growth during gestation, with birth weight potentially representing a stronger predictor of growth restriction than gestational age (Klebanoff & Yip, 1987). Reduced maternal birth weight may result in a reduction in the size of the organs potentially interfering with the growth of reproductive organs (Shah & Shah, 2009). This may explain intergenerational patterns of low birth weight in the absence of clear intergenerational effects for preterm births. Otherwise, intergenerational effects may be reflective of genetic risks, as hypothesised by
Svensson et al (2006). In saying this, the influence of shared environmental and trans-generational psychosocial risks cannot be overlooked. Generational patterns of low birth weight births may be explained through learned patterns of eating behaviours or the modelling of specific maternal reproductive health practices from mother to daughter (Pike & Rodin, 1991; Scaglioni, Salvioni, & Galimberti, 2008).

Non-significant intergenerational effects of small for gestational age births revealed in this study are at odds with findings reported by Farina et al. (2010), Jaquet et al. (2005), Klebanoff et al. (1997) and Selling et al. (2006). A relatively small sample is likely to have limited observed frequencies of maternal and infant adverse outcomes. The current sample may have been too small to adequately reflect normal variations in small for gestational age births reflected in the general population. In contrast, Selling et al (2006) reported utilising a sample of 38,720 mother-offspring pairs, which likely resulted in an improved ability to develop a more representative sample and greater ability to detect potential effects. Therefore, true estimates of risk are not necessarily reflected in the current findings. Irrespective of this, it is not clear why the findings are so discrepant from previous studies demonstrating a significant link between maternal and infant small for gestational age births. The evidence base specifically examining intergenerational patterns of small for gestational age births is relatively small and as such points to a need for additional prospective studies to clarify variances in the findings.

Variations in the current findings from previous research may be influenced by differences in subtypes of maternal small for gestational age births (Clayton et al., 2007). Castrillo et al (2014) reported that separation of these outcomes in their analyses likely contributed to different associations and further information regarding potential mechanisms. This may be reflected in findings reported by Farina et al. (2010), who in their sample of only full term small for gestational age infants, revealed twice the effect size of that reported by Klebanoff et al. (1997). In the current sample, 18 mothers were born small for gestational age, of which, three were born with low birth weight and none preterm. Two of those women had a small for gestational age birth, accounting for half of the small for gestational age births to mothers born small for gestational age. Frequencies of low birth weight and preterm subtypes of maternal and infant small for gestational age births are presented in

148
appendix E. Low birth weight has been shown to be a greater predictor of intrauterine growth compared to gestational age (Klebanoff & Yip 1987). The degree of intrauterine growth restriction in mothers may have impacted on growth patterns in offspring. More severe growth restriction in mothers born with low birth weight may be associated with greater risk, whilst small but healthy weight mothers may incur lesser risks for next generation offspring. This may explain significant increases in risk of small for gestational age births to mothers born low birth weight or preterm, but an absence of continuity in small for gestational age births.

Results from logistic regression analyses did not support the hypothesis predicting continuity of preterm births, with none of the preterm mothers having a preterm birth. This conflicts with significant intergenerational effects reported in a systematic review of the literature by Shah and Shah (2009). Given that conclusions made from that review were based only on unadjusted data, there is the potential that significant findings represent an overestimation of true effects. Selling et al. (2006), for example, reported non-significant effects when adjusting for socio economic factors, yet this adjusted odds ratio was not accounted for by Shah and Shah (2009) in their review. Porter et al. (1997) and Swamy et al. (2008) also reported significant intergenerational effects, which is contrary to results revealed in this study.

Approximately two thirds of preterm infants are born low birth weight (Tucker & McGuire, 2004). Intergenerational patterns of preterm births reported in some studies may be explained by concurrent low birth weight status in preterm mothers and infants. Non-significant results reported by Magnus et al. (1993), Selling et al. (2006), Klebanoff et al. (1997) and Castrillio et al. (2014) are more in line with findings revealed in this study, implying that gestational age is less genetically based and more likely influenced by environmental or psychosocial factors.

There is also the potential for bias in the results presented in this thesis given that the sample was comprised of a mix of parities. The risk of preterm births is significantly higher for women during their first pregnancy but that risk is reduced with each subsequent pregnancy (Ananth et al., 2001; Astolfi & Zonta, 1999). Although the majority of infants in the sample (71.8%) were the first-born \((n=135)\), 28.2% were reported to have older siblings who were not included within the ATP study. This means that there is the potential for rates of preterm births in ATP mothers
to be underrepresented in the sample. Even so, non-significant generational effects of preterm births have been reported in studies utilising samples of only first-born mothers and infants (Selling et al., 2006). With none of the preterm mothers having a preterm birth, it is unlikely that issues of parity have significantly influenced the overall findings.

Findings from bivariate correlations were indicative of intergenerational patterns of birth weight from mother to child. However, length of gestation does not appear to exert significant intergenerational effects. The underlying mechanisms remain unclear, although transmission of risk from mother to offspring is likely resultant from interaction of genetic and environmental influences (Ramakrishnan et al., 1999). Findings from this thesis have important implications for maternal and infant care, with intergenerational effects potentially resulting in a compounding effect and increasing numbers of affected offspring. This may already be partially reflected in trends indicating rising incidence rates of these outcomes (Donahue et al., 2010). With this may come an increase in morbidity associated with restricted in uterine growth and low birth weight births (Barker et al., 2005; Hack et al., 2002). Women born low birth weight ought to be considered at risk of low birth weight or small for gestational births. Preconception screening of a woman’s own developmental and birth history may be important in identifying potential risks. This may facilitate the development of adaptive maternal and reproductive care practices before, during and after pregnancy. Reducing other preventable lifestyle or psychosocial risks may be particularly important for women born low birth weight in order to prevent accumulative risks and achieve optimal reproductive health during pregnancy (Chomitz, Cheung, & Lieberman, 1995).

9.8.2 Mediating effect of adolescent disordered eating on intergenerational patterns of adverse birth outcomes

It was hypothesised that adolescent disordered eating would mediate a relationship between maternal adverse birth outcomes and infant small for gestational age births. At the a priori level of acceptable error this hypothesis was not supported, with the indirect effects of Drive for Thinness scores and disordered eating ‘Risk’ falling outside 95% confidence intervals. This does not necessarily infer that further
examination of these relationships should be deferred. The influence of adolescent disordered eating on intergenerational patterns of risk is an area that, to date, has received little empirical investigation meaning that analyses conducted in this study are largely exploratory. The current analyses are based on only the first 188 women from the ATP with available data on infant outcomes, with generation three infant data collection still within the early stages. Small frequencies of maternal and infant birth outcomes, with some outcomes including less than ten cases, means that this sample may not be representative of the general population. In other words, non-significant findings may have resulted from insufficient data in which to assess these relationships and may not necessarily indicate an absence of effects.

Given limitations in available data and exploratory nature of analyses, application of less conservative error estimates, or 90% confidence intervals, may be appropriate (Cohen, 1992). The indirect effects of adolescent disordered eating on the relationship between maternal and infant small for gestational age births fell within 90% confidence intervals, indicating a statistically significant effect (CIL= 0.004, CIU=0.384, CIL=0.014, CIU=0.548). Reported direct effects are consistent with a mediation effect, with Drive for Thinness scores and disordered eating ‘Risk’ significantly related to both maternal and infant small for gestational age. This relationship is described as an indirect only mediation effect, with maternal small for gestational age births not exerting a significant direct effect on similar outcomes in offspring (Zhao et al., 2010). This has implications for the interpretation of reported findings, with indirect only effects more likely to be consistent with the theorized framework and less influenced by other omitted mediator variables on the direct causal pathway (Zhao et al., 2010). Yet, these findings are indicative of early discoveries in relation to intergenerational reproductive risk and are not sufficient to rule out or confirm potential mediating effects.

These findings add to genetic based explanations of intergenerational patterns of small for gestational age births (Svensson et al., 2006; Jaquet et al., 2005). Mediation effects, in the absence of continuity between maternal and infant small for gestational age births, suggest that psychological factors, in addition to genetic of biological factors, play a significant role in the development of these birth outcomes. On the other hand, continuity in maternal and infant low birth weight births, and non-
significant mediation effects, suggest a relatively strong biological basis for these outcomes. Regardless, it is probable that both biological and environmental influences play a role in transmission of birth weight from one generation to the next.

Findings from this study provide preliminary support for intergenerational cycles of risk (Bulik et al., 2005; Linna et al., 2014). It has been suggested that maternal weight at birth can influence maternal genotypes and predispose women to greater difficulties in maintaining adequate weight across the lifespan resulting in greater risk for adverse pregnancy outcomes (Bulik, 2005). Findings from this study are consistent with this premise, with being small at birth significantly associated with a Drive for Thinness and disordered eating ‘Risk’ in adolescence, and consequent increases in risk of later small for gestational age births. Adolescent disordered eating may represent an important psychological factor that perpetuates the cycle of small for gestational age births from one generation to the next. This means that potential genetic predispositions may therefore be circumvented through targeted interventions aimed at developing positive eating behaviours in adolescence.

9.8.3 Post-hoc analyses: Effects of adolescent disordered eating and maternal birth outcomes on risk of small for gestational age births

In the second study reported in Chapter seven, it was hypothesised that adolescent disordered eating, at 15 to 16 years of age, would increase the risk of low birth weight, preterm or small for gestational age births. Findings indicated that adolescent disordered eating, based on Drive for Thinness scores or being ‘At Risk’ of an eating disorder, significantly predicted risk of small for gestational age births. The third study of this thesis revealed a relationship between maternal birth outcomes and infant small for gestational age births. This finding indicated further exploration of maternal and adolescent predictors of small for gestational age risk. Given this, initial analyses were re-run to assess whether the effects of adolescent disordered eating on small for gestational age births remained after adjusting for maternal birth outcomes or if this relationship was better accounted for by maternal characteristics at birth. Post-hoc analyses conducted in this study aimed to extricate the relationships between maternal birth outcomes, adolescent disordered eating and risk of small for gestational age births.
gestational age births. This represents a rare opportunity that to date has not been adequately addressed within the literature.

Findings from adjusted regression models revealed that mothers born with low birth weight were at a significantly increased risk of small for gestational age births. However, very large effect sizes and confidence intervals invite caution when interpreting results, with small frequencies of maternal low birth weight births ($n=7$) likely contributing to a lack of precision in estimating effects. Overall, this finding is consistent with preliminary analyses and prior research (Shah & Shah, 2009) identifying a link between maternal low birth weight and next generation small for gestational age births. If this finding is repeated with narrower confidence intervals in further analysis, when the sample increases, it will have important clinical implications, indicating that risks for the next generation may be identified prior to birth. Not only does this finding provide support for preconception models of reproductive health but extends current DOHaD theory back further in development by emphasising the importance of a mother's own gestation for birth outcomes in consequent offspring.

In the model predicting G3 small for gestational age births, based on Drive for Thinness scores, maternal birth weight was found to be a significant predictor of small for gestational age births, although this risk not significant in the model that included disordered eating ‘Risk’ in adolescence. Decreases in risk associated with increasing maternal birth weight is an important finding, indicating that higher maternal birth weight may be protective factor in relation to risk of small for gestational age births. In the current sample, maternal birth weight ranged from 1.23 to 4.83kgs. Few G2 participants ($n=5$) were identified as being born with large birth weight (above 4.5kgs), meaning that decreases in risk of small for gestational age births may not apply to women reporting within larger birth weight ranges. There is the potential that higher birth weight incurs similar or different, although significant, risks such as type 2 diabetes in adulthood (Harder, Rodekamp, Schellong, Dudenhausen, & Plagemann, 2007). Thus, there may be an optimal birth weight range in which to promote positive developmental outcomes.
The earlier empirical study of this thesis revealed a significant increase in risk of G3 small for gestational age births to women identified as being ‘At Risk’ of an eating disorder in adolescence. When adjusting for G2 maternal low birth weight births, disordered eating ‘Risk’ no longer accounted for a significant portion of G3 small for gestational age births; however was verging on significance ($p = .055$). Disordered eating ‘Risk’ remained a significant predictor of G3 small for gestational age births when adjusting for only overall G2 maternal birth weight and gestational age. This has important implications with the majority of studies included in the systematic literature review for this thesis that examined the risk of small for gestational age births for women with a history of disordered eating, not adjusting for maternal birth outcomes. This may, in part, explain observed discrepancies between study findings, in potentially neglecting to adequately account for early maternal indicators of risk. This study may therefore be one of the first to examine risk of small for gestational births using prospective intergenerational data obtained periodically from infancy through to adolescence and pregnancy.

The effects of disordered eating ‘Risk’ on small for gestational age births were observed to dissipate when adjusting for maternal low birth weight births. This may suggest that biological effects related to weight status or starvation effects, initially associated with disordered eating ‘Risk’, may be better accounted for by maternal low birth weight births. Significant correlations revealed between maternal low birth weight births and disordered eating ‘Risk’, indicate that this is likely representative of a confounding variable. This type of explanation is consistent with the proposition that infants born to mothers with low birth weight may be predisposed to ongoing difficulties maintaining weight throughout the lifespan and at a greater risk of developing disordered eating behaviour as well as adverse birth outcomes (Bulik, 2005; Favaro et al., 2006). Interestingly, in bivariate analyses maternal low birth weight was not significantly correlated with BMI nor was BMI significantly associated with infant small for gestational age births, implying that other factors may underlie these associations. Overall, there is the potential that biological influences, in the form of maternal low birth weight, exert a stronger influence on risk of small for gestational age births. The potential influence of disordered eating ‘Risk’ cannot be ruled out, with smaller frequencies of infant outcomes meaning that significant effects
may have been unable to be detected. Thus, replication within larger samples is required in order to understand these relationships further.

Whilst measures of disordered eating ‘Risk’ touch on physical starvation effects by accounting for BMI, Drive for Thinness scores measure more of the psychological underpinnings of disordered eating. Drive for Thinness scores remained a significant predictor of small for gestational age births when adjusting for maternal birth outcomes. Considering that in bivariate analyses maternal birth weight and low birth weight births were not significantly associated with Drive for Thinness scores it may be inferred that psychological factors, associated with the Drive for Thinness measure, contribute unique risks to offspring as originally proposed in the second study of this thesis. What this suggests is that, for some women, psychological factors associated with disordered eating may contribute to a proportion of small for gestational age births. This finding reinforces the importance of a preconception approach to reproductive care that extends from early life to consider a mother's own gestation, to adolescence, adulthood and pregnancy. The implications of these findings, in the context of results revealed in the second study of this thesis, will be further discussed in the final chapter of this thesis.

CHAPTER 10: OVERALL DISCUSSION

10.1 Chapter overview

This chapter provides a brief review of the overall aims and research questions of this thesis. Included in this chapter is a recap of the current literature and gaps within the current evidence base in relation to preconception care. Key findings from this thesis are discussed in the context of DOHaD theory and implications of these findings are reviewed. Finally, strengths and limitations of this thesis are discussed as well as directions for future research.
10.2 Literature review

Low birth weight, preterm and small for gestational age births account for approximately 75% of overall neonatal morbidity and mortality (Goldenberg et al., 2008). Despite continued attempts to reduce the incidence of these outcomes and an overall improvement in reproductive knowledge and care, the problem remains, signifying a need for further research in this area (Green et al., 2005). Theories of Developmental Origins of Health and Disease (DOHaD) have emphasised the importance of early life experiences, in particular neonatal development and infancy, in the development of disease and wellbeing in later life. Findings derived from epidemiological studies of infant and adult mortality have provided a foundation for examination of maternal weight and nutrition in the development of low birth weight, preterm and small for gestational age births (Swanson et al., 2009; Weck et al., 2008). Yet, the focus to this point has been largely on exposures occurring during the gestational period (Misra et al., 2003). This thesis investigated the proposition that some determinants of low birth weight, preterm and small for gestational age births, may originate well before conception. Examination of risk occurring prior to gestation, such as disordered eating behaviour, may provide targets for early intervention aimed at circumventing preventable instances of adverse birth outcomes.

The first study presented in this thesis was a systematic review of the current literature examining the risk of low birth weight, preterm and small for gestational age births in women with a history of disordered eating. Review of the current evidence base provided early indications of risk of low birth weight, preterm and small for gestational age births for women with a history of disordered eating, in particular AN. Few studies specifically examined the effects of preconception bulimic behaviours on risk of low birth weight, preterm or small for gestational age births, though it has been suggested that bulimic behaviours incur different pathways of risk. For the most part, significant findings in relation to preconception disordered eating have been associated with use of large prospective clinical samples. Yet, replication of these findings within prospective community samples was yet to be demonstrated. A lack of available prospective longitudinal designs and observed disparities across study findings invite some caution when interpreting overall findings.
Overall, current research was found to be reflective of traditional principles of DOHaD theory, with the focus primarily on the effects of disordered eating occurring during pregnancy or in the period immediately prior to conception. Only one study included in the review specifically examined the risk of adolescent onset disordered eating on later pregnancy and birth outcomes (Wentz et al., 2009), revealing a significant gap in relation to available prospective studies of preconception risk. Current Centre for Disease Control (CDC) recommendations have emphasised the importance of a lifespan approach to reproductive health, indicating that the preconception period should be extended to include the onset of reproductive maturation in adolescence (Johnson et al., 2006). However, the development of effective preconception intervention remains dependent on the emergence of high quality empirical evidence and support (Jack et al., 2008; Korenbrot et al., 2002).

10.3 Aims and research questions

The central objective of this thesis was to address noted gaps in the literature by examining the effects of preconception disordered eating on low birth weight, preterm and small for gestational age births. The aim of the first study was to systematically summarise and review what is currently known about preconception disordered eating. The second and third studies drew on prospective longitudinal data, obtained from 188 female participants who had given birth to 83 male and 105 female infants, to examine the effects of adolescent disordered eating, at 15 to 16 years of age, on risk of low birth weight, preterm and small for gestational age births. This thesis also aimed to explore the role of adolescent disordered eating in intergenerational transmission of adverse birth outcomes from mother to infant.

Based on findings from a systematic review of the current literature base, it was hypothesised that adolescent disordered eating behaviour, based on Drive for Thinness scores and disordered eating ‘Risk’, would significantly increase the risk of low birth weight, preterm or small for gestational age births. The third study of this thesis aimed to expand on the previous two studies by examining the role of disordered eating in intergenerational patterns of low birth weight, preterm and small for gestational age births. Substantive evidence has indicated intergenerational patterns of birth weight from mother to offspring (Farina et al., 2010; Ramakrishnan
et al., 1999). Emerging, although discrepant, evidence in relation to intergenerational transmission of preterm births inferred a need for further examination and clarification of these associations (Selling et al., 2006; Shah & Shah, 2009). As such, it was hypothesised that low birth weight, preterm and small for gestational age births would be significantly related between mothers and infants.

Findings revealing a link between adverse birth outcomes and the development of disordered eating (Andrews & Brown, 1999; Favaro et al., 2006) also contributed to preliminary theories around intergenerational cycles of risk in disordered eating populations (Linna et al., 2014; Bulik et al., 2005). Findings of this nature raised the question of potential mediating effects, with disordered eating hypothesised to sit on the causal pathway from maternal birth outcomes to infant small for gestational age births. Therefore, it was hypothesised that the relationship between maternal birth outcomes and infant small for gestational age births would be mediated by disordered eating behaviours in adolescence.

10.4 Key study findings and implications

At the beginning of this thesis it was hypothesised that preconception disordered eating would predict low birth weight, preterm or small for gestational age births. Findings from logistic regression analyses only partially supported this hypothesis with Drive for Thinness and disordered eating ‘Risk’ not contributing to a significant proportion of risk of low birth weight and preterm births. In contrast, Drive for Thinness scores and disordered eating ‘Risk’ were associated with a significant increase in risk of small for gestational age births. Increasing Drive for Thinness scores were associated with small, although significant, increases in risk of small for gestational age births (OR: 1.104). Women identified as being ‘At Risk’ of an eating disorder in adolescence were approximately three times more likely to have a small for gestational age birth. Bulimia scores did not significantly predict risk of low birth weight, preterm or small for gestational age births, which is consistent with the majority of previous findings (Conti et al., 1998; Linna et al., 2014). This suggests that poor nutrition or restricted eating patterns associated with anorexic subtypes may incur different pathways of risks relative to individuals presenting with bulimic
symptoms. These findings provide early support for the theory that reproductive risks may vary depending on clinical subtypes, as discussed in Chapter four of this thesis.

The main finding from this thesis is a significantly increased risk of small for gestational births for women reporting higher Drive for Thinness scores and disordered eating ‘Risk’, in adolescence at 15 to 16 years of age. This is an important finding, indicating that eating attitudes and behaviours in adolescence may predispose women to poorer reproductive outcomes more than 10 years later. Incidence rates of AN and BN are reported to be highest among girls in middle and late adolescence, with eating disorders representing the third most common chronic disease in adolescence (Portela de Santana et al., 2011). Furthermore, considerable increases in the proportion of sub clinical symptoms, particularly in adolescent populations infers a growing potential for ongoing harms within the general population (Chamay-Weber et al., 2005; Sancho et al., 2007). In Chapter four of this thesis it was suggested that a longer or more chronic course, associated with adolescent onset disordered eating, may incur greater risks in comparison to symptoms occurring later in life (Hebebrand & Remschmidt, 2001). Findings from this thesis may provide support for this premise, indicating that adolescent disordered eating behaviours may have long-term impacts for pregnancy outcomes in adulthood, although it is acknowledged that disordered eating was not subsequently measured in the ATP during adulthood and pregnancy.

Non-significant effects in relation to low birth weight and preterm births suggest that intergenerational risks are reduced within the general population compared to more clinical samples where significant effects have been revealed (Linna et al., 2014; Sollid et al., 2004). The findings from this thesis are consistent with the premise that long-term risk may vary as a function of symptom severity and degree of weight loss, length of disorder and rate of weight loss (Herpertz-Dahlmann, 2008). Increasing severity of disordered eating may increase the risk of very low birth weight births, whilst sub clinical symptoms may predispose women to small for age but normal weight infants. On the other hand, non-significant effects in relation to low birth weight and preterm births may indicate that long-term risks, beginning in adolescence, are attenuated over time. Given that symptoms observed in the current sample are likely to be milder in severity, compared to clinical samples, findings
revealing significant increases in risk of small for gestational age births are indicative of cause for concern. This suggests that potential reductions in risk, associated with sub clinical symptoms, occurring over time may still incur significant consequences. This finding signifies the critical importance of further examination of the effects adolescent disordered eating within clinical samples as these populations may represent those at greatest risk.

However, when accounting for the potential influence of maternal birth outcomes, maternal low birth weight was found to supersede risk of small for gestational age births associated with disordered eating ‘Risk’ in adolescence. Results indicating an increased risk of small for gestational age births to women born with low birth weight are in concordance with the findings of Shah and Shah (2009) as discussed in Chapter eight of this thesis. Recent findings have cited the proportion of low birth weight births in Australia at 6% (Blencowe et al., 2012). This represents a relatively large proportion of the population who may be at an increased risk of later adverse birth outcomes, such as small for gestational age births. This finding has important clinical implications, inferring that indicators of next generation birth risk, in the form of small for gestational age births, may be present prior to birth. This emphasises the importance of preconception care for women at risk, or those born with low birth weight, with the development of early health and reproductive care practices vital in generating optimal pregnancy outcomes in such women.

Whilst the risk of small for gestational age births, based on disordered eating ‘Risk’, was reduced when adjusting for maternal low birth weight, Drive for Thinness scores remained a significant predictor of small for gestational age births. In saying this, reported effect sizes remain small implying that the overall magnitude of risk may be marginal. Conclusions around the underlying causes or mechanisms or risk cannot be rendered from the current analyses although findings from this thesis may provide support for hypotheses predicting long-term effects as a result of adolescent disordered eating. Hormonal changes occurring as a result of starvation effects during adolescence may impact on reproductive functioning including decreases in ovary and uterus size or length (Hoffman et al., 2011; Mason et al., 2007). Similarly, reduced ovarian volume in infants born small for gestational age has been hypothesised to occur as a result of conditions imposed on the mother during development, such as
restricted in uterine growth during a mother's own gestation (Ibanez et al., 2000). It may be that both maternal low birth weight and adolescent disordered eating result in permanent changes in reproductive functioning which increases consequent risk of small for gestational age births. Findings from this thesis provide support for DOHaD theory and the relative importance of early life and gestation for later development and wellbeing (Wadhwa et al., 2009), although extends current theory further back by emphasising the critical importance of the adolescent period as well as a mother's own gestational experience on birth outcomes.

The final study of this thesis aimed to examine continuity of low birth weight, preterm and small for gestational age births from mother to offspring and explore the role of disordered eating in mediating intergenerational patterns of risk. Initial analyses revealed that mothers born low birth weight are at a significantly increased risk of having a low birth weight birth, supporting hypotheses predicting intergenerational continuity from mother to offspring. Similarly, mean birth weight was significantly correlated between mother and infant. Hypotheses predicting continuity between maternal and infant preterm and small for gestational age births were not supported. Repeating patterns of low birth weight births across generations may indicate an accumulation of potential risks across generations. Findings from this thesis fit with the premise that offspring birth weight may be determined by constraints placed on the mother during gestation. In uterine growth restriction observed in the mother may result in permanent changes in growth throughout development, altering the in utero environment and foetal development in consequent pregnancies (Drake & Walker, 2004). Low birth weight has been shown to be a strong predictor of in uterine growth restriction (Klebanoff & Yip 1987) inferring that maternal low birth weight status may increase the risk of similar outcomes in offspring. Overall, findings suggest that length of gestation, compared to weight at birth, carries fewer intergenerational risks.

Based on 95% confidence intervals, adolescent disordered eating did not significantly mediate the relationship between maternal birth outcomes and infant small for gestational age births. However, application of less conservative error estimates revealed a significant mediating effect in relation to risk of small for gestational age births from mother to infant. Conclusions based on these findings
remain tentative, representing insufficient evidence to reject or accept the null hypothesis. This infer a need for further replication to clarify potential effects. Potential mediation effects, in the absence of direct effects between maternal and infant small for gestational age births, suggest that psychological factors play an important role in the transmission of small for gestational age births from one generation to the next. This finding is indicative of the relative importance of adolescent disordered eating, with indirect only effects such as these more likely to be consistent with the theorized framework and less influenced by other omitted mediator variables on the direct causal pathway (Zhao et al., 2010).

Results of this study are consistent with theories of intergenerational cycles of risk proposed by Bulik (2005) and Linna et al. (2014) outlined in Chapter eight of this thesis. Maternal weight at birth may influence maternal genotypes and growth throughout development and consequent pregnancies; however, this process may be mediated or perpetuated by disordered eating in adolescence. Positive eating patterns during development may be increasingly important for women born small for gestational age, to circumvent later risks during pregnancy. Psychological factors may exercise greater influence in cases where biological risks are relatively reduced such as small but normal weight infants. Interventions aimed at reducing adolescent exposures may decrease risks during pregnancy and birth but also exert positive effects for following generations. Overall, findings from this thesis cautiously suggest that both biological and psychological factors, which occur and interact across the lifespan, exert underlying influence in the development of adverse birth outcomes.

The results from this thesis have important implications for the interpretation of previous findings, with few studies adjusting for maternal birth outcomes when examining risk of low birth weight, preterm and small for gestational age births in women with a history of disordered eating. Similarly, the majority of studies investigating intergenerational patterns of birth weight and gestational age utilised data obtained from linked medical records. This meant that little information was obtained in relation to factors occurring throughout development, such as disordered eating, limiting the assessment of potential mediating or moderating variables underlying the relationship between maternal and infant adverse birth outcomes. This thesis may therefore be one of the first to prospectively examine risks of these adverse births.
10.5 Strengths and limitations

One of the main strengths of this thesis is that it draws on over 20 years of prospective data from three generations of ATP participants. This represents a rare opportunity to prospectively investigate intergenerational effects and patterns of risk from infancy, adolescence and pregnancy. The methodological approach adopted in the ATP study addresses a number of methodological limitations noted within previous studies. Prospective longitudinal data obtained in this thesis help to reduce issues of selection and self-report bias and contribute to an improved ability to examine trajectories of risk and provide evidence of a temporal link between exposure and outcome variables (Austin et al., 1994; Mann, 2003; Schulz & Grimes, 2002). Three important criteria have been proposed in the development of effective intergenerational designs (Serbin & Karp, 2004). Firstly, individuals within the study must be observed at the same age or developmental stage across generations. Secondly, data should be prospective rather than retrospective. Lastly, data should be obtained from multiple measures or sources (Cairns, Cairns, Xie, Leung & Hearne, 1998; Serbin & Karp, 2004). Methodological procedures utilised within the ATP, for the most part, fulfil these criteria described.

The potential effects of preconception adolescent disordered eating on pregnancy and birth outcomes, have to date, remained a relatively under-researched area of knowledge. This is likely due to practical limitations associated with conducting long-term intergenerational research. For this reason, analyses conducted in this thesis represented preliminary and exploratory investigations into these relationships, with multiple variables and models tested in order to explore potential effects. It is acknowledged that by increasing the number of analyses conducted, the risk of type II error; or the likelihood of falsely obtaining a significant result, increases also (Price & Glenn, 2015). Regardless, findings from this thesis are important in identifying directions for future research and empirical analysis.
Relatively few cases of low birth weight, preterm and small for gestational age births may impact on the conclusions that can be drawn from this thesis. The sample may have therefore been too small to adequately reflect normal variations in birth outcomes or subtypes, potentially resulting in a reduced ability to detect potential effects, particularly those that are small in magnitude. This is exacerbated by the investigation of low prevalence eating disorders (Keski-Rahkonen et al., 2007; Smink et al., 2013). Interpretation of findings, particularly for outcomes where less than 10 cases were identified, should be made with caution, with small frequencies contributing to significant reductions in the precision and validity of estimated effects (Hosmer & Lemeshow, 2004). Considering this, findings remain tentative, with results not necessarily inferring an absence or presence of true effects. Replication of analyses using larger prospective samples may clarify the nature of these relationships. Small numbers also meant that both first-born and subsequent births were included in the sample, with only 71% of infants reported being the first-born. This may also have implications for the interpretation of findings, with risk of preterm births known to be higher in first pregnancies (Ananth et al., 2001; Astolfi & Zonta, 1999). Rates of preterm births may be underrepresented in the sample, possibly reducing the generalizability of presented results. As discussed previously, ongoing recruitment of G3 data aims to address these limitations through larger replication of these findings.

This thesis addressed noted gaps in the current literature base by examining effects of adolescent disordered eating behaviour on pregnancy outcomes. Analyses revealed a significantly increased risk of small for gestational age births to women reporting adolescent disordered eating occurring approximately 10 years prior at 15 to 16 years of age. However, disordered eating behaviours were not measured during G3 waves of ATP data collection resulting in an inability to control for the potential effects of disordered eating during pregnancy or to consider it as a mediator in the intergenerational pathway. To reiterate briefly, this has implications for the interpretation of presented findings, with reported effects potentially influenced by direct harms resulting from disordered eating behaviours occurring during pregnancy. There is the potential that adolescent disordered eating, based on the Drive for Thinness scores, increases the risk of small for gestational age births by increasing the likelihood that disordered eating behaviours continue throughout pregnancy.
Nevertheless, it may be inferred that maladaptive eating behaviours and attitudes in adolescence contribute to potential long-term risks, either through reproductive or hormonal changes in adolescence or by predisposing individuals to the continuation of maladaptive behaviours during pregnancy.

A reliance on self or parent-report measures may introduce a degree of bias to reported findings. Use of parent report data on G3 birth outcomes, during later waves of data collection, may introduce a degree of subjective bias. It is acknowledged that there is the potential for nurse reported data on G2 birth outcomes, obtained during the initial wave of data collection, to be more accurate than parent reports obtained during later assessments. In saying this, bias occurring as a result of parent reports is likely to be minimal, with parent report shown to be an adequate measure of assessing birth outcomes in children (Lederman & Paxton, 1998; Pless & Pless, 1995). The aim of the ATP is to address potential issues of bias associated with use of parent report data by cross-referencing data with hospital records that are being made available through data linkage. Use of self-report measures within disordered eating populations has been associated with an underestimation of symptoms due to attempts to conceal symptoms and levels of associated shame and secrecy (Fichter & Quadflieg, 2000; Morrill & Nickols-Richardson, 2001; Makino, et al., 2004). Some evidence has suggested that self-report measures may represent a viable alternative to more formal diagnostic assessments in reducing potential stigma associated with face-to-face approaches, particularly for adolescents (Micali & House, 2011; Mond et al., 2007). The measures used in this thesis are not without their limitations, although empirical findings have shown that subscales of the EDI significantly differentiate individuals with eating disorder symptoms from non-clinical controls (Clausen et al., 2011; Garner, 2004). The inclusion of a disordered eating ‘At Risk’ measure, which incorporated data on BMI, aimed to address some of these limitations and lend weight to self-reported data by providing an additional source to assess potential physical starvation effects associated with disordered eating.

As discussed in Chapter five of this thesis, subscales of the EDI represent only population-based indicators of characteristics of disordered eating. There is some evidence of criterion related validity, with higher associations observed between women with bulimic subtypes of disordered eating, compared to restricting subtypes,
and scores on the Bulimia subscale of the EDI (Garner et al., 1983; Milos et al., 2004). Despite this, a degree of overlap between subscales of the EDI and disordered eating symptoms means that this measure cannot be used to identify or diagnose various clinical subtypes. Bulimic samples, for example, have also shown elevated scores on the Drive for Thinness subscale that are based on characteristics associated with AN (Garner, 1983). Hence, this measure cannot be used to adequately assess or differentiate clinical subtypes. Whilst Drive for Thinness and Bulimia subscales may tap into symptom profiles consistent with anorexic or bulimic subtypes (Garner et al., 1983), conclusions based on these findings represent only indicators of risk. It also recognized that exclusion of the Body Dissatisfaction subscale of the EDI may have limited analyses and consequent interpretations. Further examination of the effects of adolescent disordered eating on pregnancy outcomes, using measures of body dissatisfaction, may be indicated.

Similarly, it is acknowledged that the disordered eating ‘At Risk’ variable requires further validation to assess the ability of this measure to correctly identify individuals who are actually engaging in disordered eating behaviours. In saying this, the theoretical foundations and empirical research underlying the development of the EDI-RF form on which the ‘At Risk’ variable is based provides some support for its ability to differentiate clinical presentations from controls, or individuals who do not engage in disordered eating behaviours (Garner, 2004). Future studies that examine specific clinical profiles or subtypes are required to develop more definitive conclusions. Therefore, risks reported in this study may not be generalizable to specific disordered eating populations.

Across the 32 years of the ATP, attrition has occurred at a rate of about 1% per annum; however, more female participants have been retained over time than men. Overall for women, response rates for self-report at each wave of data collection were in excess of 80% of the retained sample. Although common in longitudinal cohort studies, particularly those spanning large timeframes, it is argued that attrition not exceeding 20% at follow up is acceptable (Song & Chung, 2010). The overall sample was found to include families from a diverse range of backgrounds and circumstances, although compared to the retained sample non-participating families were more likely to be from a lower socio economic background (Letcher et al.,
This should be considered when interpreting results, with SES status shown to be strongly related to low birth weight births (Hughes & Simpson, 1995). Findings suggesting that disordered eating populations are over represented among non-respondents in general population studies may indicate limitations in the generalizability of reported findings (Beglin & Fairburn, 1992). Despite this, missing data analyses indicated that patterns of missingness were likely to be completely random, suggesting that issues of non-response bias may be minimal. Issues of attrition may be particularly relevant given low prevalence rates for eating disorders, potentially contributing to difficulties identifying disordered eating cases (Smink et al., 2013).

Although a range of covariates have been shown to contribute to risk of low birth weight, preterm or small for gestational age births, including anxiety symptoms (Seckl, 2008; Wadhwa et al., 2004) and prior obstetric or medical factors (Lopez, Smith, & Gutierrez, 2002; Fedrick & Adelstein, 1978; Meis et al., 1998; Mercer et al., 1999), these variables were not included in the analyses. In addition, small frequencies of multiple births ($n=2$) and IVF use ($n=8$) meant that these variables were unable to be included within analyses despite considerable evidence demonstrating an increased risk of low birth weight, preterm and small for gestational age births as a result of multiple births and IVF (Blondel et al., 2002; Blondel et al., 2006; Luke, 1994). In saying this, none of the women in the current sample, who reported undergoing IVF, experienced a low birth weight, preterm or small for gestational age birth. This indicates that exclusion of data in relation to IVF use is unlikely to have impacted on overall findings. Regardless, these variables should be considered in future research to strengthen the quality of future findings and interpretations.

### 10.6 Recommendations and future directions

This thesis represents one of the first to prospectively examine the long-term impacts of adolescent disordered eating behaviour on pregnancy outcomes in adulthood. The findings from this thesis represent only preliminary insights into the potential effects of preconception disordered eating. Considering that reported findings are based on data obtained from only the first 188 ATP participants with
complete data on G3 birth outcomes examined, further replication is required in order to generate more reliable conclusions and address noted limitations. Recruitment and data collection in relation to the Generation Three (G3) study remains in the early stages, with the aim of the ATP to recruit 1000 G3 infants in the coming years. In particular, replication of these findings within clinical samples represents a critical area of further research, with these individuals potentially representing those at the greatest risk. The ATP provides a unique opportunity for continued examination of intergenerational processes and preconception risks.

Overall, findings from this thesis provide preliminary evidence of the effects of adolescent disordered eating, measured using the Drive for Thinness subscale of the EDI, on risk of small for gestational age births in young adulthood. Such findings infer the importance of preventative interventions that target maladaptive eating behaviours and attitudes in adolescence and emphasise the relevance of a lifespan approach to reproductive health recommended by the CDC (Johnson et al., 2006). Analyses of eating disorder prevention programs indicate that multi session prevention programs, which are selected and interactive, compared with universal and didactic, remain most effective in reducing eating pathology (Stice & Shaw, 2004; Stice, Shaw & Marti, 2007). Education around the long-term impacts of nutrition, eating behaviours and reproductive functioning may be pivotal in reducing risk in adolescent populations. Targeted interventions aimed at reducing pathological eating behaviours and attitudes may be particularly relevant for individuals born low birth weight, or those at a greater risk of developing disordered eating symptoms.

Furthermore, findings from this thesis may suggest that women born low birth weight ought to be considered at risk of low birth weight or small for gestational births. Preconception screening of a woman’s own developmental and birth history, occurring as early as adolescence, may be important in identifying potential risks. This may facilitate the development of adaptive maternal and reproductive care practices before, during and after pregnancy. Reducing other preventable lifestyle or psychosocial risks, such as maladaptive eating patterns, may be particularly important for women born low birth weight in order to prevent accumulative risks and achieve optimal reproductive health during pregnancy (Chomitz et al., 1995).
An important question for future research may be whether observed intergenerational effects are transmitted onto third generation offspring. Some findings have suggested that risks associated with maternal low birth weight dissipate across generations from grandparent to grandchild (Painter et al., 2008; Veenendaal et al., 2013); however, this remains an interesting area for further research. Investigation of outcomes in third generation offspring may provide important information on the role of disordered eating in transmission of risk and whether self-perpetuating cycles, proposed by (Linna et al., 2014; Bulik et al., 2005), repeat across multiple generations. Research addressing patterns of risk across multiple generations may help to explain increasing and unchanged trends in lower birth weight births (Donahue et al., 2010; Martin, Hamilton, Ventura et al., 2012) despite advancements in reproductive care, with risks observed in one generation potentially resulting from exposures occurring in previous generations (Painter et al., 2008).

Further investigation of potential gender differences in the development of risk of adverse birth outcomes may represent an interesting area for further research considering growing prevalence rates of subclinical symptoms and disordered eating in young men and adolescents (Kjelsas, Bjornstrom & Gotestam, 2004; Muise, Stein, & Arbess, 2003). Similarly, intergenerational transmission of risk was measured along maternal lines. Although some findings have indicated that transmission of risk is stronger along maternal lines (Jaquet et al., 2005), investigation of paternal factors may contribute to understandings of potential mechanisms of risk, particularly theories of genetic inheritance. The precise mechanisms of risk from adolescent disordered eating to small for gestational age births remain speculative. Examining the biological, psychological and social mechanisms of risk may identify causal processes involved in the development of adverse birth outcomes and the development of specified interventions aimed at reducing these risks.

10.7 Conclusions

The current study drew on prospective intergenerational data obtained from the Australian Temperament Project (ATP) to test the hypothesis that adolescent disordered eating would increase the risk of low birth weight, preterm and small for gestational age births. The major finding of this thesis is a small but significantly
increased risk of small for gestational age births to women reporting disordered eating behaviours in adolescence, based on Drive for Thinness scores on the EDI. Furthermore, findings from this thesis indicated that women ‘At Risk’ of an eating disorder in adolescence were approximately three times more likely to have a small for gestational age birth. Although revealing non-significant effects when adjusting for G2 maternal low birth weight births, risk of small for gestational age births based on disordered eating ‘Risk’ in adolescence was verging significance. This represents an important finding requiring further investigation within larger prospective samples. Examination of intergenerational continuity of adverse birth outcomes revealed that low birth weight births but not preterm or small for gestational age births are significantly correlated between mother and offspring. Finally, results from this thesis revealed that adolescent disordered eating may mediate the relationship between maternal and offspring small for gestational age births. Overall findings from this thesis remain preliminary although draw on important areas for future research and replication using prospective empirical designs.

Findings from this thesis, in the context of Developmental Origins of Health and Disease theory, emphasise the critical importance of the preconception period, spanning from a mother’s own gestation to adolescence, in the development of adverse birth outcomes. This thesis highlights the importance of a lifespan approach to reproductive health, consistent with recent Centre for Disease Control recommendations (Johnson et al., 2006), indicating that the preconception period should include the onset of puberty or sexual maturation. This finding underscores the importance of the adolescent period in developing positive health trajectories into adulthood and pregnancy and has implications for the prevention and management of small for gestational age births. These findings have clinical implications in the early identification of women who may be at greater risk, suggesting that that may occur prior to becoming pregnant. Preventative interventions aimed at reducing small for gestational age births may be best targeted prior to conception and during adolescence. Preventative interventions in adolescence may have positive flow on effects in reducing physical and psychological risks for following generations.
REFERENCES


Newnham, J. P. (2007). The developmental origins of health and disease (DOHaD)- why is it so important to those work in fetal medicine? *Ultrasound in Obstetrics and Gynecology, 29*, 121-123.


APPENDICES

Appendix A: Description of measures used

This appendix presents a description of the measures used as part of this thesis and the overall Australian Temperament Project (ATP). For further details regarding the nature of these measures and psychometric properties refer to Chapter six.

Adolescent disordered eating

Disordered eating behaviours at 15 and 16 years of age were measured using an adapted version of the Eating Disorder Inventory (EDI). The EDI is a 64-item, self-report, multi-scale measure designed to assess the psychological and behavioural traits consistent with AN and BN (Garner et al., 1983). Nineteen items from the EDI were administered to ATP participants at 15 and 16 years of age, which represented three of the eight core EDI subscales; Drive for Thinness, Bulimia and Body Dissatisfaction. Total summed scores derived from seven items from the Drive for Thinness subscale and seven items from the Bulimia subscale were used for analyses in this thesis. Items were rated on a six-point scale where 1=never, 2=rarely, 3=sometimes, 4=often, 5=very often and 6=always. The items that comprise the Drive for Thinness subscale (items one through to seven) and Bulimia subscale (items eight through to fourteen) of the EDI are as follows:

1. I eat sweets and carbohydrates without feeling nervous
2. I think about dieting
3. I feel extremely guilty after overeating
4. I am terrified of gaining weight
5. I exaggerate or magnify the importance of weight
6. I am preoccupied with the desire to be thinner
7. If I gain a kilo, I worry that I will keep gaining
8. I eat when I am upset
9. I stuff myself with food
10. I have gone on eating binges where I have felt that I could not stop
11. I think about bingeing (overeating)
12. I eat moderately in front of others and stuff myself when they have gone
13. I have thought of trying to vomit in order to lose weight
14. I eat or drink in secrecy

*Depressive symptoms*

Depressive symptoms at 15 and 16 years of age were measured using an adapted version of the Short Mood and Feelings Questionnaire (SMFQ; Angold, Costello, & Messer, 1995). The SMFQ is a brief 13-item, self-report scale designed to detect clinical depression in children and adolescents. Items measure affective and cognitive symptoms of depression, including some somatic and behavioural symptoms including feeling miserable, low energy, loneliness, self-hatred and anhedonia. Twelve of these items were administered to ATP participants at 15 and 16 years of age. Total summed scores, ranging from 0 to 24, were used to assess the presence and severity of depressive symptoms, with higher scores indicating greater levels of depressive symptoms. This scale is comprised of a three-point Likert-type response format where 0=rarely or never, 1=sometimes and 2=very often. The items that comprise this measure are as follows:

1. I am restless, find it hard to sit still
2. I feel miserable or unhappy
3. I don’t enjoy anything at all
4. I feel so tired I just sit around and do nothing
5. I feel I am no good anymore
6. I cry easily
7. I hate myself
8. I think I can never be as good as other kids
9. I feel lonely
10. I think nobody really loves me
11. I am a bad person
12. I do everything wrong
### Appendix B: Search strategy for Psych Info, Medline, Pubmed and CINAHL Complete

#### Table B.1 Search strategy and search terms

<table>
<thead>
<tr>
<th>Psych INFO</th>
<th>Medline complete</th>
<th>Pubmed</th>
<th>CINAHL Complete</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Subject terms=eating disorders or anorexia nervosa or bulimia or Free text=bulimi* or anorexi* or disordered eating</td>
<td>1 Subject terms=eating disorders or anorexia or anorexia nervosa or bulimia or bulimia nervosa or Free text=bulimi* or anorexi* or disordered eating</td>
<td>1 Subject terms=eating disorders or anorexia or anorexia nervosa or bulimia or bulimia nervosa or Free text=anorexi* or bulimi* or disordered eating</td>
<td>1 Subject terms= Eating disorders or Bulimia nervosa or Bulimia or Anorexia Nervosa or Anorexia or Free text= disordered eating or anorexi* or Bulimi*</td>
</tr>
<tr>
<td>2 Subject terms=pregnancy outcomes or premature birth or obstetrical complications or birth weight or Free text= low birth weight or gestational age</td>
<td>2 Subject terms=pregnancy outcomes or premature birth or obstetrical complications or birth weight or gestational age or infant or very low birth weight or infant extremely low birth weight or gestational age or infant, small for gestational age or Free text=obstetric outcome* or birth outcome*</td>
<td>2 Subject terms=infant, low birth weight or infant, very low birth weight or infant extremely low birth weight or gestational age or infant, small for gestational age or Free text= pregnancy outcomes or Free text= pregnancy outcomes or Free text= low birth weight or preterm birth</td>
<td>2 Subject terms=pregnancy outcomes or Birth weight or childbirth, premature or Infant, low birth weight or Infant, very low birth weight or gestational age or Infant, small for gestational age or Free text= pregnancy outcomes or Free text= low birth weight or preterm birth</td>
</tr>
<tr>
<td>3 (1 and 2)</td>
<td>3 (1 and 2)</td>
<td>3 (1 and 2)</td>
<td>3 (1 and 2)</td>
</tr>
</tbody>
</table>
Appendix C: Technical Summaries

<table>
<thead>
<tr>
<th>ID Number</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Authors</td>
<td>Abraham, S., King, W., and Llewellyn-Jones, D.</td>
</tr>
<tr>
<td>Year published</td>
<td>1994</td>
</tr>
<tr>
<td>Title</td>
<td>Attitudes to body weight, weight gain and eating behaviour in pregnancy</td>
</tr>
<tr>
<td>Journal</td>
<td>Journal of Psychosomatic Obstetrics and Gynaecology</td>
</tr>
<tr>
<td>Volume, pages</td>
<td>15(4), pp. 189-195</td>
</tr>
<tr>
<td>Study Name</td>
<td></td>
</tr>
</tbody>
</table>

STUDY DESIGN

<table>
<thead>
<tr>
<th>Year</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Design</td>
<td>Cross sectional</td>
</tr>
<tr>
<td>Location</td>
<td>Australia</td>
</tr>
<tr>
<td>Sample size</td>
<td>$n=100$ (ED=24)</td>
</tr>
<tr>
<td>Mean age</td>
<td>27 years</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
</tr>
<tr>
<td>Sample type</td>
<td>Community</td>
</tr>
<tr>
<td>Retained sample/attrition</td>
<td>110 women met criteria for inclusion in the study. One hundred of those women agreed to complete the questionnaire 3-5 days after the birth.</td>
</tr>
</tbody>
</table>

MEASUREMENT

| Exposure variable (& measure) | Past or current disorder eating behaviour was assessed retrospectively by self-report questionnaire three days after birth. Participants were asked "do you think you have or have had problems with disordered eating?" or had engaged in techniques that they believed would ‘control’ their body weight either before or during pregnancy. |
| Outcome variable at each wave (up to 4) | Data on birth weight was obtained from hospital records. Infant birth weight was measured in kilograms. Low birth weight births were defined as those with a birth weight below the 25th percentile. |
| Covariates | Body Mass Index (BMI) |

RESULTS

Women reporting disordered eating behaviour were significantly more likely to give birth to low birth weight infant (chi square: 6.33; df = 1; $p = < 0.02$) and were more likely to experience antenatal complications.
**STUDY DESIGN**

<table>
<thead>
<tr>
<th>Year</th>
<th>1981-1984</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Design</td>
<td>Historical observation cohort paired with a case control study</td>
</tr>
<tr>
<td>Location</td>
<td>New Zealand</td>
</tr>
<tr>
<td>Sample size</td>
<td>AN n=66, controls n=98</td>
</tr>
<tr>
<td>Mean age</td>
<td>Mean age at time of first pregnancy 24.5 years, controls= 23.7 years</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
</tr>
<tr>
<td>Sample type</td>
<td>Clinical</td>
</tr>
<tr>
<td>Retained sample/attrition</td>
<td>Participation rate reported at 86.4% for women with a history of anorexia and 91.7% for controls. Attrition rates between groups were not significantly different.</td>
</tr>
</tbody>
</table>

**MEASUREMENT**

<table>
<thead>
<tr>
<th>Exposure variable (&amp; measure)</th>
<th>Disordered eating cases were identified from records of the Eating Disorders Service at the Princess Margaret Hospital in Christchurch. Cases were defined as any women seen by the Eating Disorders Service between 1981-194 who met DSM-III or DSM-III-R criteria for definite or probable anorexia nervosa.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome variable at each wave</td>
<td>Data on gestational weight, preterm and small for gestational age births were obtained by face-to-face (91.4%) or telephone as part of a structured psychiatric interview using the diagnostic interview for genetic studies.</td>
</tr>
<tr>
<td>Covariates</td>
<td>Body Mass Index (BMI), fertility treatment and maternal age.</td>
</tr>
</tbody>
</table>

**RESULTS**

Offspring of women with anorexia nervosa were significantly more likely to be preterm (chi square: 3.48, P=<=0.05) and of lower birth weight (t value: 6.4, P=<=0.01) compared to offspring of controls. Offspring of women with a history of anorexia without bulimia had significantly lower body weight than women with anorexia and bulimia. Rates of small for gestational age births were not significantly different between groups. Pregnancy outcomes were not significantly different between women with active versus remitted anorexia nervosa.
<table>
<thead>
<tr>
<th>ID Number</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year published</td>
<td>2009</td>
</tr>
<tr>
<td>Title</td>
<td>Birth outcomes in women with eating disorders in the Norwegian mother and child cohort study (MoBa).</td>
</tr>
<tr>
<td>Volume, pages</td>
<td>42(9), pp. 9-18</td>
</tr>
<tr>
<td>Study Name</td>
<td>Norwegian mother and child cohort study (MoBa)</td>
</tr>
</tbody>
</table>

**STUDY DESIGN**

| Year | 1999-2006 |
| Study Design | Prospective cohort |
| Location | Norway |
| Sample size | n=35929 (AN=35, BN=304) |
| Mean age | AN=26.6, BN=29.8, BED=30.0, EDNOS=28.4, Controls=29.9 |
| Sex | Female |
| Sample type | Community |
| Retained sample/attrition | Of the initial 74,200 mother–child records reported, 35,929 (48%) met criteria for inclusion in the study. From 1999–2006, 42% of invited mothers agreed to participate in the study. |

**MEASUREMENT**

| Exposure variable (& measure) | Data on past or current anorexia nervosa, bulimia nervosa, binge eating disorder and EDNOS was obtained retrospectively at 18 weeks gestation. Questionnaires included items on disordered eating behaviour and were designed in accordance with DSM-IV criteria. |
| Outcome variable | Data on preterm births, defined at less than 37 weeks, birth weight and small for gestational age were obtained from the Medical Birth Registry of Norway (MBRN) after 16 weeks of gestation, through mandatory notification by midwives and doctors. |
| Covariates | Smoking, household income, education, parity, maternal age, maternal pre-pregnancy BMI, gestational weight gain |

**RESULTS**

Birth outcomes were not significantly different between disordered eating and control groups. Risk of preterm births (RR: 0.83; CI: 0.12-5.9), small for gestational age births (RR: 0.87; CI: 0.3-2.5) were comparable between anorexia and control groups. Similarly, individuals with bulimia were not significantly more likely to have a low birth weight (RR: 1.5; CI: 0.85-2.8), preterm (RR: 0.86; CI: 0.47-1.6) or small for gestational age births (RR: 1.1; CI: 0.73-1.6).
### STUDY DESIGN

<table>
<thead>
<tr>
<th>Year</th>
<th>1994-1995</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Design</td>
<td>Case control</td>
</tr>
<tr>
<td>Location</td>
<td>Australia</td>
</tr>
<tr>
<td>Sample size</td>
<td>ED $n=88$ and controls $n=86$</td>
</tr>
<tr>
<td>Mean age</td>
<td>Not reported</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
</tr>
<tr>
<td>Sample type</td>
<td>Community</td>
</tr>
<tr>
<td>Retained sample/attrition</td>
<td>Assessment questionnaires were completed and returned by 76%, 94%, and 87% of the small for gestational age, preterm and control groups, respectively.</td>
</tr>
</tbody>
</table>

### MEASUREMENT

| Exposure variable (& measure) | Data on past anorexia nervosa, bulimia nervosa and EDNOS were obtained retrospectively one-week post partum through semi-structured interviews and self-report using the Eating Disordered Inventory (EDI). Retrospective diagnosis of a clinical eating disorder was determined based on DSM-IV criteria. The presence of maternal “normative” weight and shape concerns were assessed using a modified version of the Eating Disorder Examination (EDE). |
| Outcome variable at each wave | Low birth weight and preterm births were defined at those below 2500g and 37 weeks respectively. Data on low birth weight, preterm and small for gestational age births were obtained from hospital birth registers. |
| Covariates | Maternal smoking, alcohol and caffeine use. |

### RESULTS

Previous disordered eating behaviour did not significantly increase the risk of low birth weight or preterm births. Women delivering small for gestational age births reported elevated eating disorder psychopathology on the EDI and more disturbances in eating behaviour before and during pregnancy. Unique predictors of low birth weight and small for gestational age births were low maternal pre-pregnancy body weight, smoking, low maternal weight gain, and elevated Bulimia scores on the EDI.
**STUDY DESIGN**

<table>
<thead>
<tr>
<th>Year</th>
<th>Data collected from 1965-2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Design</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>Location</td>
<td>Scotland</td>
</tr>
<tr>
<td>Sample size</td>
<td>n=804 (ED=134)</td>
</tr>
<tr>
<td>Mean age</td>
<td>Mean age at first delivery AN=26.8, matched non AN women=26.9, non AN women=24.9</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
</tr>
<tr>
<td>Sample Type</td>
<td>Clinical</td>
</tr>
<tr>
<td>Retained sample/attrition</td>
<td>The original cohort consisted of 597 individuals presenting from 1965 to 2007 inclusive. Of these, 180 were matched as having at least one pregnancy. Four women were omitted due to having twin births and 42 women reported that their first pregnancy predated a diagnosis of AN. The current sample consisted of 134 women and 670 controls, which gave birth to 1144 infants.</td>
</tr>
</tbody>
</table>

**MEASUREMENT**

<table>
<thead>
<tr>
<th>Exposure variable (&amp; measure)</th>
<th>Data on anorexia nervosa was obtained prospectively based on case-register or case-record diagnoses. Anorexia diagnosis was based on significant recorded weight loss at presentation, amenorrhea and or evidence of characteristic psychopathology and no other diagnosis.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome variable at each wave</td>
<td>Low birth weight and preterm births were defined as those less than 2500g and before 37 respectively. Data on birth outcomes were obtained from the Aberdeen Maternity and Neonatal Databank (AMND).</td>
</tr>
<tr>
<td>Covariates</td>
<td>BMI, smoking, social class and marital status.</td>
</tr>
</tbody>
</table>

**RESULTS**

Risk of low birth weight births was significantly increased in mothers with a history of anorexia (unadjusted RR: 1.89, CI: 1.10–3.23; adjusted RR: 1.61, CI: 0.89–2.90). A history of anorexia did not significantly predict risk of preterm births (RR: 1.30, CI: 0.71–2.39). Furthermore, women with a history of anorexia were at a greater risk of intrauterine growth restriction in consequent births (RR: 1.54; CI: 1.11–2.13).
STUDY DESIGN

<table>
<thead>
<tr>
<th>Year</th>
<th>1973 to 1996 who gave birth during 1983 to 2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Design</td>
<td>Prospective cohort</td>
</tr>
<tr>
<td>Location</td>
<td>Sweden</td>
</tr>
<tr>
<td>Sample size</td>
<td>n=828582 (ED=1000)</td>
</tr>
<tr>
<td>Mean age</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
</tr>
<tr>
<td>Sample type</td>
<td>Clinical</td>
</tr>
<tr>
<td>Retained sample/attrition</td>
<td>All women above 10 years of age, who had been discharged with a main diagnosis of anorexia nervosa between 1973-1996 were identified from the Swedish Hospital Discharge Register.</td>
</tr>
</tbody>
</table>

MEASUREMENT

<table>
<thead>
<tr>
<th>Exposure variable (&amp; measure)</th>
<th>Diagnoses were consistent with the International Classification of Diseases ICD-8 and ICD-9.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome variable at each wave</td>
<td>Data on birth weight (grams), gestational age, small for gestational age status (according to birth weight curve) was obtained from the Swedish Medical Birth Register.</td>
</tr>
<tr>
<td>Covariates</td>
<td>Year of birth of child, maternal age and cigarette smoking.</td>
</tr>
</tbody>
</table>

RESULTS

A history of anorexia nervosa was not associated with an increased risk of adverse birth outcomes. Risk preterm births (OR: 0.8; CI: 0.4–1.5), small for gestational age births (OR: 1.0, CI: 0.7–1.4) were not significantly different in women with anorexia compared to controls. Offspring to women with a history of anorexia had a significantly lower mean birth weight (mean 3387g) compared with those born to women in the general population (mean 3431g, P = 0.005) after adjusting for maternal age and year of birth.
STUDY DESIGN

<table>
<thead>
<tr>
<th>Year</th>
<th>1997-2001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Design</td>
<td>Prospective cohort</td>
</tr>
<tr>
<td>Location</td>
<td>Sweden</td>
</tr>
<tr>
<td>Sample size</td>
<td>ED ( n=49 ), controls ( n=68 )</td>
</tr>
<tr>
<td>Mean age</td>
<td>ED=29.3 years, controls=30.0 years</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
</tr>
<tr>
<td>Sample Type</td>
<td>Community</td>
</tr>
<tr>
<td>Retained sample/attrition</td>
<td></td>
</tr>
</tbody>
</table>

MEASUREMENT

<table>
<thead>
<tr>
<th>Exposure variable (&amp; measure)</th>
<th>Past disordered eating including anorexia nervosa, bulimia nervosa and EDNOS, were measured through interviews conducted by trained midwives at prenatal clinics. Women were classified according to DSM-IV criteria.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome variable at each wave (up to 4)</td>
<td>Data on birth weight (grams), preterm birth and intrauterine growth restriction were obtained from medical records.</td>
</tr>
<tr>
<td>Covariates</td>
<td>Maternal Body Mass Index (BMI)</td>
</tr>
</tbody>
</table>

RESULTS

Women with a history of disordered eating delivered offspring with significantly lower birth weight (\( p<0.001 \)) and an increased risk of small for gestational age births (\( p< .05 \)) compared with controls. Risk of preterm births was not significantly different between disordered eating and control groups (\( p<0.33 \)).
Retarded head growth and neurocognitive development in infants of mothers with a history of eating disorders: longitudinal cohort study

STUDY DESIGN

Year | August 1997 to June 2001
Study Design | Longitudinal cohort with nested case control
Location | Sweden
Sample size | ED n=47, controls n=65
Mean age | ED=29.3, controls=30.0
Sex | Female
Sample type | Community
Retained sample/attrition | The initial study population comprised 49 women with a history of disordered eating and 67 controls. No attrition was observed in the control group.

MEASUREMENT

Exposure variable (& measure) | Prior eating disorders (anorexia, bulimia or EDNOS) were initially diagnosed by interview based on DSM-IV diagnostic criteria. Diagnoses were confirmed from medical records when available. The mean duration of eating disorders was 9 years (range 3–15 years) and the duration of recovery before study recruitment was 3.2 years.
Outcome variable at each wave | Data on birth weight, gestational age and small for gestational age births were obtained from medical records at respective child health Centre’s in Stockholm.
Covariates | BMI, child’s sex.

RESULTS

Women with a history of anorexia reported significantly low birth weights (SD: -0.66, CI: -1.25 -0.06) compared to controls. Women with a history of disordered eating were at a significantly increased risk of small for gestational age births. Birth weight in women with a history of bulimia (SD -0.62, CI: -1.24-0.00) was not significantly different from controls. Gestational age and rates of preterm births were similar between groups.
STUDY DESIGN

Year: 1995-2010
Study Design: Prospective longitudinal cohort
Location: Finland
Sample size: $n=7397$ (AN=302, BN=724)
Mean age: AN=29.4, BN=30.4, BED=30.2 and controls=29.1
Sex: Female
Sample type: Clinical
Retained sample/attrition: A register search on pregnancy, obstetric, and perinatal outcomes was conducted on 2257 patients and 9028 unexposed women. All births were included except for multiple births ($n=104$).

MEASUREMENT

Exposure variable (& measure): Data on lifetime eating disorder, bulimia nervosa and binge eating disorder were obtained from hospital records from individuals treated in the eating disorders clinic at the Helsinki University Central Hospital. Diagnoses were based on ICD-10 criteria.
Outcome variable at each wave: Data on low birth weight births (<2500g), very low birth weight (<1500g), preterm births (<37 weeks), very preterm births (<28 weeks) and small for gestational age births were obtained from the Medical Birth Register, which covers all delivery hospitals in Finland.
Covariates: Maternal age, parity, marital status and smoking status.

RESULTS

Women with a history of anorexia were at a significantly increased risk of low birth weight births (OR: 2.16, CI: 1.3-3.58) very preterm (OR: 4.59, CI: 1.25-16.87) and small for gestational age births (OR: 2.20, CI: 1.23-3.93). Women with a history of bulimia nervosa were at an increased, although not statistically significant, risk of low birth weight (OR: 1.37, CI: 0.90-2.07), preterm (OR: 1.28, CI: 0.85-1.91) and small for gestational age births (OR: 1.51, CI: 0.92-2.48).
## STUDY DESIGN

<table>
<thead>
<tr>
<th>Year</th>
<th>1991-1992</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Design</td>
<td>Longitudinal prospective cohort</td>
</tr>
<tr>
<td>Location</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>Sample size</td>
<td>n=12,254 (AN=171, BN=199)</td>
</tr>
<tr>
<td>Mean age</td>
<td>AN=28.9, BN=28.2, AN &amp; BN=29.2, controls=28.2 years</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
</tr>
<tr>
<td>Sample type</td>
<td>Community</td>
</tr>
<tr>
<td>Retained sample/attrition</td>
<td>All pregnant women expecting to deliver their baby between April 1991 and December 1992 were recruited. It is estimated that 85–90% of eligible women took part in the study.</td>
</tr>
</tbody>
</table>

## MEASUREMENT

<table>
<thead>
<tr>
<th>Exposure variable (&amp; measure)</th>
<th>Data on anorexia, bulimia and combined anorexia and bulimia, were obtained at 12 weeks gestation from women by asking whether they had any current or past history of psychiatric problems, including depression, schizophrenia, alcoholism, anorexia nervosa, bulimia nervosa or any other psychiatric disorder. Pre-pregnancy weight and height were also obtained.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome variable at each wave</td>
<td>Data on birth weight (grams adjusted for sex and age) and preterm births (&lt;37 weeks gestation) were obtained from obstetric records.</td>
</tr>
<tr>
<td>Covariates</td>
<td>Recent or past history of psychiatric problems (depression, schizophrenia, alcoholism), alcohol and smoking intake before and during 1st/2nd trimester, parity, maternal age, employment status and relationship status.</td>
</tr>
</tbody>
</table>

## RESULTS

Women with a history of anorexia had offspring with significantly lower mean birth weight (OR: -75.1, CI: -143.6 to -6.5, p=.001) compared to controls. Risks of preterm and small for gestation age births were comparable between disordered eating and control groups. Women reporting other psychiatric disorders were at in increased risk of low birth weight births (OR:-36.4, CI:-64.0 to -8.8).
<table>
<thead>
<tr>
<th>ID Number</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Authors</td>
<td>Micali, N., Stavola, B. D., Dos-Santos-Silva, I., Graaff, J. S., Jansen, P. W., Jaddoe, V. W. V., Hofman, A., Verhulst, F. C., Steegers, E. A. P. and Tiemeier, H.</td>
</tr>
<tr>
<td>Year published</td>
<td>2012</td>
</tr>
<tr>
<td>Title</td>
<td>Perinatal outcomes and gestational weight gain in women with eating disorders: a population-based cohort study.</td>
</tr>
<tr>
<td>Volume, pages</td>
<td>119(12), pp. 1493-1502</td>
</tr>
<tr>
<td>Study Name</td>
<td></td>
</tr>
</tbody>
</table>

**STUDY DESIGN**

| Year | Delivery date between April 2002 and January 2006. |
| Study Design | Prospective cohort |
| Location | Netherlands |
| Sample size | \( n=5256 \) (AN=129, BN=209) |
| Mean age | AN=30.6, BN=30.5, AN and BN=30.8 & controls= 30.4 |
| Sex | Female |
| Sample type | Community |
| Retained sample/attrition | Estimated participation rate was approximately 61% for all live born children and parents living in the area at the time of recruitment. 8880 women were recruited in pregnancy, with 6493 women (74.6%) consenting to postnatal participation. Data were missing for 1176 women (18.1%). The final sample comprised 5256 women and their babies. |

**MEASUREMENT**

| Exposure variable (& measure) | Lifetime anorexia, bulimia and anorexia and bulimia were measured by self-report from a pregnancy questionnaire completed at 20 weeks gestation. |
| Outcome variable at each wave | Data on birth weight (grams), preterm (<37 weeks) and small for gestational age births were obtained prospectively from questionnaires conducted by midwives and hospital registers. |
| Covariates | Depression, anxiety, psychosis, manic episodes, maternal age, education, ethnicity, pregnancy weight, height, smoking and alcohol use. |

**RESULTS**

Risk of low birth weight, preterm and small for gestational age births were comparable for women with a history of disordered eating compared to controls. The mean birth weight of offspring born to underweight mothers with an eating disorder was 3275 g (SD 382.8) compared to healthy weight women with an eating disorder (3488 g, SD=566.0). Results indicated a trend towards lower birth weight births in underweight women after adjusting for gestational age, gender of the baby, maternal age, education, ethnicity and parity (156.6; CI: 354.3-41.0).
**STUDY DESIGN**

<table>
<thead>
<tr>
<th>Year</th>
<th>1973-1993</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Design</td>
<td>Prospective follow up</td>
</tr>
<tr>
<td>Location</td>
<td>Denmark</td>
</tr>
<tr>
<td>Sample size</td>
<td>n=1202 (ED=302)</td>
</tr>
<tr>
<td>Mean age</td>
<td>AN maternal age &lt; 25 n=122 and &gt;25 n=382, control maternal age &lt;25 n=509 and &gt;25 n=1043</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
</tr>
<tr>
<td>Sample type</td>
<td>Clinical</td>
</tr>
<tr>
<td>Retained sample/attrition</td>
<td>2056 singleton deliveries were included in the study. Of which, 302 women were hospitalized with an eating disorder before giving birth to 504 children, and 900 women who were without a previous hospitalization for an eating disorder gave birth to 1552 children.</td>
</tr>
</tbody>
</table>

**MEASUREMENT**

<table>
<thead>
<tr>
<th>Exposure variable ( &amp; measure)</th>
<th>Past disordered eating; anorexia or bulimia nervosa was assessed using ICD-8 diagnostic codes; 306.50 for anorexia nervosa, 306.58 for other specified feeding disturbances, and 306.59 for feeding disturbances unspecified. Diagnostic criteria were based on a Danish adaptation of the Glossary of Mental Disorders. All disordered eating cases had been hospitalized within 8 years prior to conception.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome variable at each wave</td>
<td>Data on birth weight (grams), low birth weight (&lt;2500g), preterm births (&lt;37 weeks) and birth weight for gestational age were obtained from medical birth registers.</td>
</tr>
<tr>
<td>Covariates</td>
<td>Maternal age, parity and marital status, sex of child and smoking status</td>
</tr>
</tbody>
</table>

**RESULTS**

Risk of low birth weight was twice as high in women with a history of an eating disorder compared to controls (OR: 2.2, CI: 1.4-3.2). Risk of preterm and small for gestational age births were 70% and 80% higher, respectively, in women with an eating disorder compared to controls (OR: 1.7, CI: 1.1-2.6; OR: 1.8, CI: 1.3-2.4; OR: 1.8, CI: 1.3-2.4 respectively).
### ID Number 13

**Authors** Waugh, E. and Bulik C. M.

**Year published** 1999

**Title** Offspring of women with eating disorders

**Journal** International Journal of Eating Disorders

**Volume, pages** 25 (20), pp. 123-133.

### STUDY DESIGN

<table>
<thead>
<tr>
<th>Year</th>
<th>May-August 1995</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Design</td>
<td>Case control</td>
</tr>
<tr>
<td>Location</td>
<td>New Zealand</td>
</tr>
<tr>
<td>Sample size</td>
<td>ED ( n = 10 ) and controls ( n = 10 )</td>
</tr>
<tr>
<td>Mean age</td>
<td>ED = 30.1, controls = 30.8</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
</tr>
<tr>
<td>Sample type</td>
<td>Clinical</td>
</tr>
<tr>
<td>Retained sample/attrition</td>
<td></td>
</tr>
</tbody>
</table>

### MEASUREMENT

<table>
<thead>
<tr>
<th>Exposure variable (&amp; measure)</th>
<th>Prior anorexia nervosa and bulimia nervosa was diagnosed using diagnostic interviews for genetic studies and structured clinical interview based on DSM-III-R criteria. Drive for Thinness, Bulimia and Body Dissatisfaction scales from the Eating Disorders Inventory, were also completed.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome variable at each wave</td>
<td>Data on birth weight (grams) and gestational age (&lt;39 weeks) were obtained by maternal self-report and maternal health nurse reports.</td>
</tr>
<tr>
<td>Covariates</td>
<td>Smoking and alcohol</td>
</tr>
</tbody>
</table>

### RESULTS

Offspring to women with a history of disordered eating were significantly lighter in weight (13%, 523.5g) compared to controls. Rates preterm births were comparable between disordered eating and control groups with all children born between 39-42 weeks. No differences were observed in birth weight of infants, born to mothers with an active eating disorder, to those who were not symptomatic during pregnancy.
<table>
<thead>
<tr>
<th>STUDY DESIGN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Year</strong></td>
</tr>
<tr>
<td><strong>Study Design</strong></td>
</tr>
<tr>
<td><strong>Location</strong></td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
</tr>
<tr>
<td><strong>Mean age</strong></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
</tr>
<tr>
<td><strong>Sample type</strong></td>
</tr>
<tr>
<td><strong>Retained sample/attrition</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MEASUREMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exposure variable (&amp; measure)</strong></td>
</tr>
<tr>
<td><strong>Outcome variable at each wave</strong></td>
</tr>
<tr>
<td><strong>Covariates</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Offspring mean birth weight was significantly lower for women with past anorexia (3,347.9 gram; median: 3,400; SD: 548.4, range: 1,925–4,500, p=0.03) compared to controls (3,553.8 gram; median: 3,650; SD: 600.7; range: 1,900–4,760). Risk of preterm births was comparable between groups. None of the women in the anorexia group reported experiencing a preterm birth, although two preterm births were reported in women included in the control group.</td>
</tr>
</tbody>
</table>
Appendix D: Results from post hoc logistic regression analyses including the whole sample of 188 participants

Analyses conducted in the second study in Chapter seven of this thesis, which examined the effects of preconception disordered eating on adverse birth outcomes, were re-run post hoc to adjust for maternal birth outcomes based on findings obtained in the third study revealing significant correlations between maternal and infant birth outcomes. Post hoc analyses of multivariate outliers, based on Cook’s Distance values, revealed two potential multivariate outliers for models regressing adolescent disordered eating adjusting for maternal low birth weight, preterm and small for gestational age births and one outlier in models adjusting for maternal birth weight and gestational age. Overall, two cases were identified as being multivariate outliers. Of the two outliers, one case represented a participant who reported having a small for gestational age birth and the other case, a participant who reported having an infant of normal birth weight. The participant, who had a small for gestational age birth, indicated that they were not born small for gestational or low birth weight and were not classified as being ‘At Risk’ of an eating disorder. In contrast, the participant who had a normal weight infant reported being born small for gestational age and low birth weight and was classified as being ‘At Risk’ of an eating disorder. Both women reported having a BMI of 17 in adolescence.

Review of the overall accuracy of each model, after removal of identified outliers, revealed that the percentage of small for gestational age cases correctly classified had increased, although not significantly as did the amount of overall variance explained by each model. Removal of these cases resulted in a change in the statistical significance of predictor variables included in the model, although only small differences in the size of effects, indicating that the overall precision in estimating these effects had improved. For models where more than one outlier was identified, each case was excluded separately to enable further investigation of the influence of each case on the overall data. Analyses were rerun (n=187) with and without each of these cases to assess the individual impact of each case. The overall variance explained by the model, when these cases were removed, was observed to increase slightly (n=188). Both cases appeared to exert similar influence on the overall results.
Given that identified outliers were observed to exert undue influence on the overall data, as evidenced by changes in the statistical significance of effects and consequent interpretation of results, it was deemed appropriate to exclude these cases from final analyses. Results from post hoc logistic regression analyses reported in Chapter nine of this thesis are based on a total sample of \( n=186 \). Results from post hoc logistic regression analyses, which included the whole sample of 188 participants, are presented in Table D.1 and Table D.2 below.

Post hoc logistic regression analyses, which utilised the total sample of \( n=188 \), revealed that Drive for Thinness scores no longer significantly predicted risk of G3 small for gestational age births when adjusting for G2 maternal low birth weight (OR: 1.079, CI: .999-1.165, \( p=.053 \)). It should be noted that although not statistically significant at \( p=.05 \), this finding was verging on significance. When adjusting for only G2 maternal overall birth weight (kgs) and gestational age (weeks), Drive for Thinness scores remained a significant predictor of G3 small for gestational age births (OR: 1.090, CI: 1.010-1.177). Furthermore, disordered eating ‘Risk’ in adolescence was not a significant predictor of G3 small for gestational age births (OR: 2.494, CI: .789-7.889; OR: 2.881, CI: .934-8.893) when adjusting for G2 maternal birth outcomes.

G2 maternal low birth weight births, was found to significantly predict risk of G3 small for gestational age births (OR: 12.0, CI: 1.242-115.904; OR: 9.992, CI: 1.130-88.355). Results indicated that G2 women born with low birth weight were approximately 9 to 12 times more likely to have a G3 small for gestational age birth. Continues measures of G2 maternal birth weight was also found to significantly predict risk of small for gestational age births (OR: .250, CI: .074-.847; OR: .247, CI: .074-.827). These findings suggest that as G2 maternal birth weight increases, the risk of small for gestational age births in subsequent infants decreases. None of the other predictor variables (G2 preterm births, G2 gestational age, maternal age, BMI or depressive symptoms) contributed to a significant portion of risk of G3 small for gestational age births.
Table. D.1 Logistic regression analyses assessing Drive for Thinness and disordered eating ‘Risk’ on infant small for gestational age births adjusting for maternal low birth weight, preterm and small for gestational age births

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio (CI)</th>
<th>B</th>
<th>Sig</th>
<th>Odds Ratio (CI)</th>
<th>B</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drive for Thinness</td>
<td>1.079 (0.999-1.165)</td>
<td>0.076</td>
<td>0.053</td>
<td>ED Risk</td>
<td>2.494 (1.789-7.889)</td>
<td>0.914</td>
</tr>
<tr>
<td>Maternal Age</td>
<td>.695 (.453-1.064)</td>
<td>-0.364</td>
<td>0.094</td>
<td>Maternal Age</td>
<td>.677 (.447-1.025)</td>
<td>-0.390</td>
</tr>
<tr>
<td>Depression</td>
<td>.905 (.765-1.071)</td>
<td>-0.100</td>
<td>0.244</td>
<td>Depression</td>
<td>.909 (.772-1.071)</td>
<td>-0.095</td>
</tr>
<tr>
<td>BMI</td>
<td>.899 (.725-1.115)</td>
<td>-0.106</td>
<td>0.335</td>
<td>G2 LBW</td>
<td>9.992 (1.130-88.355)</td>
<td>2.302</td>
</tr>
<tr>
<td>G2 LBW</td>
<td>12.0 (1.242-115.904)</td>
<td>2.485</td>
<td>0.032*</td>
<td>G2 Preterm birth</td>
<td>2.620 (.370-18.563)</td>
<td>0.961</td>
</tr>
<tr>
<td>G2 Preterm birth</td>
<td>2.42 (.320-18.300)</td>
<td>0.884</td>
<td>0.392</td>
<td>G2 SGA</td>
<td>2.228 (.448-11.082)</td>
<td>0.801</td>
</tr>
<tr>
<td>G2 SGA</td>
<td>2.016 (395-10.302)</td>
<td>0.701</td>
<td>0.400</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Sig at p< .05

Table. D.2 Logistic regression analyses regressing Drive for Thinness and disordered eating ‘Risk’ on infant small for gestational age births adjusting for maternal birth weight and gestational age

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio (CI)</th>
<th>B</th>
<th>Sig</th>
<th>Odds Ratio (CI)</th>
<th>B</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drive for Thinness</td>
<td>1.090 (1.010-1.177)</td>
<td>0.086</td>
<td>0.027*</td>
<td>ED Risk</td>
<td>2.881 (1.934-8.893)</td>
<td>1.058</td>
</tr>
<tr>
<td>Maternal Age</td>
<td>.691 (.455-1.049)</td>
<td>-0.37</td>
<td>0.083</td>
<td>Maternal Age</td>
<td>.678 (.453-1.014)</td>
<td>-0.389</td>
</tr>
<tr>
<td>Depression</td>
<td>.909 (.771-1.073)</td>
<td>-0.095</td>
<td>0.26</td>
<td>Depression</td>
<td>.912 (.777-1.070)</td>
<td>-0.092</td>
</tr>
<tr>
<td>BMI</td>
<td>.891 (.719-1.103)</td>
<td>-0.116</td>
<td>0.29</td>
<td>G2 birth weight</td>
<td>.247 (.074-827)</td>
<td>-1.397</td>
</tr>
<tr>
<td>G2 birth weight</td>
<td>.250 (.074-847)</td>
<td>-1.388</td>
<td>.026*</td>
<td>G2 Gestational age</td>
<td>.927 (.710-1.210)</td>
<td>-0.076</td>
</tr>
<tr>
<td>G2 Gestational age</td>
<td>.911 (692-1.201)</td>
<td>-0.093</td>
<td>0.51</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Sig at p< .05

Note: G2 birth weight and gestational age were regressed separately from G2 low birth weight, preterm and small for gestational age births as these outcomes are derived from data on birth weight and gestational age.
Appendix E: Frequencies of low birth weight, preterm and small for gestational age births amongst mothers and infants born low birth weight, preterm or small for gestational age.

In the current sample, 11 G3 infants were born low birth weight, of which five were preterm and seven were small for gestational age. Ten G3 infants were born preterm, with five of these also being low birth weight and one small for gestational age. 19 G3 infants were born small for gestational age. Of those, seven were low birth weight and one was preterm. Seven G2 mothers were born low birth weight, of those four were preterm and three were small for gestational age. Ten G2 mothers were born premature, with four of these women also born with low birth weight. 18 G2 mothers were born small for gestational age, of which, three were born with low birth weight and none preterm. Subtypes of low birth weight, preterm and small for gestational age births in G2 mothers and G3 infants are presented in Table E.1 and Table E.2.

Two small for gestational age mothers who were also born low birth weight had a small for gestational age infant, which was also born with low birth weight. This accounted for half of the small for gestational age births to mothers born small for gestational age. None of the G2 small for gestational age mothers were born preterm. The remaining G2 small for gestational age births (n=15) represented mothers who were born small, although normal weight for gestational age. Frequencies of low birth weight and preterm subtypes of small for gestational age births, in mothers and infants, are presented in Table E.3.

Table E.1. Subtypes of maternal (G2) low birth weight, preterm and small for gestational age births

<table>
<thead>
<tr>
<th>G2 Low birth weight</th>
<th>G2 Preterm births</th>
<th>G2 SGA</th>
</tr>
</thead>
<tbody>
<tr>
<td>G2 Low birth weight</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>G2 Preterm births</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>G2 SGA</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>
Table E.2. Subtypes of infant (G3) low birth weight, preterm and small for gestational age births

<table>
<thead>
<tr>
<th>Subtype</th>
<th>G3 Low birth weight</th>
<th>G3 Preterm births</th>
<th>G3 SGA</th>
</tr>
</thead>
<tbody>
<tr>
<td>G3 Low birth weight</td>
<td>11</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>G3 Preterm births</td>
<td>5</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>G3 SGA</td>
<td>7</td>
<td>1</td>
<td>19</td>
</tr>
</tbody>
</table>

Table E.3. Frequencies of low birth weight and preterm births among subtypes of low birth weight and preterm types of small for gestational age births

<table>
<thead>
<tr>
<th>Subtype</th>
<th>G3 Low birth weight (n=11)</th>
<th>G3 Preterm births (n=10)</th>
<th>G3 SGA (n=19)</th>
<th>G3 Low birth weight SGA (n=7)</th>
<th>G3 Preterm birth SGA (n=1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G2 LBW (n=7)</td>
<td>3</td>
<td>0</td>
<td>5</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>G2 Preterm births (n=10)</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>G2 SGA (n=18)</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>G2 Low birth weight SGA (n=3)</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>G2 Preterm SGA (n=0)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>