

**Mothers with Recurrent Depression:
Co-occurring Psychopathology and Parenting as
Risks for Offspring Psychopathology**

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2012

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Declaration and statements

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Summary

Offspring of depressed mothers are at increased risk of developing a variety of psychopathologies. Risk factors and mechanisms for the development of these heterogeneous outcomes are poorly understood. Disruptions in the mother-child relationship may be one mechanism by which maternal depression increases risk for offspring psychopathology. Many adults with depression present with co-occurring psychopathology, but how these co-occurring problems affect offspring risk, or impact upon the mother-child relationship, has rarely been considered.

Data were from the Early Prediction of Adolescent Depression study. Mothers with a history of recurrent major depressive disorder and their adolescent offspring were assessed three times between 2007 and 2011. Mothers completed questionnaires assessing their own depression severity and co-occurring psychopathology (anxiety, antisocial behaviour (ASB), and alcohol misuse). Offspring psychopathology (presence of psychiatric disorder, symptoms of depression, anxiety and disruptive behaviour disorder (DBD)) were assessed using the Child and Adolescent Psychiatric Assessment. The mother-child relationship was assessed using parent-rated questionnaires and an interviewer-rated speech sample.

Co-occurring problems in mothers predicted *new-onset* psychiatric disorder in offspring; this remained significant after controlling for maternal depression severity. When investigating the specificity of risk for offspring, maternal co-occurring ASB was specifically associated with offspring DBD, whereas maternal depression severity predicted offspring depression. The mother-child relationship mediated the effect of maternal depression severity on risk for offspring psychopathology. However this was better accounted for by co-occurring maternal ASB, which predicted both maternal warmth and hostility. Maternal

hostility was a specific risk factor for offspring DBD. Bidirectional effects were observed between offspring DBD and maternal hostility.

Findings highlight the importance of assessing co-occurring psychopathology in mothers with recurrent depression when considering risk for offspring. Parenting interventions that reduce hostility may be beneficial for preventing or reducing adolescent DBD, particularly when depressed mothers report additional ASB. Furthermore, interventions that reduce offspring DBD may also show benefits for the mother-child relationship.

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Chapter 1. Introduction

This thesis examines risk factors and mechanisms for psychopathology in high-risk offspring of parents with recurrent depression. It focuses on co-occurring psychopathology in mothers with recurrent depression, and family relationships as risk factors for offspring psychopathology. This chapter will first discuss the epidemiology of child and adolescent mental health problems, demonstrating why it is important to examine risk factors for the development of psychopathology in adolescents. This will be followed by a discussion of maternal depression and the impact on offspring. This chapter will then consider co-occurring psychopathology in adults with recurrent depression, and examine whether additional psychopathology in parents with depression is associated with increased risk for offspring. Mechanisms for the intergenerational transmission of risk for psychopathology will be discussed, briefly discussing genetic transmission, before considering environmental transmission, focusing on parenting. The role of the parent-child relationship, and the impact this has on risk for offspring psychopathology will be discussed. Following this I will discuss research which investigates the association between family relationships and offspring psychopathology. I will summarise findings and challenges and how they may be overcome. Lastly, I will outline the aims of the current study, and consider how the study design is able to address the aims.

1. Child and adolescent mental health problems

Adolescent mental health problems are common. Table 1.1 shows a summary of recent studies of rates of psychopathology in adolescents from the general population. Estimates of the prevalence of psychopathology vary as studies use different age ranges for their definition of adolescence, different time periods to assess prevalence of disorder, as well

Table 1.1: Recent key studies identifying rates of psychopathology in general population samples of adolescents

Study	Sample size	Child age (years)	Method of assessment/ taxonomy	Country	Time period	Rate of psychiatric diagnosis
(Fergusson & Horwood, 2001)	1000	15	CIDI DSM-III-R	New Zealand	12 months	22.0%
(Romano, Tremblay, Vitaro, Zoccolillo, & Pagani, 2001)	2000	14-17	DISC DSM-III-R	Canada	6 months	20.1%
(Costello, Mustillo, Erkanli, Keeler, & Angold, 2003)	1420	Three cohorts aged 9, 11, 13 Followed up until aged 16	CAPA DSM-IV	United States	3 months	22.8%
					Course of study	37.7%
(Green, McGinnity, Meltzer, Ford, & Goodman, 2005)	4051	11-16	DAWBA DSM-IV	United Kingdom	1 month	11.5%
(Lynch, Mills, Daly, & Fitzpatrick, 2006)	723	12-15	K-SADS DSM-IV	Ireland	1 month	15.6%
(Kessler et al., 2012)	10,148	13-17	CIDI and K-SADS DSM-IV	United States	1 month	23.4%
					12 months	40.3%

Abbreviations: CIDI, Composite International Diagnostic Interview; DISC, Diagnostic Interview Schedule for Children; CAPA, Child and Adolescent Psychiatric Assessment; DAWBA, Development and Well-being Assessment; K-SADS, Kiddie Schedule for Affective Disorders and Schizophrenia.

as using different assessments, and taxonomies. Evidence suggests that there is a modest increase in all psychiatric disorders from childhood to adolescence.

A recent review suggested that approximately 1 in 5 adolescents had a psychiatric disorder (Costello, Copeland, & Angold, 2011) with the most commonly reported disorders in adolescence being behaviour disorders, anxiety disorders, and depression (Costello et al., 2011; Kessler et al., 2011; Rutter, 2007b), with UK prevalence estimates of 7.0%, 4.4%, and 1.3% respectively (Green, McGinnity, Meltzer, Ford, & Goodman, 2004). Rates of depression increase sharply in adolescence (Costello et al., 2011), and are estimated to be two times greater in female than male adolescents (Essau, Conradt, & Petermann, 2000; Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993). Antisocial behaviours also increase (Rutter, 2007b), with males being more likely to be aggressive and antisocial than female adolescents (Lewinsohn et al., 1993; Maughan, Rowe, Messer, Goodman, & Meltzer, 2004; McDermott, 1996).

Associated impairment and prognosis

The presence of a psychiatric disorder in adolescence is associated with a range of negative outcomes including poor academic performance, substance misuse, impaired social functioning, and suicide risk (Combs-Ronto, Olson, Lunkenheimer, & Sameroff, 2009; Costello et al., 2011; Costello et al., 2003). Adolescent psychiatric disorder is also a strong predictor of later psychopathology and future psychosocial impairment (Costello et al., 2003; Kim-Cohen et al., 2003). A follow-back of a prospective longitudinal study found that of those adults with a psychiatric disorder, three-quarters had received a diagnosis before the age of 18 years, and half before the age of 15 years (Kim-Cohen et al., 2003). Many had a history of conduct disorder and/or oppositional defiant disorder, which may be particular risk factors for future psychiatric disorders (McGee et al., 2011). Depression in adolescence is

also a risk factor for future psychiatric disorder, with 40-70% of adolescents experiencing recurrence within 5 years (Rutter, Kim-Cohen, & Maughan, 2006). Moreover, both depression, and antisocial behaviours can show persistence into adulthood (Costello et al., 2003).

Child comorbidity

The term ‘comorbidity’ refers to the co-occurrence, either concurrently or over time (‘sequential’ or ‘successive’) of two distinct disorders within one individual (Rutter, 1997). Comorbidity can be homotypic (a phenomenon that changes little over time) or heterotypic (a process with different manifestations across time) (Angold, Costello, & Erkanli, 1999). Epidemiological studies have demonstrated that comorbidity in adolescents is common, exceeding chance expectations (Caron & Rutter, 1991), with depression being almost as strongly related to disruptive behaviours (conduct disorder/oppositional defiant disorder) as it is to anxiety (Angold et al., 1999). Although this co-occurring psychopathology in children and adolescents is considered to be the rule rather than the exception (Angold et al., 1999; Avenevoli, Stolar, Li, Dierker, & Merikangas, 2001), it is rarely taken into consideration. Any associations found between putative risk factors and a specific child outcome could be due to co-occurring symptoms in the offspring. Inconsistencies between studies could be due to different patterns of comorbidity in different samples. In addition, assessing co-occurring psychopathology may help to elucidate mechanisms for one or both disorders; conditions may differ in terms of origin, correlates or causes depending on whether the condition is comorbid or occurs in isolation. Although not a central focus of the current thesis, the co-occurrence of psychopathology in offspring is common and will be taken into account. There are several theoretical explanations for the presence of comorbid psychopathology (Angold et al., 1999; Rutter, 1997) and these are outlined below:

- (i) **It may be a different manifestation of the same disorder:** Anxiety and depression frequently co-occur and it has been hypothesised that they may be manifestations of the same disorder. If comorbid disorders are episodic in nature it is possible to determine whether the remission and recurrence of one disorder is associated in time with the other. Also, treatment that is specific to the one disorder may lead to loss of symptoms in the other. Research suggests that, for the development of DSM-V, mood and anxiety disorders should be collapsed into an overarching class of emotional disorders, with subcategories for distress disorders (major depression, dysthymic disorder, generalized anxiety disorder, posttraumatic stress disorder), and fear disorders (panic disorder, agoraphobia, social phobia, specific phobia) (Watson, 2005).
- (ii) **There may be two stages of the same disorder:** This is a variant of the first explanation and suggests that there may be a single disease process which is an age-dependent expression of the same disorder. For example, there is evidence that anxiety and depression may be manifestations of the same underlying disorder (Merikangas et al., 1998; Merikangas, Risch, & Weissman, 1994), as anxiety disorders typically begin in childhood and tend to precede depressive disorders (Avenevoli et al., 2001; Kessler, Chiu, Demler, & Walters, 2005; Weissman et al., 2005). Longitudinal studies have also identified continuities from childhood conduct problems to adult antisocial personality disorder (Fergusson & Horwood, 1995; Fergusson, Lynskey, & Horwood, 1996; Rutter, 1997). Oppositional defiant disorder typically precedes conduct disorder and may be an earlier stage of the same disorder (Angold et al., 1999; Rutter, 1997).

- (iii) **It may arise from the same or correlated risk factors:** The aetiologies of many disorders are multi-factorial, and causal factors may not be diagnosis-specific. Therefore two disorders may share certain risk factors. For example, family adversity, child abuse/neglect, and parent psychopathology are all associated with a range of problems including conduct problems and depressive disorders (Angold et al., 1999; Rutter, 1997).
- (iv) **The comorbid conditions are distinct:** Comorbidity represents the co-occurrence of two meaningful and distinct conditions, for example, it has been hypothesised that depressive disorders that co-occur with conduct disorders are distinct from depressive disorders that occur without co-occurring problems; individuals may have a lower risk of depression recurrence and bipolar disorder, but a higher risk of personality disorder and criminality (Harrington, Rutter, & Fombonne, 1996; Rutter, 1997).
- (v) **One condition may predispose individuals to another condition:** For example, the development of adolescent conduct problems has been found to predispose adolescents to risk for future psychopathology (Kim-Cohen et al., 2003), including depression (Fergusson et al., 1996; Mason et al., 2004). However, this may be due, in part, to conduct problems generating stressful life events (Champion, Goodall, & Rutter, 1995) which, in turn predict future depression (Pine, Cohen, Johnson, & Brook, 2002). Depressive disorders have also been identified as a risk factor for future alcohol misuse (Dixit & Crum, 2000). Depression in adolescence also predicts a range of disorders in adult life including anxiety, substance misuse and bipolar disorders, as well as suicidal behaviour and depressive disorders in adulthood (Costello et al., 2011; Costello et al., 2003). Therefore risk factors and pathways that predispose adolescents to one disorder

are associated with risk factors and pathways that predispose adolescents to another disorder. If one disorder precedes the other, it offers a potential way in for intervention and prevention strategies.

Importance of identifying and understanding risk for psychopathology

Given evidence that the prevalence of psychopathology increases across the course of adolescence, and that it has associated concurrent and future impairments, it is important to study this developmental period to better understand the development of psychopathology. Risk factors may be temporally different in adolescence compared to other developmental periods (Copeland, Shanahan, Costello, & Angold, 2009). Additionally, many adolescent are not being identified as needing services (Ford, Goodman, & Meltzer, 2003), even in groups at high-risk of developing psychopathology (Potter et al., 2012). There is an unmet need and it is therefore important to identify high-risk groups to target for early intervention and prevention strategies. Moreover, it is also necessary to identify mechanisms for the development of psychopathology in order to inform intervention strategies.

2. Maternal Depression as a risk factor for child and adolescent psychopathology

The current thesis focuses on maternal depression, one of the most well established risk factors for offspring psychopathology (Beardslee, Versage, & Gladstone, 1998; Hammen & Brennan, 2003; Wickramaratne & Weissman, 1998). Symptoms of DSM-IV (American Psychological Association, 1994) defined depression are summarised in Table 1.2. For a diagnosis of major depressive disorder, patients must have at least one core symptom plus additional symptoms for a total of 5 or more symptoms. These symptoms must persist for at least 2 weeks and cause clinically significant distress or impairment.

Adult depression is a common psychiatric disorder with prevalence estimates that range from 6% to 17% (Blazer, Kessler, McGonagle, & Swartz, 1994). It is more common in

women than men, with a gender ratio of around 2:1 from adolescence onwards (Kessler, 2003). Risk of depression is highest in women of child-bearing age, with point prevalence rates ranging from 8% to 12% (Lovejoy, Graczyk, O'Hare, & Neuman, 2000; Weissman & Olfson, 1995). Additionally, depression is often recurrent, causing the largest amount of non-fatal burden in the world (Üstün, Ayuso-Mateos, Chatterji, Mathers, & Murray, 2004). Therefore a large number of children are exposed to maternal depression.

Table 1.2: DSM-IV symptoms of major depressive disorder

Core symptoms	<ul style="list-style-type: none"> • Depressed mood most of the day, nearly every day • Loss of interest or pleasure in almost all activities nearly every day
Additional symptoms	<ul style="list-style-type: none"> • Fatigue or loss of energy nearly every day • Feelings of worthlessness or excessive guilt nearly every day • Recurrent thoughts of death, recurrent suicidal ideation, suicide attempt or a specific plan for committing suicide • Diminished ability to think or concentrate, or indecisiveness nearly every day • Psychomotor agitation or retardation nearly every day • Insomnia or hypersomnia nearly every day • Weight loss or weight gain, or decrease or increase in appetite nearly every day

Offspring of depressed parents are at increased risk of developing a psychiatric disorder compared to offspring of non-depressed parents (Beardslee et al., 1988; Goodman et al., 2011; Orvaschel, Walsh-Allis, & Ye, 1988; Weissman et al., 1984), including depression, anxiety and disruptive behaviour disorders (Halligan, Murray, Martins, & Cooper, 2007; Lee & Gotlib, 1989; Olino et al., 2008; Radke-Yarrow, Nottelmann, Martinez, Fox, & Belmont, 1992; Wickramaratne & Weissman, 1998). Community samples also highlight that depression in parents increases risk of offspring internalising problems such as depression and anxiety (Klein, Lewinsohn, Seeley, & Rohde, 2001; Lieb, Isensee, Höfler, Pfister, & Wittchen, 2002) and externalising problems and substance misuse (Lieb, Isensee, Höfler, Pfister, et al., 2002; Luoma et al., 2001). These key studies are summarised in Table 1.3.

However, there is substantial heterogeneity in response to maternal depression with not all children going on to develop psychopathology (Brennan, Le Brocque, & Hammen, 2003). It is necessary to understand which children are at greatest risk of developing psychopathology for the effective targeting of intervention strategies. Furthermore, offspring of depressed parents are at increased risk of developing a range of disorders, as summarised in Table 1.3 (Kim-Cohen, Moffitt, Taylor, Pawlby, & Caspi, 2005; Lieb et al., 2000; Radke-Yarrow et al., 1992; Weissman, Warner, Wickramaratne, Moreau, & Olfson, 1997; Wickramaratne & Weissman, 1998). It is important to understand the mechanisms through which maternal depression impacts on offspring adjustment (Rutter, 1990) and to understand risk factors for the development of different psychiatric disorders in offspring. Different disorders are likely to require different interventions. At present the reasons for these heterogeneous outcomes are unclear.

Most studies have assessed risk of psychopathology in offspring of depressed parents compared to non-depressed parents (see Table 1.3). Different designs are needed to test the variation of risk within a high-risk group, and few studies have sufficient power to test this

inter-generational transmission of risk (Brennan et al., 2000; Fendrich, Warner, & Weissman, 1990; Hammen & Brennan, 2003; Weissman, Pilowsky, et al., 2006; Weissman et al., 1997).

Table 1.3: Key studies demonstrating parent depression as a risk factor for offspring psychopathology

Study	Study name and/or Description	Sample size	Age range of child at baseline	Follow-up periods	Measure of child outcome	Measure of parent depression	Risk for offspring
Clinical Studies							
(Halligan et al., 2007)	Prospective longitudinal study of children who were or were not exposed to postnatal depression (PND)	94 offspring and their mothers	2 months	Child age 18-months, 5 years, 8 years, 13 years	K-SADS	SCID	Maternal PND associated with increased risk for offspring psychiatric disorder. Maternal PND increased risk for offspring depression only if later episodes of maternal depression
(Weissman, Wickramaratne, et al., 2006)	Longitudinal study of offspring at high and low risk for depression due to parent depression status (1 or more, or neither parent depressed)	220 offspring	6-23 years	Offspring age 35 years	SADS-L	SADS-L	Maternal depression associated with increased risk of offspring anxiety, depression, and substance dependence. Rates of disorder were three times higher in offspring of depressed compared to offspring of non-depressed mothers
(Wickramaratne & Weissman, 1998)	Longitudinal study of offspring at high and low risk for depression due to parent depression status (1 or more, or neither parent depressed)	182 offspring from 91 families	6-23 years	2 years and 10 years after initial assessment	SADS-L	SADS-L	Parent depression associated with increased risk of offspring depression (eight-fold), anxiety (three-fold), and conduct (five-fold) compared to offspring of non-depressed parents

Study	Study name and/or Description	Sample size	Age range of child at baseline	Follow-up periods	Measure of child outcome	Measure of parent depression	Risk for offspring
(Radke-Yarrow et al., 1992)	Three groups of mothers were recruited: (i) bipolar illness (ii) unipolar depression (iii), and non-depressed controls.	100 mothers and their offspring (pairs of siblings)	Younger aged 1 ½ -3 ½; Older 5-8 years	3 years after initial assessment	CAS, CBCL	SADS-L	Offspring of mothers with unipolar depression were more likely to have behaviour problems.
(Anderson & Hammen, 1993)	Offspring of unipolar, bipolar, medically ill, and non-depressed mothers	96 offspring and their mothers	8-16 years	6-month intervals for 3 years	K-SADS	SADS-L	Rates of depression were 45% in children of mothers with unipolar depression compared to 11% in non-ill mothers.
(Hammen, Burge, Burney, & Adrian, 1990)	Offspring of unipolar, bipolar, medically ill, and non-depressed mothers	96 offspring and their mothers	8-16 years	6-month intervals for 3 years	K-SADS	SADS-L	Offspring of mothers with unipolar depression had the highest rates of disorder.
(Lee & Gotlib, 1989)	Offspring of (i) clinically depressed psychiatric patients, (ii) non-depressed psychiatric patients, (iii) non-depressed medical patients, (iv) non-depressed non patients	71 mothers and their offspring	7-13 years	6-8 weeks later	CAS, CBCL	HRSD, BDI, SADS	Children of depressed mothers developed significantly more internalising symptoms than offspring of mothers with medical problems, or offspring of non-medical mothers. There was a trend for an association between mother depression and offspring externalising problems.

Study	Study name and/or Description	Sample size	Age range of child at baseline	Follow-up periods	Measure of child outcome	Measure of parent depression	Risk for offspring
(Beardslee et al., 1988)	Children of parents with serious affective disorders	153 offspring in 81 families	6-19 years	4 years after initial assessment	Diagnostic Interview of Children and Adolescents	SADS-L	There was an increased risk of psychopathology in offspring of parents with an affective psychiatric disorder (63%) compared to offspring of parents with a non-affective illness (53%) or parents with no disorder (35%).
(Orvaschel et al., 1988)	Offspring of parents with recurrent depression and non-depressed parents	107 offspring	6-17 years	-	K-SADS	SADS-L	41% of high-risk children met criteria for at least 1 disorder, compared with 15% of low-risk children.
(Weissman et al., 1984)	Pilot family study of offspring at high and low risk for depression due to parent depression status	194 offspring	6-18 years	-	Screening instrument unspecified in paper	SADS-L	Parent depression was associated with a three-fold increased risk of offspring DSM-III psychiatric disorder
Community studies							
(Korhonen, Luoma, Salmelin, & Tamminen, 2012)	Population sample of 327 mothers and their offspring	191 mother-child pairs	birth	Child aged 16-17 years	CBCL; YSR	EPDS	Maternal depression at child aged 16-17 years associated with adolescent behavioural and emotional problems

Study	Study name and/or Description	Sample size	Age range of child at baseline	Follow-up periods	Measure of child outcome	Measure of parent depression	Risk for offspring
(Pawlby, Hay, Sharp, Waters, & O'Keane, 2009)	Community sample of antenatal patients and their offspring	151 mother-child pairs	Birth	Child aged 4, 11, and 16 years	CAPA	SADS-L	14% of adolescents were diagnosed with a depressive disorder at 16 years. Every depressed adolescent had been exposed to maternal depression
(Hay, Pawlby, Waters, & Sharp, 2008)	Community sample of antenatal patients and their offspring	121 mother-child pairs	Birth	Child aged 11, 16 years	CAPA	CIS; SADS-L	Internalising disorder and disruptive behaviour disorders in adolescence were predicted by the extent of exposure to maternal depression.
(Klein, Lewinsohn, Rohde, Seeley, & Olino, 2005)	Oregon Adolescent Depression Project (OADP). A Large community sample of parents and their offspring.	775 adolescents	14-18 years	1 year after initial assessment; and at child age 24 years	T1: K-SADS T2 and T3:LIFE	SCID-NP	Maternal depression was associated with an increased risk for child depression (62% vs 46%) and anxiety (25% vs 19%).
(Brennan, Hammen, Katz, & Le Brocque, 2002)	Community sample of families from a larger birth cohort, the Mater University of Queensland Study of Pregnancy (MUSP)	522 families	Birth	Child aged 6 months, 5 years, 15 years	K-SADS	SCID	Parent depression was associated with offspring externalising disorder and depressive disorders.

Study	Study name and/or Description	Sample size	Age range of child at baseline	Follow-up periods	Measure of child outcome	Measure of parent depression	Risk for offspring
(Lieb, Isensee, Höfler, Pfister, et al., 2002)	Early Development Stages of Psychopathology Study (EDSP), a prospective longitudinal study	2427 offspring and both parents	14-24 years	20 months and 42 months after initial assessment	M-CIDI	M-CIDI	Parent depression was associated with an increased risk for offspring depression, substance misuse, anxiety
(Luoma et al., 2001)	Prospective longitudinal study	147 mother-child pairs	Birth	Child aged 8-9 years	CBCL symptoms	EPDS	There was a lack of association between maternal depression symptoms and offspring internalising symptoms. There was an association between maternal depression and offspring externalising problems.

Abbreviations: BDI, Beck Depression Inventory; CAPA, Child and Adolescent Psychiatric Assessment; CAS, Child Assessment Interview; CBCL, Child Behaviour Checklist; CES-D, Centre for Epidemiological Studies depression Scale; CIS, Clinical Interview Schedule; DIS, Diagnostic Interview Schedule; EPDS, Edinburgh Postnatal Depression scale; HRSD, Hamilton Rating Scale for Depression; K-SADS, Kiddie Schedule for Affective Disorders and Schizophrenia; LIFE, Longitudinal Interval Follow-up Evaluation; M-CIDI, Munich Composite International Diagnostic Interview; SADS (-L), Schedule for Affective Disorders and Schizophrenia (-Lifetime version); SCID(-NP), Structured Clinical Interview for DSM-IV Axis I disorders (non-patient version); YSR, Youth Self Report.

Variation in risk among offspring of mothers with depression

Depression is highly heterogeneous, with mothers varying considerably in their experience of depression, and this likely affects risk for offspring psychopathology.

Features such as depression age of onset, severity and chronicity, timing, and remission have been found to explain some of the variation in risk for offspring (Brennan et al., 2000; Hammen & Brennan, 2003; Warner, Mufson, & Weissman, 1995).

Age of onset: An early age of onset of parent depression (before 30 years) has been associated with an increased risk for depression and anxiety in offspring (Janzing et al., 2009; Warner et al., 1995; Weissman, Warner, Wickramaratne, & Prusoff, 1988). However, findings are not consistent, with some studies failing to find such associations (Harrington et al., 1997; Kendler, Gardner, & Prescott, 1999; Lieb, Isensee, Höfler, & Wittchen, 2002; Milne et al., 2009). Furthermore, age of onset of depression is associated with poorer depression outcomes; it is confounded with other features of depression such as increased severity and chronicity (e.g. greater number of depression episodes and longer episodes).

Severity and chronicity: Severity and chronicity of parent depression have been associated with increased risk for offspring psychiatric disorder (Janzing et al., 2009; Keller et al., 1986). Severity of maternal depression has been associated with adolescent offspring risk for depression more than chronicity; however, the converse was true for non-depressive outcomes such as conduct problems (Hammen & Brennan, 2003). Additional research has identified that duration of current maternal depression is associated with child outcomes, with longer ongoing depressive episodes being associated with increased risk for offspring internalising and externalising symptoms (Foster, Webster, Weissman, Pilowsky, Wickramaratne, Rush, et al., 2008), suggesting that chronicity of parent depression may increase risk for offspring psychopathology.

Timing: Maternal depression in the first year of life has been found to predict future psychopathology in offspring, including internalising problems (Fihrer, McMahon, & Taylor, 2009). However, evidence suggests that this risk may be due to subsequent episodes of maternal depression (Halligan et al., 2007), with risk for offspring future externalising symptoms being mediated by concurrent maternal depression (Fihrer et al., 2009). This suggests that recent exposure to maternal depression may be an important risk factor for the development of offspring psychopathology.

More recent evidence suggests that exposure to recent parental depression was associated with an increased risk for offspring psychiatric disorder and depression symptoms in adolescents (Hammen, Burge, & Adrian, 1991; Mars et al., 2012) and higher rates of child behaviour problems in young children (Brennan et al., 2000) in a dose-response relationship (Kim-Cohen et al., 2005).

Studies of treating parents with depression are also useful for identifying the nature of risk to offspring associated with variation in maternal depression. These studies focus on maternal remission and any associated reductions in offspring psychopathology. A study of mothers being treated for their recurrent depression assessed the association between maternal depression remission and risk for offspring psychopathology in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study. A decrease in maternal depression symptoms was associated with a decrease in offspring internalising and externalising symptoms in these high-risk offspring of mothers with depression (Foster, Webster, Weissman, Pilowsky, Wickramaratne, Talati, et al., 2008; Garber, Ciesla, McCauley, Diamond, & Schloedt, 2011; Pilowsky et al., 2008; Weissman, Pilowsky, et al., 2006). Offspring of parents who did not remit and had more severe depression were therefore at greater risk. Research suggests that variation in maternal depression remission, and successful treatment of parent depression may have some

effect on offspring risk for psychopathology, although this is unlikely to be sufficient (Gunlicks & Weissman, 2008).

Evidence suggests that variations in maternal depression features explain some of the variation in risk for offspring psychopathology. However, it is also important to consider that adult depression is often accompanied by additional psychopathology. Less attention has been paid to whether comorbid problems in depressed mothers index risk of psychopathology in offspring.

3. Maternal co-occurring psychopathology

Approximately 50% of adults with a mental health problem have at least one other concurrent diagnosable disorder (Clark, Watson, & Mineka, 1995). It is now widely accepted that ‘pure’ depression (depression occurring without other co-occurring problems) is the exception rather than the rule; depression frequently co-occurs with other disorders (Kessler, DuPont, Berglund, & Wittchen, 1999; Rohde, Lewinsohn, & Seeley, 1991). In community samples of adults with depression, the most common comorbid problems are anxiety (Brown, Campbell, Lehman, Grisham, & Mancill, 2001; Coryell et al., 2012; Hirschfield, 2001), antisocial behaviour (Kim-Cohen et al., 2005; Zoccolillo, 1992) and substance misuse (Grant & Harford, 1995; Merikangas et al., 1998; Swendsen & Merikangas, 2000). These comorbid problems have each been associated with increased severity of depression symptoms and increased impairment compared to depression alone (Kessler et al., 1999; Kim-Cohen et al., 2005; Moffitt et al., 2007), as well as a more chronic course of depression and an earlier age of onset (Hill, Pickles, Rollinson, Davies, & Byatt, 2004; Jaffee et al., 2002; Rohde et al., 1991). The associations between depression and each of these co-occurring problems will now be discussed.

It is well-established that major depression and anxiety frequently co-occur, with up to 20% of adults with major depressive disorder also having a diagnosis of generalised anxiety disorder over the course of 12 months (Kessler et al., 1994; Rohde et al., 1991). Estimates of lifetime co-occurrence are almost 50% (Regier, Rae, Narrow, Kaelber, & Schatzberg, 1998; Zimmerman & Chelminski, 2003). Rates of anxiety in those with depression exceed rates of anxiety in non-depressed adults, with lifetime estimates of anxiety in non-depressed adults estimated to be between 5% to 10% (Anseau, Fischler, Dierick, Mignon, & Leyman., 2005; Wittchen, 2002; Wittchen, Zhao, Kessler, & Eaton, 1994). These co-occurring symptoms have been associated with increased impairment when compared to depression alone (Kessler et al., 1999).

Broadly, antisocial behaviour (ASB) is a cluster of symptoms involving hostility or aggression towards others. However, the definition of ASB varies widely across studies (for example violations of social norms, disruptive or aggressive behaviours) and therefore it is difficult to estimate prevalence rates of ASB in the general population; however a nationally representative sample of adults estimated the prevalence of adult ASB to be around 12% (Compton, Conway, Stinson, Colliver, & Grant, 2005). Antisocial behaviour is more common in men than women, in contrast to depression (Eme & Kavanaugh, 1995; Piccinelli & Wilkinson, 2000). ASB can co-occur with depression, however the co-occurrence of ASB and depression has received little attention, despite strong sequential links between antisocial behaviour and future depression (Fergusson et al., 1996; Kim-Cohen et al., 2003; Mason et al., 2004; McGee et al., 2011), and evidence that it is associated with increased functional impairment compared to depression alone (Kim-Cohen, Caspi, Rutter, Tomas, & Moffitt, 2006; Kim-Cohen et al., 2005).

Alcohol abuse and dependence are maladaptive patterns of drinking that cause distress or impairment. Approximately 5% of adults reach criteria for alcohol dependence over a 12-month period (Andrews, Henderson, & Hall, 2001; Bijl, Ravelli, & van Zessen,

1998). Alcohol problems can co-occur with depression, with 9% of women with depression also meeting criteria for alcohol dependence concurrently (Merikangas et al., 1998; Swendsen & Merikangas, 2000). Furthermore, co-occurring alcohol problems adversely affect course, treatment and prognosis of depression (Grant & Harford, 1995).

4. Co-occurring psychopathology in mothers and risk to offspring

Studies suggest that parent anxiety, ASB and alcohol misuse are each associated with risk for psychopathology in offspring (Blazei, Iacono, & McGue, 2008; Burstein, Ginsburg, & Tein, 2010; Hussong et al., 2007; McClure, Brennan, Hammen, & Le Brocque, 2001; Ohannessian et al., 2004; Puttler, Zucker, Fitzgerald, & Bingham, 1998; Van Der Bruggen, Stams, & Bogels, 2008; Van Meurs, Reef, Verhulst, & Van Der Ende, 2009). However, it is unclear whether each of these problems, when they co-occur with parent depression, are associated with increased risk for offspring psychopathology. Additionally, it is unclear whether the cumulative burden of the overall number of co-occurring problems in parents is associated with increasing risk for offspring psychopathology. Only a few studies have considered this issue.

In a regionally representative sample, the number of maternal comorbid disorders (depression, panic disorder, generalised anxiety disorder, substance dependence and antisocial personality disorder) increased risk for offspring psychopathology, suggesting that there may be an additive risk of the number of parent psychiatric disorders as a risk for any psychopathology in offspring (McLaughlin et al., 2012). However, this study was cross-sectional, with offspring (as adults) reporting on their parent's psychopathology retrospectively. Additionally, this study did not utilise a high-risk design; crucially, it is unclear whether the presence of parent co-occurring problems cumulatively increases risk for offspring psychopathology, or whether the presence of any psychopathology indexes increased adversity.

It has not been tested whether co-occurring problems in parents increase risk for psychopathology in offspring of mothers with recurrent depression. Additionally, given that the presence of co-occurring problems in parents with depression are each associated with increased parent depression severity (Grant & Harford, 1995; Kessler et al., 1999; Kim-Cohen et al., 2005), it is important to test whether any effect of co-occurring psychopathology in risk for offspring is independent of maternal depression severity.

It is also unclear whether co-occurring psychopathology in parents with recurrent depression demonstrates specificity of risk to offspring: Do specific co-occurring problems in mothers with recurrent depression predict specific problems in offspring? Studies that have considered the effect of co-occurring psychopathology in parents with recurrent depression have primarily focused on the co-occurrence of depression and anxiety, but typically not considered additional co-occurring problems such as antisocial behaviour or alcohol misuse.

Parent co-occurring anxiety and risk to offspring

Studies assessing co-occurring anxiety in parents with depression and the impact on offspring have typically assessed parent panic disorder, and the associations with offspring anxiety and depression. Research suggests that the presence of parent panic disorder comorbid with depression may not demonstrate an additive risk to offspring; parent panic disorder (regardless of comorbid major depressive disorder) was associated with increased risk of offspring anxiety, whilst parent major depressive disorder (regardless of comorbid panic disorder) was associated with increased risk of offspring depressive disorders and disruptive behaviour disorders both cross-sectionally (Biederman et al., 2001), and at a five-year follow-up (Biederman et al., 2006). These studies suggest that co-occurring panic disorder in parents with depression may have specific links with offspring anxiety disorders. However, the age range of the offspring in

these studies was large, spanning young childhood to early adulthood (age 2 to 25 years at first assessment), and patterns of risk may be different for different developmental periods. Additionally, the groups of parents with depression alone or panic disorder alone were small. It is important to consider that many parents experience significant anxiety symptoms that do not fit this diagnostic category, particularly as several studies have suggested that the developmental pattern of comorbidity of generalised anxiety disorder versus panic disorder with depression differs. Evidence suggests that panic disorder tends to follow the onset of depression while generalised anxiety disorder often precedes the onset of depression (Lewinsohn, Zinbarg, Seeley, Lewinsohn, & Sack, 1997; Merikangas et al., 2003), suggesting different aetiologies. The impact of co-occurring parent anxiety problems on offspring psychopathology therefore remains unclear.

Parent co-occurring antisocial behaviour and risk to offspring

To date, only two studies have assessed the co-occurrence of antisocial behaviour in parents with depression. Kim-Cohen et al (2005) utilised a large high-risk sample of offspring of mothers who had their first child before the age of 20 years. Parent history of antisocial behaviour accounted for some of the association between maternal depression and offspring antisocial behaviour. A high-risk study of offspring of depressed parents found similar results; both parent major depressive disorder and history of childhood disruptive behaviour disorder conferred risk for offspring disruptive behaviour disorders (Hirschfeld-Becker et al., 2008). This research suggests that the elevated rates of disruptive behaviour disorder (DBD) in offspring of parents with depression may be due, in part, to parent history of ASB. However, both these studies assessed the effects of parent ASB on young children. It is not clear whether the risk for psychopathology will be the same in adolescent offspring of depressed parents. In addition these studies relied on parents' retrospective recall of their own disruptive behaviours in childhood.

Furthermore, these studies focused on disorder-specific transmission from parent to child (i.e. parent antisocial behaviour leading to increased offspring disruptive behaviours), therefore it is not clear whether parent co-occurring ASB represents a general risk factor for child psychopathology, or instead increases risk for conduct problems specifically in offspring of depressed parents.

Parent co-occurring alcohol problems and risk to offspring

Parent problem drinking is associated with increased risk for offspring psychopathology, particularly disruptive behaviour disorder (Loukas, Fitzgerald, Zucker, & von Eye, 2001; Loukas, Zucker, Fitzgerald, & Krull, 2003; Puttler et al., 1998), but also other problems including anxiety and depression (Eiden, Molnar, Colder, Edwards, & Leonard, 2009). However, these studies did not assess samples of parents with depression. Therefore it remains unclear whether the overlap between problem drinking and depression contributes to risk for child psychopathology observed in parents with recurrent depression.

The majority of studies examining the intergenerational transmission of risk associated with problem drinking have focused on a very young age group of children, with only one study assessing the trajectories of offspring from pre-school to adolescence, although this study assessed only boys (Loukas et al., 2003). None of these studies assessed the effects of *maternal* alcohol problems on risk for offspring psychopathology but focused on paternal alcohol problems. Therefore it is unclear how maternal alcohol use affects risk for offspring psychopathology, and how parent alcohol misuse affects risk for *adolescent* offspring.

In summary, there is well-established evidence of the co-occurrence of parent depression and other forms of psychopathology (such as anxiety, ASB and alcohol

problems), and these additional problems in parents may have a negative impact on child outcomes. However, it is not apparent whether specific types of comorbid parent problems are associated with increased risk of specific child psychopathology, or if they are general risk factors associated with increased risk for a range of offspring psychopathology in offspring of depressed parents. These studies have primarily focused on one disorder at a time, and it is therefore difficult to assess the pattern of familial transmission. However, some family studies have assessed the intergenerational transmission of different disorders and this will now be discussed.

5. Mechanisms of intergenerational transmission

Family studies can be used to test whether there is specific inter-generational transmission of risk of a particular disorder or whether there is a shared predisposition for two (or more) disorders. If there is an association between two (or more disorders) these disorders may be causally associated, or share common aetiology. Alternatively, if there is no association between disorders, these disorders may not have shared aetiology. Research has assessed the intergenerational transmission of both internalising and externalising problems simultaneously.

A family study examined the familial transmission of depression, anxiety and alcoholism in relatives of probands with depression or no psychopathology (Merikangas et al., 1994). Depressed probands were categorised according to the presence or absence of lifetime alcoholism and anxiety. The presence of lifetime diagnoses were assessed in first degree relatives. Rates of alcoholism were increased in relatives of probands with alcoholism suggesting that alcohol problems were uniquely transmitted. In contrast, anxiety was elevated among relatives of all depressed probands compared to controls; nearly all the transmission between anxiety and depression was shared. This suggests that depression and anxiety may share aetiology (Merikangas et al., 1994). This finding was

extended by a nationwide survey of the U.S. population (aged 15 – 54 years) that examined the familial aggregation of a range of psychiatric disorders (major depression, generalised anxiety disorder, antisocial personality disorder, alcohol abuse, and drug abuse)(Kendler, Davis, & Kessler, 1997). The transmission of disorders was best explained by underlying vulnerabilities to internalising and to externalising disorders (Kendler et al., 1997), suggesting that there was moderate specificity of risk transmitted across generations. Therefore co-occurring psychopathology in parents with recurrent depression may explain in part the heterogeneity of outcomes in offspring. However, few studies thus far have attempted to assess whether co-occurring psychopathology in mothers with recurrent depression shows specific links with child problems.

Genetically sensitive designs are needed to estimate the contribution of genes and environment when estimating risk to offspring; parent psychopathology may index particularly high genetic or environmental stress. As discussed next, studies that use genetically sensitive designs highlight that although the intergenerational transmission of risk for internalising and externalising problems are accounted for in part by genetic factors, environmental factors also play a role.

Although heritability estimates vary, genetically sensitive studies consistently demonstrate moderate to high heritability for depression (Kendler, Gatz, Gardner, & Pedersen, 2006; Sullivan, Neale, & Kendler, 2000; Thapar & McGuffin, 1994), with environmental factors also having a substantial role in the intergenerational transmission of depression (Eley, Deater-Deckard, Fombonne, Fulker, & Plomin, 1998; Harold et al., 2010; Lewis, Rice, Harold, Collishaw, & Thapar, 2011; Silberg, Maes, & Eaves, 2010; Singh et al., 2011; Van Den Oord, Boomsma, & Verhulst, 1994).

Genetically sensitive designs assessing the intergenerational transmission of externalising problems suggest that although heritability estimates are high (Baker, Jacobson, Raine, Lozano, & Bezdjian, 2007; Scourfield, Van den Bree, Martin, &

McGuffin, 2004; Singh et al., 2011), environmental processes also account for the association between maternal ASB and offspring externalising problems (Bornovalova, Hicks, Iacono, & McGue, 2010; Harold et al., 2010; Hicks, Krueger, Iacono, McGue, & Patrick, 2004; Silberg et al., 2010; Van Den Oord et al., 1994).

Adoption studies provide support for environmental transmission of both depression and disruptive behaviours; parent depression is associated with increased risk for both offspring disruptive behaviours and depression in both adopted and non-adopted offspring (Tully, Iacono, & McGue, 2008). Risk for psychopathology may also not be disorder-specific. Both genes and environmental factors may increase risk for internalising and externalising problems in children and adolescents (Burcusa, Iacono, & McGue, 2003; Ehringer, Rhee, Young, Corley, & Hewitt, 2006; O'Connor, McGuire, Reiss, Hetherington, & Plomin, 1998; Silberg et al., 1994; Silberg et al., 2010; Subbarao et al., 2008).

Despite these inconsistencies, these genetically sensitive studies are important, highlighting that genes only partially account for the intergenerational transmission of risk; non-inherited factors also have an important role in the development of psychopathology. One psychosocial risk factor that has received considerable attention is that of disruptions in parenting. Impairments in parenting are associated with increased risk for offspring psychopathology. Parenting disruptions may mediate the effect of maternal depression on risk for offspring psychopathology. However, less is known about whether co-occurring psychopathology has any effect on disruptions to parenting, and whether this in turn has an effect on risk for child psychopathology. Additionally, less attention has been paid to the direction of effects between parenting and child psychopathology; whether there are any child effects on parenting, and/or vice versa, in adolescent offspring of depressed mothers.

6. Parenting

There is considerable evidence to suggest that parent depression is associated with adverse family environment, including disruptions to parenting, and to the parent-child relationship (Goodman & Gotlib, 1999; Muris, Schmidt, Lambrichs, & Meesters, 2001). Mothers who suffer from depression are reported to show more hostility and less warmth compared to parents without depression, they are also more likely to use resolution strategies such as coercion or withdrawal, and to use harsh or inconsistent punishments. These disruptions in parenting are one mechanism through which maternal depression may exert effects on offspring (Blatt-Eisengart, Drabick, Monahan, & Steinberg, 2009; Downey & Coyne, 1990; Elgar, Mills, McGrath, Waschbusch, & Brownridge, 2007; Foster, Webster, Weissman, Pilowsky, Wickramaratne, Talati, et al., 2008; Goodman, Adamson, Riniti, & Cole, 1994; Goodman & Gotlib, 1999; Keenan-Miller, Hammen, & Brennan, 2010; Kim-Cohen et al., 2005; Marmorstein & Iacono, 2004; McCarty & McMahon, 2003; Muris et al., 2001; Schwartz, Dorer, Beardslee, Lavori, & Keller, 1990). It is important to consider that disruptions to parenting may be accounted for, at least in part, by co-occurring psychopathology in parents with recurrent depression. This will be discussed after outlining the association between parenting disruptions and child psychopathology. The current thesis focuses on the constructs of maternal warmth and hostility as putative mediating mechanisms of risk for offspring psychopathology.

Parenting and the association with children's psychopathology

Offspring internalising problems: Community studies suggest that disruptions in parenting are associated with child internalising symptoms (Psychogiou, Daley, Thompson, & Sonuga-Barke, 2007; Stubbe, Zahner, Goldstein, & Leckman, 1993). Research assessing clinical samples of children presenting with internalising problems

have also identified an association between parenting disruptions and offspring psychopathology. Hostility and criticism were increased in mothers when the children had current or remitted depression compared to controls with no psychopathology, with no significant differences between current and remitted groups (Silk et al., 2009). Furthermore, an additional study suggested that mothers of children with depressive disorders were more critical compared to mothers of children with other psychopathology (Attention Deficit Hyperactivity Disorder; ADHD), but no differences were found between the control group (with no disorder) and the ADHD group (Asarnow, Tompson, Woo, & Cantwell, 2001). Parent criticism has also been associated with increased risk for the onset of subsequent episodes of depression (Silk et al., 2009). These findings suggest that maternal criticism may be important for the development or maintenance of depression.

Research suggests that disruptions in parenting may be an important mediating mechanism explaining the association between parent depression and offspring psychopathology; one study found that the parent-child relationship mediated the association between parent depression and adolescent depression (Davies & Windle, 1997). However, findings are inconsistent. Recent findings suggest that maternal depression and parenting disruptions are each independent risk factors associated with offspring depression (Tompson et al., 2010), or that maternal parenting factors are not related to offspring internalising symptoms (Foster, Webster, Weissman, Pilowsky, Wickramaratne, Talatj, et al., 2008; Frye & Garber, 2005). Therefore more research is needed to test whether maternal warmth or hostility increase risk for offspring depression, and whether these aspects of parenting mediate the effects of maternal depression on risk for offspring depression.

Offspring externalising problems: Community studies suggest that the associations between disruptions in parenting and offspring disruptive behaviours may be

stronger than between parenting and internalising problems (Combs-Ronto et al., 2009; Gershoff, 2002; Psychogiou et al., 2007; Stubbe et al., 1993). Disruptions in parenting may have a causal role in the development of offspring antisocial behaviour (Burt, McGue, Krueger, & Iacono, 2005; Caspi et al., 2004).

Parenting disruptions have also been examined in parents of offspring presenting to services with offspring conduct problems. Maternal criticism has been found to distinguish between children with conduct disorders compared to other groups (emotional disorders, and control group) (Vostanis, Nicholls, & Harrington, 1994). This suggests that maternal criticism may be a specific risk factor associated with offspring conduct disorder. Maternal lack of warmth was also associated with offspring conduct disorder. However, although lowest in children with conduct disorder, maternal lack of warmth was still significantly associated with offspring depression (Vostanis & Nicholls, 1995; Vostanis et al., 1994), suggesting that it may be a general risk factor associated with offspring psychopathology. However, where children are recruited through services due to the presence of psychiatric disorder it is not clear whether disruptions in parenting represent a risk factor for the development of psychopathology, or a response to offspring psychopathology.

High-risk studies of offspring of depressed parents have examined whether parenting mediated the effect of maternal depression on risk for offspring psychopathology. The effect of parent depression severity on risk for pre-adolescent offspring externalising problems has been found to be mediated by negative parent-child relationships (McCarty & McMahon, 2003), and by maternal positivity (Foster, Garber, & Durlak, 2008). However, findings are inconsistent, with some studies suggesting that maternal depression and parenting disruptions each have independent associations with offspring externalising problems (Nelson, Hammen, Brennan, & Ullman, 2003).

Therefore more research is needed to test whether parenting mediates any effect of maternal depression on risk for offspring DBD.

Findings suggest that disruptions in parenting in depressed parents are associated with risk for offspring psychopathology, and that the association between negative parenting and child psychopathology is stronger than effects found for positive parenting (Lovejoy et al., 2000; McCarty & Weisz, 2002).

It is important to note that for many studies it is unclear whether impairments in parenting are causally related to offspring psychopathology as the temporal pattern of associations is often inferred; studies are largely cross-sectional or do not assess both parenting and child symptomatology at the same time point and therefore are unable to test the direction of effects. Additionally, not all studies utilised high-risk samples of offspring of parents with clinically diagnosed depression; risk for offspring may not be the same in high-risk groups.

Parenting and co-occurring parent psychopathology

Few studies have considered the potential impact of additional psychopathology on parenting in parents with depression. Co-occurring psychopathology may, at least in part, explain the association between maternal depression and offspring symptomatology. Family risk factors, including suboptimal parenting, are common in families in which parents evidence *any* psychopathology, not just in parents with depression (Fendrich et al., 1990).

There is surprisingly little available information regarding parenting characteristics of parents with anxiety that co-occurs with depression (Berg-Nielsen, Vikan, & Dahl, 2002). One study found that parent anxiety that co-occurred with depression was associated with lower parental care compared to parents with depression alone, or anxiety disorders alone (Alnæs & Torgersen, 1990).

Recent studies have recruited mothers with anxiety and found that although maternal anxiety was associated with increased parental rejection and criticism towards their children compared to mothers with no history of anxiety disorders (Hirschfield, Biederman, Brody, Faraone, & Rosenbaum, 1997; Lieb et al., 2000), these impairments were better accounted for by maternal depression (McClure et al., 2001). This suggests that maternal depression may be associated with disruptions in parenting over and above parent anxiety.

There is preliminary evidence that depressed mothers with co-occurring ASB symptoms may provide especially poor quality care-giving environments. They are rated as more hostile and less understanding compared to parents with no psychopathology (Jaffee, Belsky, Harrington, Caspi, & Moffitt, 2006; Johnson, Smailes, Cohen, Kasen, & Brook, 2004). In a study of depressed mothers with younger children, maternal depression comorbid with a history of ASB was associated with lower warmth and greater maternal hostility than depression alone (Kim-Cohen et al., 2006). The extent to which co-occurring psychopathology in mothers with recurrent depression explains the associations between maternal depression, parenting and child psychopathology remains unclear. In addition, where associations have been observed between parenting and child psychopathology, it is important to consider whether parenting affects risk for offspring psychopathology, or whether offspring psychopathology increases disruptions to parenting, or both. This will now be discussed.

Direction of effects

Transactional theory purports that there are reciprocal relationships in which children are influenced by their environment, and also influence their environment; children are influenced by parenting behaviours, but their behaviour also elicits particular reactions from parents. Reciprocal effects between individuals and social contexts have

long been highlighted by developmental psychologists (Bell, 1968; Sameroff, 1975).

Despite this, few studies have considered a transactional approach or explicitly examined the direction of effects, particularly in families where a parent has recurrent depression.

Research has mainly focused on parent effects on children, including parenting as a predictor of offspring symptoms or behaviours. Additionally, much previous research has been cross-sectional, or has not assessed both parenting and child symptomatology at multiple time points. Therefore temporal associations could not be ascertained; the effects of parenting on child psychopathology are inferred (Asarnow et al., 2001; Caspi et al., 2004; Foster, Garber, et al., 2008; Nelson et al., 2003; Peris & Baker, 2000; Silk et al., 2009). It is not clear whether negative parenting has effects on child psychopathology, or whether child psychopathology has effects on parents, or both (Bell, 1968).

Research that has assessed the direction of effects has primarily focused on parenting as a risk for offspring conduct problems in high-risk groups of younger children, providing evidence for bidirectional effects (Combs-Ronto et al., 2009; Gross, Shaw, Moilanen, Dishion, & Wilson, 2008; Miner & Clarke-Stewart, 2008). However, all these studies assessed young children, and do not assess the direction of effects between parenting and *adolescent* offspring symptomatology. Adolescence is a period of transition when offspring are developing their autonomy and therefore may be an important developmental period in which to assess the relationship between parenting and child psychopathology. Additionally these studies did not assess the direction of effects between parenting and offspring psychopathology in families where parents suffer with recurrent depression, a high-risk group where disruptions to the parent-child relationship have been reported.

The vast majority of studies have focused on child disruptive behaviours but fewer studies have examined the direction of effects between parenting and child

symptoms of depression and anxiety, and evidence here is inconsistent. Some studies report child effects of depression/anxiety on parenting across time (Hale III et al., 2011), whereas others have reported parent effects on offspring emotional adjustment (Rueter, Scaramella, Wallace, & Conger, 1999). Bidirectional effects between parenting and offspring internalising symptoms have also been reported (Branje, Hale III, Frijns, & Meeus, 2010; Hipwell et al., 2008). More research is needed testing the direction of effects between parenting and offspring anxiety and depression symptoms. In addition, research is needed assessing the direction of effects (between offspring depression and anxiety symptoms and parenting) in high risk groups of parents with recurrent depression. It is important first to test whether parenting mediates any effect of parent psychopathology on risk for offspring psychopathology and this ideally requires data from at least three time points so that the risk (parent depression), mediator (parenting), and outcome (child psychopathology) can be separated in time.

7. Summary

Children of depressed parents are at increased risk of developing psychopathology. However, outcomes are heterogeneous, with not all children going on to develop psychopathology. It is important to understand risk factors and mechanisms that help to explain this variation in outcomes. Furthermore, those that do develop psychopathology have heterogeneous outcomes, developing a range of problems including depression, anxiety and disruptive behaviour disorders. It is crucial to understand what may explain this heterogeneity of outcome in offspring to better understand the aetiology of adolescent psychopathology in this high-risk group, and for the development of intervention strategies.

Features of maternal depression have been examined as possible risk factors that may explain the heterogeneity of outcomes in offspring. However, adults with depression

can also present with additional psychopathology, including anxiety, antisocial behaviour, and alcohol misuse. These co-occurring problems have each been associated with increased depression severity and impaired functioning compared to depression alone. There are still several important gaps in our understanding of how this co-occurring psychopathology in parents may impact on risk for adolescent offspring. First, it is unclear whether the burden of co-occurring psychopathology in mothers with depression indexes risk of child psychopathology, independent of maternal depression severity. Second, is it unclear whether the type of co-occurring psychopathology in mothers with recurrent depression is associated with risk for specific child outcomes, or whether these co-occurring problems represent general risk factors for all offspring psychopathology.

Maternal depression severity has been associated with disruptions in parenting and the parent-child relationship (Goodman & Gotlib, 1999; Muris et al., 2001). These disruptions in the mother-child relationship may mediate the effect of maternal depression on risk for offspring psychopathology. However, there are also several important gaps in our understanding of the role of parenting as a risk mechanism for offspring psychopathology in the context of maternal depression. First, there are few studies that investigate mother-child interactions with older children. Adolescence is a period of transition when the parent-child relationship is changing (Steinberg, 2001). It is also a time when rates of psychopathology typically increase. It is therefore an ideal time to explore potential mechanisms of risk. Second, it is not clear whether negative parenting has effects on child psychopathology, or whether child psychopathology has effects on parents, or both (Bell, 1968). Third, it is unclear whether parenting effects are specific to particular forms of psychopathology (e.g. disruptive behaviour problems, depression or anxiety). It is particularly important to identify risk factors that differentially predict outcomes, not only to improve our understanding of aetiology and

the course of psychopathology, but also to improve the targeting of interventions. It is likely that different interventions will be necessary for those at risk of developing different disorders. At present, although there is evidence that family factors may be risk markers for child psychopathology, it is not known whether there is any specificity of risk in offspring of depressed mothers. Fourth, it is not clear whether problems in parenting in these high-risk families reflect other co-occurring parent psychopathology such as antisocial behaviour; co-occurring psychopathology is rarely considered. Impairments in parenting are potentially modifiable and therefore important to understand for intervention strategies.

8. Rationale of current study

Aims

Maternal depression is a well-established risk factor for offspring psychopathology. However, adult depression can often co-occur with additional psychopathology, and how this co-occurring psychopathology in mothers with recurrent depression affects risk for adolescent psychopathology is not well understood. Therefore, in this thesis, I utilised longitudinal data to examine the effect of maternal co-occurring psychopathology in mothers with recurrent depression on risk for offspring psychopathology. Mothers and their adolescent offspring were assessed on three occasions over four years. This thesis is divided into four results chapters, each of which are either published or under review. The specific aims of each study were as follows:

The first aim of this thesis was to test whether the burden of co-occurring psychopathology (anxiety, ASB, and harmful drinking) in mothers with recurrent depression impacted on offspring risk for the development of psychopathology, after adjusting for baseline maternal depression severity. These analyses utilised longitudinal

data to predict whether maternal co-occurring psychopathology at Time 1 predicted the presence of new-onset psychiatric disorder in offspring (at either Time 2 or Time 3). Additional confounders were also considered, including the presence of financial difficulties, other features of maternal depression course, and offspring symptomatology prior to each assessment.

The second aim was to test whether specific co-occurring psychopathology in depressed mothers (Time 1) demonstrated any specificity of risk for offspring symptomatology (Time 3); whether symptoms of ASB, anxiety, and alcohol use in parents with recurrent depression showed specific links with child symptoms of depression, anxiety, and DBD.

The third aim was to examine whether impairments in the mother-child relationship mediated effects of maternal depression severity on offspring symptomatology, after accounting for co-occurring psychopathology in the depressed mothers. Maternal depression severity and co-occurring antisocial behaviour were considered at the first assessment (Time 1). Maternal warmth and hostility were the constructs of the parent-child relationship that were considered, and were assessed at Time 2. Child outcomes were symptoms of depression and disruptive behaviour disorder at Time 3.

The fourth aim was to test the direction of effects between maternal hostility/warmth and offspring symptoms of depression, and disruptive behaviour disorder (across Time 2 and Time 3).

The current study

Data for the current thesis were collected as part of the 'Early Prediction of Adolescent Depression' (EPAD) study conducted at Cardiff University, a longitudinal study of adolescent offspring of parents with recurrent depression. Families were

interviewed three times over four years. Data collection began April 2007 and was completed April 2011. The study has a number of key attributes that enable the aims to be addressed.

- (i) **Longitudinal design:** Longitudinal research is scarce, but is particularly informative; it is possible to assess the impact of parent depression and additional problems on offspring psychopathology *as it develops*. Thus, risk markers for the onset of psychopathology in offspring can be identified. Furthermore, longitudinal research can assess the temporal order of events to assess within-individual change. This is crucial; testing the direction of effects is informative for intervention and treatment programmes.
- (ii) **High-risk sample:** The use of a high-risk design takes advantage of the fact that putative risk (parent recurrent depression) is present in all of the selected population. The use of a high-risk design provides sufficient power to examine variation in outcomes among offspring of mothers with depression, rather than simply draw comparisons between offspring of depressed and non-depressed parents. In addition, the period of adolescence is thought to be a period of transition when the parent-child relationship is subject to change (McGue, Elkins, Walden, & Iacono, 2005), with rates of disorder increasing in adolescence. It is therefore a period of particular risk for the onset of psychopathology.
- (iii) **Quality of assessments:** The current study made use of research diagnostic interviews to assess the presence of recurrent depression in the parents, and to assess psychopathology in offspring. Multiple informants were used to assess offspring psychopathology. When rating the presence of a psychiatric disorder, there is evidence to suggest that construct validity may be greater when using information from multiple informants than when using a single

informant (Bird, Gould, & Staghezza, 1992; Piacentini, Cohen, & Cohen, 1992).

The use of multiple informants is the gold standard for research and clinical practice, and therefore parent and child reports were used to assess the presence of offspring psychopathology. This method also reduces effects of shared-method variance, where parents report on both their own symptomatology and that of their offspring. This is particularly important in offspring of depressed parents, as there is some debate as to whether depressed mood in parents affects their reports of offspring psychopathology (Angold & Costello, 1995; Boyle & Pickles, 1997; Hay, Pawlby, Sharp, & Schumacker, 1999; Lewis et al., 2012; Najman et al., 2000; Rice, Lifford, Thomas, & Thapar, 2007; Richters & Pellegrini, 1989; Weissman et al., 1987). Furthermore, there is evidence to suggest that different reporters are likely to report different symptoms, for example suicidal thoughts are rarely endorsed by mothers suggesting that they may be unaware of these thoughts in their children (Rice et al., 2007). In contrast, some symptoms of oppositional defiant disorder are rarely endorsed by offspring (Angold & Costello, 1995). Multiple methods (e.g. interview and questionnaire data) are useful for understanding complex phenomena; they can provide information about different aspects of a phenomenon and therefore improve understanding. The current thesis made use of multiple methods. For example, mother self-report questionnaires and interviewer-rated five minute speech samples were combined to provide a robust measure of the parent-child relationship. Finally, the current study used a prospective design. Therefore, unlike studies relying on retrospective recall, reports are likely to be more

reliable, and thus the study is able to accurately assess temporal relations between putative risk factors, mediators, and outcomes.

9. Role in the study

Measures used in the study were chosen by the principal investigators. I worked as a research assistant and was responsible for data collection across the four years of the study. I was also responsible for data entry and data checking. I devised the research questions for each results chapter and analysed the data for all papers. Advice was given regarding some of the statistical analysis approaches and was provided by Dr Stephan Collishaw, Dr Kit Elam, and Prof Gordon T. Harold as stated in the methodology chapter (analysis section). Each results chapter was written as a paper; I wrote each paper. Named co-authors contributed to the editing of papers and interpretation of results.

Chapter 2. Methodology

This chapter summarises recruitment and retention of the sample. Details of the sample and methodology specific to individual analysis will be described in the relevant chapters. The current thesis utilises data from the ‘Early Prediction of Adolescent Depression’ (EPAD) study, a prospective longitudinal study of 337 parents (315 mothers; 22 fathers) with recurrent depression and their adolescent offspring (aged 9-17 years at baseline).

1. Sample and recruitment

Inclusion and exclusion criteria

Parents were required to have a history of recurrent unipolar depression (at least two lifetime episodes, later confirmed at interview) with no previous history of a psychotic disorder, schizoaffective disorder, or mania. Parents had to be living with a child aged between 9 to 17 years that they were biologically related to. Where there was more than one eligible child per household, the youngest child was selected given the focus on examining the development of psychopathology over adolescence, and to avoid parental selection of children with the most problems.

Children were excluded from the study if they had moderate-severe intellectual disability that would impair their ability to complete assessments (IQ <50). Over the course of the study, two further families were excluded due to the depressed parent reporting a bipolar diagnosis.

Recruitment methods

Participants were recruited primarily from general practices across South Wales (n = 263; 78%), as well as from a database from a previous study of adults with recurrent

unipolar depression ($n = 64$; 19%), and community volunteers ($n = 10$; 3%). Figure 2.1 shows a flowchart of sample recruitment, and is detailed below.

General practice ($n = 263$): Sixty-two general practice surgeries from South Wales, UK assisted with recruitment. Patients with recurrent depression were identified via electronic records using depression read-codes and/or more than one repeat prescription of anti-depressant medication for at least two episodes of depression (patients with prescriptions of low doses of Amitriptyline ($<50\text{mg}$) were excluded following recommendations from a general practitioner (AKT) as these low doses are likely to be prescribed for sleep problems). Patients were initially selected for telephone screening if aged 26 to 55 years to increase the likelihood that they would have children in the study age range.

Patients identified were contacted via a letter from the surgery. Over 4000 letters were sent from 62 surgeries asking patients if they would like to hear more information regarding the research project. Surgeries sent reminder letters to non-responders after 2 weeks. No further attempts to contact the patients were made. Patients returned a reply card to the research project with their contact details if they were willing to participate. There were over 700 positive responses.

Patients were contacted by telephone to ensure suitability and confirm eligibility. There was no contact made directly from the research team prior to this. 368 eligible families agreed to participate. Of these, 263 families were interviewed (see Figure 2.1). It was not possible to ascertain whether there were any differences between those who responded and those who did not due to patient confidentiality.

Database from a previous study of recurrent depression ($n = 64$): A second source of recruitment was through a database of two studies of previously identified adults with recurrent unipolar depression from the community (Depression case control

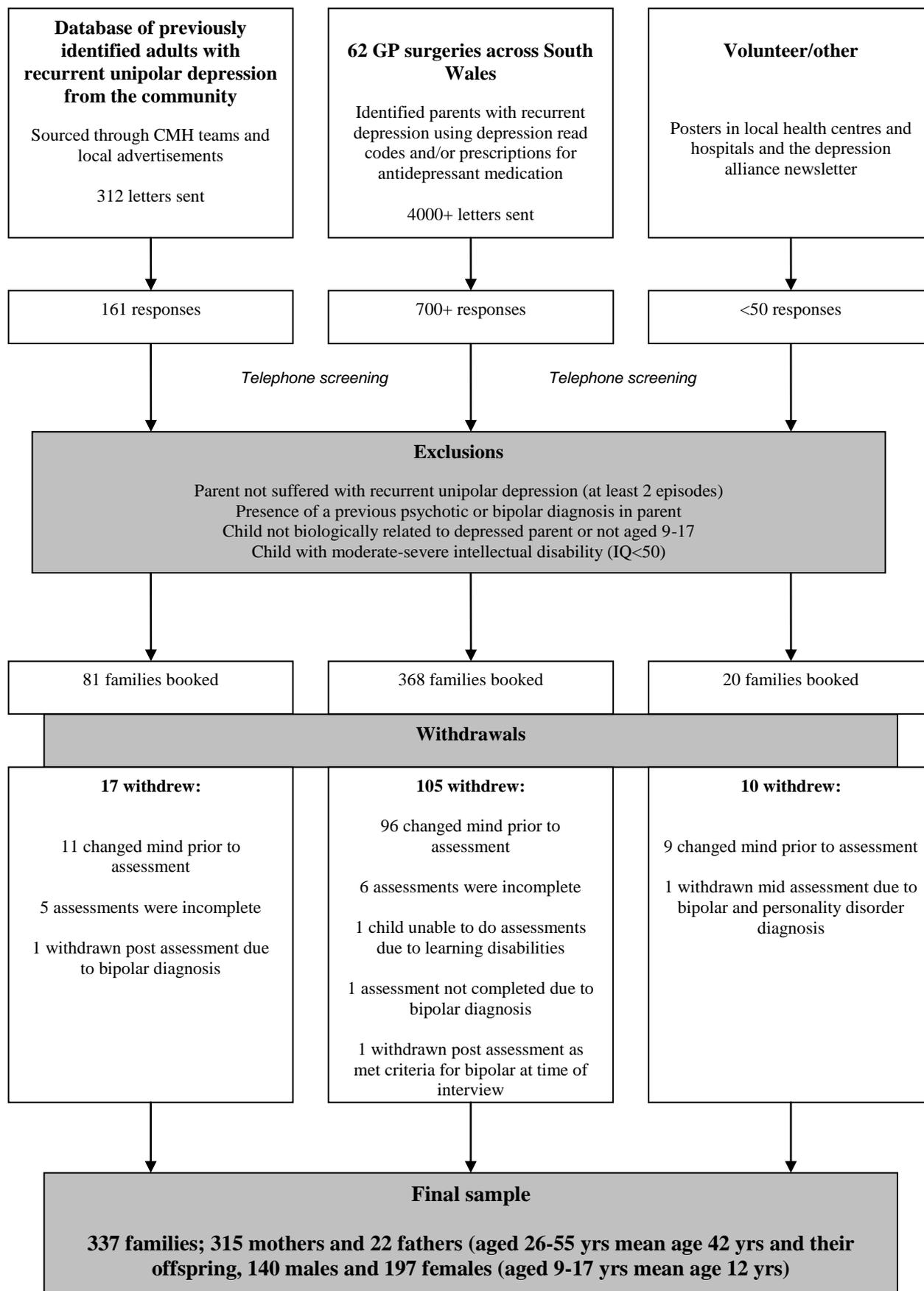


Figure 2.1: Flow chart of sample recruitment (Mars et al., 2012)

study (DECC) and Depression Network (DeNT) sibling pair Study) (Farmer et al., 2004; Korszun et al., 2004). These were sourced through Community Mental Health (CMH) teams and advertisements in local media and primary care centres. Three-hundred and twelve participants who had agreed to future contact and were between the ages 26-55 years were contacted via letter providing them with information regarding the study. There were 161 positive responses.

Community volunteers (n = 10): A final source of recruitment was a volunteer sample recruited via posters in local health centres, the University Hospital of Wales, and through an advertisement in a 'Depression Alliance' newsletter. Volunteers contacted the researchers and were provided with information regarding the study. Volunteers were subsequently contacted to screen for eligibility, and confirm participation (see Figure 2.1).

Analysis of Variance and Chi-Square tests were used to test whether there were any significant differences between families recruited from different sources. There were no significant differences between families from different recruitment sources on a number of demographics; parent gender, child age, child gender, family composition (two-parent household compared to one-parent household), self-reports of financial hardship or maternal depression severity. However, significant differences were found for parent age by recruitment source ($F(2) = 3.30, p = .038$). Post hoc tests revealed that parents from DEC/DENT were significantly older (mean = 43.2 years) than parents recruited from general practice (mean = 41.9 years).

2. Longitudinal follow-up and retention

Two follow-up assessments were conducted, with the first follow-up approximately 16 months after the baseline assessment ($SD = 2.63$), and the second follow-up conducted a further 13 months later ($SD = 1.57$). The average time between the

baseline and final assessment was 29 months ($SD = 3.59$). Retention rates at each assessment are summarised in Figure 2.2. Sample characteristics and retention are described in detail later.

Retention

Several strategies were used to encourage participation at each assessment. At the first assessment parents provided additional contact details (email address, GP contact details, details of friends or family). Between assessments, parents and children were sent newsletters at regular intervals, as well as Christmas cards, including change of address cards.

Retention at Time 2: Between assessments, two affected parents were diagnosed as having bipolar disorder and were therefore excluded (sample $n = 335$). Fourteen participants declined to participate, thus the retention rate at time two was 95.8% ($n = 321/335$). Thirty-one families completed questionnaires only (no interview data), with 86.6% ($n = 290/335$) of families participating in interviews.

Retention at Time 3: Retention at the final assessment was 92.5% (25 declined to participate $n = 310/335$). Twenty-six families completed questionnaires only, with 84.8% ($n = 284/335$) of families participating in interviews.

Retention at either follow-up: 96.7% of families (324/335) participated at either or both follow-ups (time two or time three), with interview data available regarding child psychopathology for 91.0% of families ($n = 305/335$; 305 parent reports, 295 child reports).

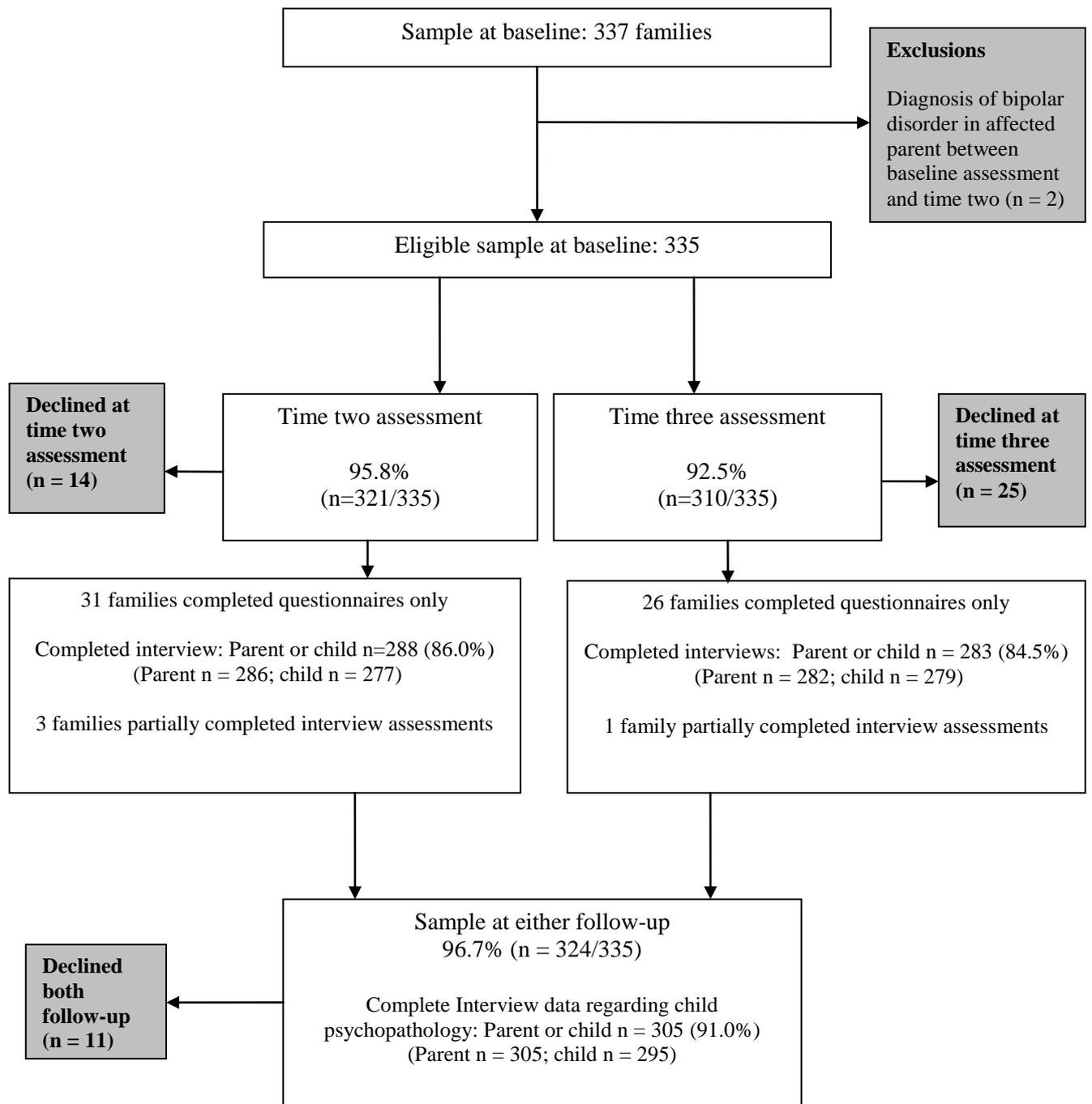


Figure 2.2: Flow chart of retention at each assessment (Mars et al., 2012)

3. Procedure

At each assessment, parents and children were sent questionnaires to complete two weeks prior to interview. Interview assessments were conducted in the family home in most cases (99.6% at each assessment), or at the university hospital. Parent and child interviews were conducted, where possible in different rooms by different interviewers. Parents and children were given a description of the study and provided written informed consent, or written assent (if under 16 years of age) at each assessment.

Assessments lasted approximately 3 hours and participants were compensated for their time (£20 voucher per family). Interviewers were aware that all index parents had a history of recurrent depression but were blind to any additional clinical problems, and child psychopathology. Interviewers were all trained psychology graduates supervised by psychiatrists at weekly meetings. Ethical approval was provided by the Multi-Regional Ethics Committee (MREC number: 06/MRE09/48).

4. Measures

Data were collected from multiple informants (parents and child) via multiple methods; semi-structured interviews (Child and Adolescent Psychiatric assessments, CAPA (Angold & Costello, 2000); Schedules for Clinical Assessment in Neuropsychiatry, SCAN (Wing et al., 1990), and questionnaires.

Parent psychopathology

Parent depression: At the baseline assessment parents provided information on the clinical features of their past depressive episodes. Parents completed a timeline using a life-history calendar approach (Caspi et al., 1996). This is a retrospective measure using life events to aid recall. A history of recurrent depression (2 or more episodes of DSM-IV major depression) was confirmed for all index parents.

Impairment of the two worst depression episodes was assessed using the Global Assessment of Functioning (GAF) Scale (American Psychological Association, 1994). The GAF scale assesses functioning in three main domains (psychosocial, occupational, relationships) on a scale of 0 to 100, with lower scores indicating greater impairment. An average of the two worst episodes was taken as a measure of past impairment. Additional retrospective data on past depression features used in the present thesis were the age of onset of depression, and average episode duration (in months).

At each assessment, presence of major depressive disorder was assessed using a semi-structured interview; the Schedule for Clinical Assessment in Neuropsychiatry (Wing et al., 1990). This established whether the parent had experienced an episode in the previous month. Regular supervision meetings were provided by an adult psychiatrist (DJS). Interviewer agreement for coding DSM-IV parent depression was perfect ($\kappa = 1$). Parents also completed the Beck Depression Inventory (BDI) (Beck, Rush, Shaw, & Emery, 1979) to assess the severity of depression symptoms at baseline and follow-ups. The BDI is a 21 item questionnaire with each item scored 0 to 3 according to severity of depression symptoms that day, with a maximum score of 63 (baseline $\alpha = .91$).

Parent anxiety: Parent concurrent anxiety was assessed using the Hospital Anxiety and Depression Scale anxiety subscale (HADS) (Zigmond & Snaith, 1983). This consists of 7 items scored from 0 to 3 according to severity of anxiety symptoms over the preceding week (e.g. 'I get sudden feelings of panic'). A total anxiety symptom score was calculated with high scores indicative of increased severity of anxiety symptoms (baseline $\alpha = .82$). A dichotomous variable was created using a cut-off score of 11 or more; this is indicative of clinically significant anxiety symptoms (Zigmond & Snaith, 1983).

Parent antisocial behaviour: Parents reported on their own current antisocial behaviour (ASB) using the Adult Self Report (ASR) questionnaire (Achenbach &

Rescorla, 2003) which is a 34 item questionnaire with each item coded 0 (absent), 1 (somewhat or sometimes true) or 2 (very true). The item 'I have never been arrested' was excluded as it referred to lifetime behaviour (baseline $\alpha = .75$). In addition to a total ASB score, a high ASB score was defined as a scale score of 1 standard deviation above the sample mean (≥ 13) as there is no established cut-point for this scale.

Parent alcohol use: Alcohol use was measured using a self-report questionnaire, the Alcohol Use Disorders Identification Test (AUDIT) (Saunders, Aaland, Babor, De La Fuente, & Grant, 1993) which is a 10 item questionnaire assessing harmful drinking within the last year. Each item is scored 0 (never) to 4 (e.g. daily or almost daily) to create a total AUDIT score (baseline $\alpha = .78$). Harmful drinking was coded according to established criteria of scores of 13 or more for women (Saunders et al., 1993).

Number of parent co-occurring clinical problems: An index of 'co-occurring problems' was created to tap the breadth of co-occurring psychopathology currently experienced by the parents with recurrent depression. The number of problems (anxiety, ASB, and harmful drinking) that reached the thresholds outlined above were summed, leading to a maximum of three possible concurrent problems in addition to recurrent depression. Rates of parents reporting 3 co-occurring problems were low ($n = 6$ at baseline), and therefore number of co-occurring problems was categorised as 0, 1, 2 or more.

Household demographics

Mothers rated their family's financial situation on a 5-point scale from 'living comfortably' to 'finding it very difficult to make ends meet'. This was dichotomised to identify families 'finding it difficult' or 'finding it very difficult' to make ends meet.

Child psychopathology

Child disorder: Child psychiatric disorder was assessed at baseline and at each follow-up using parent and child versions of the Child and Adolescent Psychiatric Assessment (CAPA) (Angold & Costello, 2000). This is a semi-structured research diagnostic interview providing a detailed assessment of child psychopathology over the preceding three months. The study considered DSM-IV diagnoses of depressive disorders (major depressive disorder, dysthymia, and depression not otherwise specified (NOS)), anxiety disorders (generalised anxiety disorder, separation anxiety, social phobia, panic disorder, agoraphobia, and obsessive compulsive disorder), disruptive behaviour disorders (DBD; oppositional defiant disorder, conduct disorder, and disruptive behaviour NOS), and attention deficit hyperactivity disorder (ADHD). Eating disorders, cyclothymia, and bipolar disorder were also assessed.

Regular supervision meetings were provided by two child and adolescent psychiatrists (AT, RP). Parent interviews and child interviews were considered separately. All children reaching diagnostic criteria for DSM-IV or ICD-10 (American Psychological Association, 1994; World Health Organisation, 1993) and subthreshold cases were reviewed by AT and RP.

Inter-rater reliability compared interviewer ratings of the presence or absence of psychiatric disorder for 20 CAPA interviews (10 parent-rated and 10 child-rated) at each time point. Agreement for the presence of offspring psychiatric disorder was excellent (average $\kappa = .92$). For the present thesis a disorder was considered to be present if a DSM-IV diagnosis was made according to information from either the parent or child interview. Rates and type of psychiatric disorder in offspring at each assessment are presented in Appendix 1.

Child new onset cases: The current thesis utilised the longitudinal data to consider risk markers for psychopathology as it developed. New onset cases were defined as the

presence of a DSM-IV psychiatric diagnosis in offspring at either of the two follow-up assessments, where there was no diagnosis at baseline. Where analyses were predicting new onset disorder (chapter 3) analyses were restricted to the subsample of children without a psychiatric disorder at baseline.

Child symptomatology; depression, anxiety, disruptive behaviour: The CAPA was used to assess dimensional DSM-IV counts of depression, anxiety and disruptive behaviour disorder (DBD; conduct disorder and oppositional defiant disorder). These were calculated using a combination of parent and child reports; where a symptom was reported by either the parent *or* the child, the symptom was considered to be present. The current thesis considered the number of DSM-IV symptoms of depression, generalised anxiety disorder, and disruptive behaviour disorder.

Inter-rater reliability assessed the agreement between raters for symptoms of depression and DBD in offspring for both parent and child interviews. Agreement between raters was excellent for child reports of depression symptoms (average $\kappa = .90$) and child reports of DBD symptoms (average $\kappa = .93$), as were parent reports of offspring depression (average $\kappa = .96$) and DBD symptoms (average $\kappa = .95$).

Parent warmth and hostility

Parent warmth and hostility towards the child were assessed via two methods using self-report questionnaire-based and interview-based measures.

Questionnaire: Parent warmth and hostility were assessed using the Iowa Youth and Families Project (IYFP) family interaction rating scales (Melby et al., 1993), a ten item self-report questionnaire. It contained two subscales assessing hostility (four items) and low warmth (six items) directed towards the study child. Each item was coded 1 - 7 with higher scores indicating higher hostility and lower warmth (hostility Time 2: $M = 12.42$, $SD = 4.20$, $\alpha = .89$; hostility Time 3: $M = 12.08$, $SD = 4.51$, $\alpha = .84$; warmth Time

2: $M = 12.61$, $SD = 6.80$, $\alpha = .93$; warmth Time 3: $M = 12.72$, $SD = 6.92$, $\alpha = .94$).

Warmth items were then reverse coded so that higher scores were indicative of higher warmth.

Interview measure: The study used a modified version of the five minute speech sample (FMSS) of expressed emotion developed by Caspi et al (2004) to assess parent warmth and hostility. Parents were asked to describe their child. They were encouraged to speak freely but a series of prompt questions were utilised to elicit responses. In the current study, two additional prompts were included to elicit responses relevant to the construct of resilience (see Table 2.1).

Table 2.1: Prompt questions from five minute speech sample of expressed emotion (Caspi et al., 2004)

Prompt questions used in the FMSS
Can you tell me what X is like?
What are they like compared to their brother or sister/other children their age?
In what way would you like them to be different?
How do you feel when they are away from you?
How do you feel when you take them out in public?
What are their strengths or good points? **
What is it like being their mum or dad, what are the good things? **

** Additional prompts added in EPAD study

Thirty interviews were randomly selected to assess inter-rater reliability and were coded by a second interviewer, blind to the initial coding of the interviews. Ratings were compared between the first and second rater. Inter-rater reliability for warmth and hostility both showed substantial levels of agreement (warmth at Time 2 $ICC = .69$; Time 3 $ICC = .68$; hostility at Time 2 $ICC = .79$, Time 3 $ICC = .85$). The measure of expressed emotion is described in more detail in Appendix 2, examining components of expressed emotion and its relationship with other variables.

Information from the two measures (EE and IYFP) was combined to create a robust measurement of the parent-child relationship constructs of hostility and warmth. The two measures of warmth (EE and IYFP) were moderately correlated ($r = .30, p = <.001$), as were the two measures of hostility ($r = .36, p = <.001$). A composite score of maternal warmth, and a composite score of maternal hostility were created from the IYFP and EE in order to utilise information from both interviewer-rated and maternal questionnaire reports. The subscales of hostility and warmth from each measure of parenting were first standardised using z-score transformations and then combined: the z-scores of hostility from each parenting measure were added together to create a composite measure of maternal hostility as were the z-scores of warmth.

Both the IYFP and EE had high levels of reliability. Although the reliability estimate for the EE measure of warmth was lower than compared to EE hostility, and IYFP measures of reliability, estimates still demonstrated substantial levels of agreement.

It should be noted that the overlap between EE and IYFP was modest. Information regarding parenting is often modest when obtained from different sources (Winsler, Madigan, & Aquilino, 2005). The EE and IYFP were combined to create a robust multi-informant measure of the mother-child relationship. Multiple methods such as this are useful for understanding complex phenomena; they can provide information about different aspects of a phenomenon and therefore improve understanding (Kendler, Myers, & Prescott, 2000). They are also the gold standard for research as well as clinical practice. It is possible that using either measure alone could change the strength of relationships observed, although the direction of associations would be unlikely to change.

5. Sample characteristics

Sample at baseline

Demographics and details of parent and child psychopathology are outlined in Table 2.2. The majority of parents recruited in the study were mothers. A small majority of offspring were female. Most offspring lived in two-parent households (70.4%); this is comparable with a recent UK epidemiological survey where 68% of children were living in two-parent households (Beaumont, 2011). Over one quarter of parents reported a low household income. All parents had a history of recurrent depression (at least two previous episodes), and almost one quarter of parents met criteria for major depressive disorder at the time of interview, with over 40% reporting additional psychopathology. Almost one quarter of offspring met criteria for DSM-IV psychiatric disorder.

Differences between retained and not retained sample

Table 2.2 also presents demographics, parent psychopathology and offspring symptomatology of families participating at either follow-up. Chi-square and t-tests considered whether there were any significant differences between families who participated at either follow-up ($n = 324$) and those who declined at both follow-up assessments ($n = 11$). Families who did not participate at either follow-up were significantly more likely to report higher parental ASB symptoms ($F(1) = 4.57, p = .033$) and higher offspring DBD symptoms ($F(1) = 4.73, p = .030$). There were no other significant differences between those who completed either follow-up and those who declined both follow-ups.

Depressed mothers only

In this thesis all analyses are conducted with depressed mothers only as the index parent, given the small number of fathers ($n = 22$). Restricting the sample to mothers resulted in a sample similar to the whole sample in terms of parent and child age, child

gender, family type, household income, and parent and child symptomatology (see Table 2.2).

Mothers who did not participate at either follow-up were significantly more likely to report higher ASB symptoms ($F(1) = 6.42, p = .012$) and their offspring had higher DBD symptoms ($F(1) = 7.33, p = .007$). There were no other significant differences between those who completed either follow-up and those who declined both follow-ups.

Table 2.2: Sample demographics, features of parent depression and co-occurring symptomatology amongst retained and non-retained families at each follow-up assessment, and at either follow-up.

Baseline characteristics	Baseline Sample	Families participating at either follow-up assessment ⁱ	Mothers baseline sample	Mothers participating at either follow-up assessment ⁱ
Total % (n)	100% (335)	96.7% (324)	100% (315)	96.2% 303
Baseline Demographics				
Mean parent age (SD)	41.61 (5.45)	41.68 (5.42)	41.26 (5.38)	41.32 (5.33)
Parent gender % female	93.5%	93.5%	100%	100%
Mean child age (SD)	12.40 (2.01)	12.38 (2.02)	12.35 (2.00)	12.32 (2.00)
Child gender % female	58.5%	59.3%	58.4%	59.1%
Family Type				
Both biological parents	57.0%	59.0%	55.6%	57.4%
Mother and step-father	13.1%	11.7%	14.0%	12.5%
Father and step-mother	0.3%	0.3%	-	-
Mother only	27.6%	27.2%	29.5%	29.0%
Father only	1.2%	0.9%	-	-
Other	0.9%	0.9%	-	-
			1.0%	1.0%
Financial Hardship	26.8%	27.2%	27.3%	27.7%
Parent Psychopathology at Baseline				
Depressed at interview %	23.8%	24.1%	23.2%	23.5%
Mean depression severity (SD)	16.62	16.45	16.53	16.36

Baseline BDI ^a	(11.19)	(11.16)	(11.22)	(11.17)
Mean anxiety score (SD)	9.25	9.22	9.26	9.21
Baseline HADS ^b	(4.53)	(4.51)	(4.52)	(4.50)
Mean Antisocial behaviour (SD)	7.80	7.66	7.57	7.58
Baseline ASR ^c	(5.01)	(4.91)	(5.00)	(4.88)
Mean alcohol use score (SD)	5.47	5.45	5.38	5.34
Baseline AUDIT scale ^d	(5.13)	(5.11)	(5.06)	(5.03)
Any co-occurring psychopathology ^e	44.7%	44.8%	44.2%	44.1%

Child Characteristics

IQ ^f	94.95	95.13	94.97	95.18
	(12.83)	(12.95)	(12.53)	(12.64)
Child Psychopathology ^g	23.7%	21.6%	21.0%	20.8%
Mean depression symptoms (SD) ^h	1.69	1.68	1.67	1.66
	(1.86)	(1.85)	(1.84)	(1.83)
Mean anxiety symptoms (SD) ^h	1.97	1.96	1.94	1.92
	(2.76)	(2.74)	(2.69)	(2.65)
Mean disruptive behaviour disorder symptoms (SD) ^h	3.04	2.99	3.05	2.99
	(2.48)	(2.44)	(2.46)	(2.41)

^a Beck Depression Inventory

^b Anxiety subscale of the Hospital Anxiety and Depression Scale

^c Adult Self Report

^d Alcohol Use Disorders Identification Test (AUDIT)

^e Number of co-occurring problems in the parent; anxiety, antisocial behaviour and harmful drinking, in addition to parent depression severity

^f IQ assessed using the Wechsler Intelligence Scale for Children-IV (WISC-IV) (Wechsler, 2003)

^g Presence of any psychiatric disorder (reported by parent or child) from Child and Adolescent Psychiatric Assessment (CAPA) (Angold & Costello, 2000)

^h DSM-IV symptoms of psychopathology in offspring reported by parent or child from CAPA (Angold & Costello, 2000)

ⁱ Families completed any assessments (questionnaires and/or interview assessments) at either follow-up

6. Analysis

Linear and logistic regression analyses used SPSS 16 unless stated otherwise. Mean imputations were conducted where there were one or two missing items on parent questionnaires (BDI, HADS, ASR, AUDIT) and where there was one missing item for offspring symptom counts (depression, anxiety, and DBD). Symptom counts that were not normally distributed were transformed prior to analysis using natural log transformations. Due to missing data on key variables, where specified in the thesis, multiple imputation was conducted. For the first results chapter core analyses were confirmed using multiple imputation (MICE procedure with 10 imputed datasets) with assistance from Doctor Stephan Collishaw using STATA (StataCorp, 2007). For subsequent results chapters multiple imputation was conducted in NORM (Schafer, 1999) for models conducted in MPLUS (Muthén & Muthén, 1998) with the assistance of Doctor Kit Elam.

Path analysis

Path analysis examines the relationship between several related constructs simultaneously. Variables of interest can be both a predictor and an outcome. Path analysis tested whether putative risk factors (maternal depression severity and co-occurring psychopathology) demonstrated any specificity of risk for offspring symptomatology. Path analysis allows multiple dependent (outcome) variables to be included in the model, thus allowing for co-occurring offspring psychopathology to be modelled (e.g. figure 2.3). Pathways (β^1 , β^2 , β^3 in figure 2.3) are each estimated simultaneously to test the specificity of risk to offspring symptomatology. Path analyses were conducted with the assistance of Doctor Stephan Collishaw, Professor Gordon T. Harold and Doctor Kit Elam.

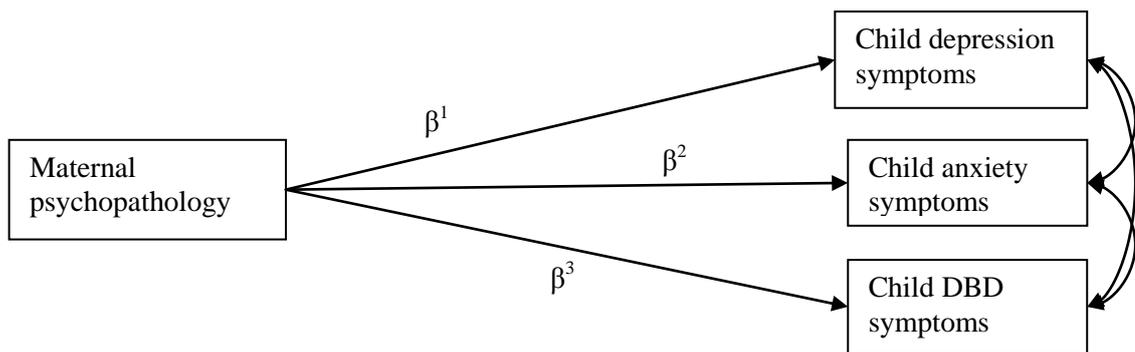


Figure 2.3: Example of a model testing the association between maternal psychopathology and offspring symptomatology

Where path analyses were conducted, model fit statistics were used to test competing models. Fit statistics used in the current thesis were: Chi-square test (χ^2), Confirmatory Fit Index (CFI); Root Mean Square Error Approximation (RMSEA), and Standardised Root Mean Square Residual (SRMR). Good model fit was indicated by a non-significant χ^2 statistic, a CFI fit of more than .98, an RMSEA fit statistic of less than .05, and an SRMR close to zero (Kline, 2005).

Mediation analysis: assessing putative mechanisms

Mediation analyses tested whether an association between a risk factor and an outcome was accounted for (mediated) by a postulated third variable (Baron & Kenny, 1986; MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002). There are several stages to test mediation. First, the direct effect between the putative predictor and the outcome is tested (figure 2.4a). Second, the associations between the predictor and the proposed mediator (figure 2.4b), and between the proposed mediator and the outcome are tested (figure 2.4c). Finally, mediation is shown if the direct effect between the predictor and the outcome (x1 to y1) is reduced when all three variables are included, but there are significant effects from x1 to x2, and from x2 to y1 (figure 2.4d). Indirect effects were

estimated with bias-corrected bootstrapping, and were considered significant if the 95% confidence interval did not include zero (MacKinnon et al., 2002). Mediation analyses were conducted in MPlus 6.12 (Muthén & Muthén, 1998).

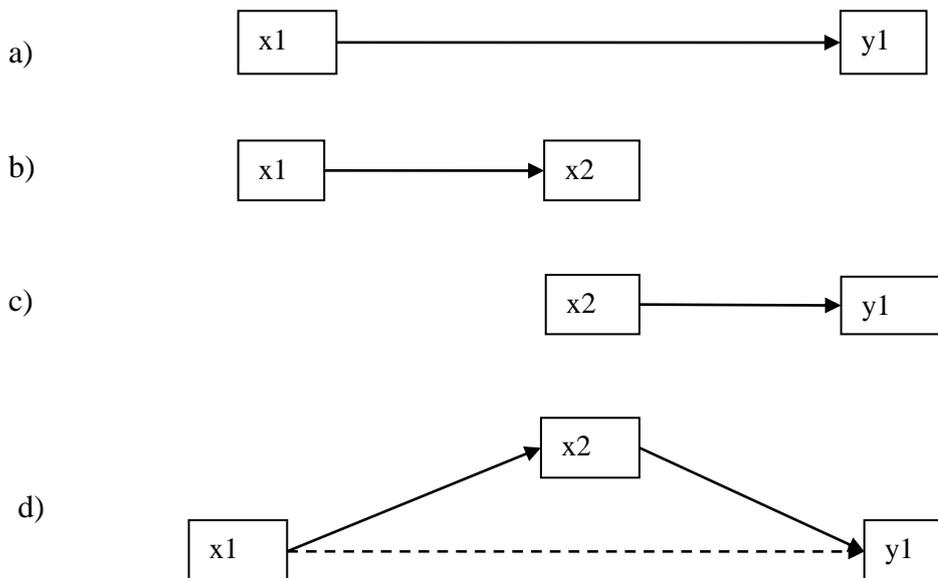


Figure 2.4: Example of steps taken to assess mediation
x1: risk factor
x2: putative mediator
y1: outcome

Testing the direction of effects

Cross-lagged path analysis: Cross lagged path analysis is a form of Structural Equation Modelling (SEM). It utilises longitudinal data to test the direction of effects where associations have been observed between variables. By accounting for reverse causation, variables can be identified as potential causal risk factors. Paths estimate concurrent associations between variables (double headed arrows in figure 2.5), and the stability between variables at different time points (paths γ^1 and γ^2). Paths γ^3 and γ^4 are partial regression coefficients and estimate the contribution of each construct at time one in accounting for each construct at time two whilst controlling for the previous levels of

the constructs (stability coefficients). All paths (depicted in figure 2.5) are estimated, therefore the model can be said to fit the observed data perfectly; no goodness of fit statistics are generated as the model is saturated.

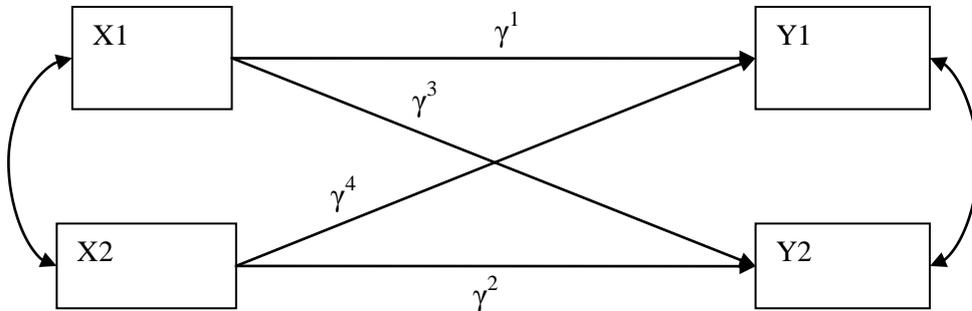


Figure 2.5: Example of a cross-lagged model assessing the direction of effect

Reciprocal effects models: Reciprocal effects models assess the influence of each variable on the other within time (β^1 and β^2 in figure 2.6), whilst simultaneously considering the stability of both variables in the model (γ^1 and γ^2 in figure 2.6). Cross lagged path analyses and reciprocal effects models were conducted in MPLUS (Muthén & Muthén, 1998).

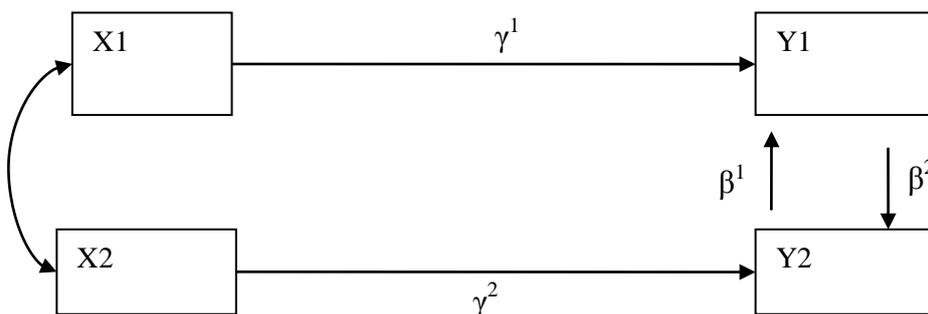


Figure 2.6: Example of a reciprocal effects model assessing the direction of effect

In each chapter of the current thesis, different data were utilised to address each of the study aims. The samples used are summarised below, and explained in detail in each relevant chapter. As stated above, due to the small number, depressed fathers ($n = 22$) were removed from all analyses in the current thesis, and therefore mothers-only were selected ($n = 315/337$), furthermore, parents with a diagnosis of bipolar disorder were also excluded from analyses ($n = 2$). Therefore for the current thesis, the total sample size was 313.

The focus of chapter 3 was on predicting new-onset psychiatric disorder in offspring over the course of the study. Analyses were therefore restricted to the subsample of children without a psychiatric disorder at baseline ($n = 242/313$). Families were required to have complete data on all baseline predictors ($n = 223$). In addition families were required to participate in either of the two follow-ups and have complete data, leading to a final sample size of 209 for chapter 3.

Chapter 4 assessed risk for offspring symptoms of depression, anxiety, and DBD. Data was used from Time 1 and Time 3 of the study. At Time three, 290/313 families participated, with complete interview data on child outcomes available for 260/313 families. Multiple imputation was conducted to generate missing data across relevant datasets, and therefore the analyses were conducted on the full samples of 313 mothers and their offspring.

For chapters 5 and 6, offspring were required to have lived at home for the duration of the study, and therefore 14 families were excluded, leaving an eligible sample of 299/313 at baseline. Analyses for chapters 5 and 6 also required that families participated at all three assessments (91.3%, $n = 273/299$).

Chapter 3

Co-occurring psychopathology in mothers with recurrent depression and risk of psychopathology to adolescent offspring

This chapter has been published:

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Chapter 3. Co-occurring psychopathology in mothers with recurrent depression and risk of psychopathology to adolescent offspring

Abstract

Background: Offspring of mothers with depression are at heightened risk of psychiatric disorder. Many mothers with depression have comorbid psychopathology. How these co-occurring problems affect child outcomes has rarely been considered.

Aims: To consider whether the overall burden of co-occurring psychopathology in mothers with recurrent depression predicts new-onset psychopathology in offspring.

Methods: Mothers with recurrent depression and their adolescent offspring (9-17 years at baseline) were assessed in 2007 and on two further occasions up to 2011. Mothers completed questionnaires assessing depression severity, anxiety, alcohol problems and antisocial behaviour. Psychiatric disorder in offspring was assessed using the Child and Adolescent Psychiatric Assessment.

Results: The number of co-occurring problems in mothers (0, 1, or 2+) predicted new-onset offspring disorder (OR=1.80, 95% CI 1.17, 2.77, $p=.007$). Rates varied from 15.7% to 34.8% depending on number of co-occurring clinical problems. This remained significant after controlling for maternal depression severity (OR=1.73, 95% CI 1.03, 2.89, $p=.040$).

Conclusion: The burden of co-occurring psychopathology amongst mothers with recurrent depression indexes increased risk of future onset of psychiatric disorder for

offspring. This knowledge can be used in targeting preventative measures in children at high risk of psychiatric disorder.

Declaration of Interest: Dr Daniel Smith has received honoraria for speaking at educational meetings organized by AstraZeneca and Lilly.

Introduction

Children of depressed mothers are at an increased risk of developing psychopathology, with a two to five fold increase in risk compared to offspring of non-depressed mothers (Singh et al., 2011; Weissman, Pilowsky, et al., 2006). However, there is much heterogeneity in outcome and it is important to better understand which aspects of maternal illness are associated with elevated risk for offspring (Avenevoli & Merikangas, 2006) as this will help better target preventative interventions to those at greatest risk of developing psychopathology.

Features of depressive illness in mothers (such as severity and chronicity) explain some of the variation in risk for psychopathology in offspring (Hammen & Brennan, 2003; Mars et al., 2012; Silberg et al., 2010; Tully et al., 2008). However, depression is often accompanied by additional psychopathology (Rohde et al., 1991) of which the most common are anxiety (Brown et al., 2001), antisocial behaviour (Zoccolillo, 1992) and substance misuse (Grant & Harford, 1995; Swendsen & Merikangas, 2000). These comorbid problems have each been associated with increased impairment in the affected adult, and with more severe depression symptoms compared to depression alone (Kessler et al., 1999; Kim-Cohen et al., 2005; Moffitt et al., 2007). Understanding of implications of these co-occurring problems in mothers for psychopathology in their offspring is limited.

Importantly, it is not yet known whether co-occurring psychopathology in mothers with depression indexes risk of child psychopathology in addition to severity of maternal depression. If co-occurring psychopathology in adults with depression is a separate index for a more severe familial depression phenotype this would be important in guiding intervention strategies for high-risk children.

Recent research by McLaughlin et al (McLaughlin et al., 2012) utilised data from the World Mental Health surveys, selected to be nationally or regionally representative, and demonstrated that total number of maternal disorders (depression, panic disorder, generalised anxiety disorder, substance dependence and antisocial personality disorder) increased risk for a psychiatric disorder in offspring. A complementary approach is to assess psychopathology in a high-risk group of mothers with recurrent depression and their offspring.

We utilised data from a longitudinal study of children of mothers with recurrent depression. Longitudinal research is scarce, but particularly informative; it is possible to assess the impact of maternal depression and additional problems on offspring psychopathology *as it develops*. Thus risk markers for the onset of psychopathology in offspring can be identified.

The primary aim of the study was to investigate whether the number of co-occurring clinical problems (anxiety, antisocial behaviour, and harmful drinking) in mothers with recurrent depression indexed increased risk of new-onset psychopathology in offspring, and whether any increased risk found was independent of variation in maternal depression severity. We hypothesized that comorbid problems in mothers with recurrent depression would increase risk of psychopathology in offspring over and above any association with maternal depression severity.

Methods

Participants

Analyses utilised data from the three-wave ‘Early Prediction of Adolescent Depression’ (EPAD) study, an observational community study of the offspring of parents with recurrent depression. Parents were recruited predominantly from primary care in South Wales, UK on the basis of treatment for at least two episodes of depression (78%);

from a previous community study of recurrent unipolar depression (19%); and from additional sources such as posters within primary care settings (3%). Participants did not differ on predictor or outcome variables according to the sampling method.

A history of recurrent depression in the parent (2 or more episodes of DSM-IV major depression) (American Psychological Association, 1994) was confirmed at interview. Families were excluded if the parent had a diagnosis of bipolar disorder during screening or at interview, the depressed parent was not biologically related to the child, the child did not live at home at baseline, or the child had moderate to severe intellectual disability ($IQ < 50$).

To provide coverage over the whole of adolescence across the course of the study, families were selected if children were aged between nine and seventeen years at the first assessment. Where there was more than one eligible child per household, the youngest child was selected given the focus on new-onset child psychopathology over adolescence, and to avoid bias in parental selection of children.

The EPAD study includes 337 parents with recurrent depression (315 mothers, 22 fathers; age 26-55 years, mean 41.7 years) and their children (197 females, 140 males; age 9-17 years, mean 12.4 years). Inclusion criteria and retention to follow-up for the present analyses are summarised in Figure 3.1. Given the small number of depressed fathers participating in the study, analyses were conducted with mothers only ($n = 315$). Preliminary analyses identified 73 children (23%) with a disorder at baseline (Table 3.1). This represents a rate in excess of that found in the general population (11.5% for ages 11-16, (Green et al., 2004)). The focus in the present paper was on the prediction of 'new-onset' offspring disorders over the course of the study. Analyses were therefore restricted to the subsample of children without a psychiatric disorder at baseline ($n = 242/315$).

Seventeen further families were excluded due to incomplete data on baseline mother psychopathology and two families were excluded where the affected parent was diagnosed with bipolar disorder by follow-up. Of the eligible baseline sample ($n = 223$), 219 (98.2%) families participated in the first follow-up assessment approximately 16 months later ($SD = 2.69$). A second follow-up was conducted a further 12 months later ($SD = 1.56$); here 214/223 (96.0%) families participated. Only two families declined to participate at both follow-up assessments, with a further 12 families having incomplete data. Therefore complete data was available on child outcomes for 209/223 (93.7%) families.

Those with missing data at either follow-up ($n = 14$) were compared on key variables to those with complete data ($n = 209$). There were no differences in terms of parent and child age and gender, parental depression age at onset and past impairment, nor number of co-occurring problems. Missing data at follow-up was however associated with higher baseline maternal depression severity (Beck Depression Inventory) (Beck et al., 1979) and with longer duration of previous depressive episodes (Appendix 3).

Procedure

The majority of assessments were conducted in the family home (99.6%) with parents and children assessed by different interviewers. Parents and children were given a description of the study and provided written informed consent, or written assent (if under 16 years of age). Assessments lasted approximately 3 hours and participants were compensated for their time. Interviewers were aware that all parents had a history of recurrent depression but were blind to any additional clinical problems in parents and child psychopathology. Interviewers were trained psychology graduates supervised weekly by psychiatrists. Ethical approval was provided by the Multi-Regional Ethics Committee.

Measures

Maternal Depression: A semi-structured interview, the Schedule for Clinical Assessment in Neuropsychiatry (Wing et al., 1990) was used to establish the presence of DSM-IV major depression over the preceding month. Twenty one percent (47/223) of mothers met criteria for a major depressive episode at baseline.

Mothers completed the Beck Depression Inventory (BDI) (Beck et al., 1979) to assess severity of symptoms of baseline depression. The BDI is a 21-item questionnaire with each item scored 0 to 3 according to severity of symptoms that day, with a maximum score of 63. A total depression severity score was calculated (range = 0-49, mean = 15.48, SD = 10.64, alpha = 0.91).

At the baseline assessment mothers also provided information on the clinical features of their past depressive episodes. A detailed description is provided by Mars et al (Mars et al., 2012). Briefly, mothers provided information about age at first episode of depression, number of episodes, and duration of each episode. They also rated impairment during worst and second-worst depressive episodes using the Global Assessment of Functioning scale (American Psychological Association, 1994) according to functioning in psychosocial, occupational, and relationships domains, with scores ranging 0 to 100 (lower scores indicating greater impairment).

Maternal Anxiety: Maternal anxiety was assessed using the Hospital Anxiety and Depression Scale (HADS) anxiety subscale (Zigmond & Snaith, 1983). Seven items were scored from 0 to 3 according to severity of anxiety symptoms over the preceding week. A total anxiety symptom score was calculated (alpha = 0.82). A dichotomous variable was created using the previously validated cut-off score of 11 or more, indicative of clinically significant anxiety (Zigmond & Snaith, 1983).

Maternal Antisocial Behaviour: Mothers reported on their own current ASB using 33 items of the 34-item Adult Self Report (ASR) questionnaire (Achenbach & Rescorla, 2003) with items coded 0 (absent), 1 (somewhat/sometimes true) or 2 (very true). The item 'I have never been arrested' was excluded as this item referred to lifetime behaviour. A total ASB score was calculated (observed range 0-23, alpha=0.75). A dichotomous variable was created using a cut-off of 1 standard deviation above the sample mean (≥ 13) as indicative of significant ASB symptoms as there is no established cut-point for this scale.

Maternal Alcohol Use: Alcohol Use was measured using the widely used and well-validated Alcohol Use Disorders Identification Test (AUDIT) (Saunders et al., 1993), a 10 item questionnaire assessing harmful drinking within the last year. Each item is scored 0 to 4 and a total AUDIT score was calculated (observed range = 0-25, alpha = 0.78). Harmful drinking was coded according to established criteria for women of a score of 13 or greater (Saunders et al., 1993).

Number of Maternal Co-occurring Clinical Problems at Baseline: An index of 'co-occurring problems' was created to tap the breadth of co-occurring psychopathology currently experienced by mothers with recurrent depression. The number of problems (anxiety, ASB, and harmful drinking) that reached the thresholds outlined above were summed, leading to a maximum of three possible concurrent problems in addition to recurrent depression. At baseline 59.6% mothers ($n = 133/223$) reported no concurrent problem, 28.7% ($n = 64$) mothers reported one concurrent problem, 10.8% ($n = 24$) reported two concurrent problems, and 0.9% mothers ($n = 2$) reported three concurrent problems. Analyses compared those with recurrent depression only, one additional clinical problem or multiple additional problems (two or three additional clinical problems; 11.7%, $n = 26$).

Child Psychopathology at Follow-up: Child psychiatric disorder was assessed using parent and child versions of the Child and Adolescent Psychiatric Assessment (CAPA) (Angold & Costello, 2000), a semi-structured research diagnostic interview providing a detailed assessment of child psychopathology over the preceding three months. The study considered DSM-IV diagnoses of depressive disorders (major depressive disorder, dysthymia, depression not otherwise specified (NOS), and adjustment disorder), anxiety disorders (generalised anxiety disorder, separation anxiety, social phobia, panic disorder, agoraphobia, and obsessive compulsive disorder), disruptive behaviour disorders (DBD; oppositional defiant disorder, conduct disorder, and disruptive behaviour NOS), and attention-deficit hyperactivity disorder (ADHD). Eating disorders, cyclothymia, and bipolar disorder were also assessed. Inter-rater reliabilities for child disorder were excellent (average kappa =.92). Case notes on individuals reaching diagnostic criteria and subthreshold cases were reviewed by two consultant child psychiatrists and DSM-IV diagnoses were agreed by consensus. A disorder was considered to be present if a diagnosis was made by either the mother or child interview (Angold & Costello, 1995). New-onset cases were defined where children received a DSM-IV psychiatric diagnosis at either of the two follow-ups, but not at baseline.

Household demographics: Family poverty and maternal education were assessed by parental self-report questionnaire, and family type (single or two-parent) was assessed at interview. Mothers rated their family's financial situation on a 5-point scale from 'living comfortably' to 'finding it very difficult to make ends meet'. This was dichotomised to identify families 'finding it difficult' or 'finding it very difficult' to make ends meet.

Analysis

Preliminary linear regression analyses assessed whether maternal depression severity (BDI score) was associated with the number of maternal comorbid clinical problems at baseline.

Primary aim: Binary logistic regression analyses tested the prospective association between number of co-occurring problems and new-onset child disorder at follow-up. Analyses were repeated controlling for mother depression severity (BDI) at baseline. Results are described as odds ratios with 95% confidence intervals. Odds ratios represent the average increase in risk across each step of the three-level predictor (0, 1, 2+ co-occurring problems).

Sensitivity analyses: Additional sensitivity analyses examined the robustness of findings.

(a) Social adversity may be an important confounding factor. Regression analyses considered whether family financial difficulty was associated with maternal depression severity, the number of co-occurring psychopathology, and child new-onset disorder.

(b) We tested whether past course and severity of parents' depressive illness might act as additional confounders of the relationship between co-occurring parent psychopathology and child new onset disorder over and above any effect of baseline parent depression severity. Analyses assessed associations between several maternal depression features (age of onset, average episode duration, average impairment) and (i) the number of maternal co-occurring problems at baseline (0, 1, 2+), and (ii) new-onset child disorder, in each case controlling for baseline maternal depression severity.

(c) The CAPA uses a three-month time frame and therefore some episodes of illness may have been missed. This may be a particular concern in relation to depression given its episodic course. For example, some children may have experienced an episode of depression at some point between assessments but not in the three months prior to

interview. We may also have incorrectly classified some children as new-onset cases if we had missed episodes of depression prior to baseline. The retrospective DSM-IV depression symptom checklists carried out at each interview allowed us to address these possibilities. Two children who we had not classified as new-onset cases reported significant depression symptoms (5+) after baseline but not at interview at either follow-up. Conversely, five children who had been classified as new-onset cases had in fact reported significant symptoms of depression (5+) prior to baseline. Analyses were repeated (i) excluding the 5 children with possible depression prior to baseline and (ii) including the 2 additional possible new-onset depression cases. As noted below, results were unchanged.

All analyses included child (baseline) age and gender as covariates. Analyses were conducted using STATA version 10 for Windows using multiple imputation (multivariate imputation by chained equations (MICE) procedure with 10 imputed datasets (Royston, 2009)) to account for incomplete data at follow-up in a small number of cases. For clarity and ease of interpretation, non-imputed numbers and percentages are presented. A p-value of $\leq .05$ was used as the established significance level.

Results

Co-occurring Psychopathology in Mothers with Recurrent Depression

Table 3.2 shows characteristics of psychopathology in mothers at baseline and sample demographics. Forty percent of this sample of mothers with recurrent depressive disorder also had significant other problems – anxiety, ASB, and/or harmful drinking. The number of co-occurring clinical problems in the mothers was associated with maternal depression severity as measured by the BDI at baseline ($\beta = .86$, $b = 9.38$, 95% CI 7.82, 10.97, $p = <.001$). On average each additional co-occurring clinical problem was associated with a 9.4 point increase in BDI score at baseline.

New-Onset Offspring Psychiatric Disorder

Among children free of disorder at baseline, 21.1% (44/209) experienced new-onset disorders across the follow-up period. These included 14 depressive disorders, 28 anxiety disorders (excluding specific phobia), 18 disruptive behaviour disorders, and 3 adjustment disorders. Rates of new-onset disorder by age and gender are summarised in Table 3.3.

Does the number of co-occurring problems in mothers predict new-onset disorder in offspring?

Figure 3.2 shows that at follow-up, rates of new-onset disorder in offspring increased according to the number of additional clinical problems in mothers and varied from 15.7% to 34.8% (no clinical problems vs. 2+ clinical problems). The number of additional clinical problems in the mother (0, 1, 2+) was associated with new-onset offspring disorder (OR = 1.80, 95% CI 1.17, 2.77, $p = .007$). This association remained after adjusting for baseline maternal depression severity (OR = 1.73, 95% CI 1.03, 2.89, $p = .040$).

The majority of new-onset cases of disorder (54.5%, 24/44) occurred in children whose mothers reported at least one comorbid problem (8/14 depressive disorder; 14/28 anxiety disorder, 12/18 disruptive behaviour disorder). Small sample sizes precluded separate testing for association between mothers' additional clinical problems and each child diagnostic group.

Sensitivity analyses

(a) Over one quarter of mothers described themselves as having financial difficulties. Those in financial difficulties reported higher depression severity ($\beta = .28$, b

= 6.64, 95% CI 3.56, 9.72, $p < .001$) and increased co-occurring psychopathology ($\beta = .15$, $b = .24$, 95% CI .03, .44, $p = .026$). However, financial hardship did not significantly predict new-onset disorder in offspring after adjusting for baseline severity (OR = .94, 95% CI 0.43, 2.07, $p = .875$).

(b) We tested severity and course of parents' depressive illness prior to baseline as additional potential confounders. Number of co-occurring problems (0, 1, 2+) in mothers with recurrent depression was associated with a younger age of depression onset (but not longer episode duration or greater impairment) when accounting for baseline maternal depression severity (Appendix 4). However maternal age of onset of depressive disorder did not significantly predict new-onset disorder in offspring (OR = .96, 95% CI 0.92, 1.00, $p = .071$, adjusting for baseline severity).

(c) Five children reported possible depression prior to the baseline assessment (five or more symptoms of depression). After excluding these cases from analyses primary findings were unchanged; parent co-occurring problems remained significantly associated with future disorder in offspring after adjusting for maternal depression severity (OR = 2.37, 95% CI 1.23, 4.57, $p = 0.01$). Two additional children reported possible depression between baseline and follow-up assessments. Including these 2 children as new onset cases also made no difference to the findings (OR = 1.87, 95% CI 1.05, 3.32, $p = 0.033$).

Discussion

It is well-established that offspring of mothers with depression are at elevated risk of developing depression and other psychiatric disorders. It is less clear how far risk for offspring psychopathology reflects the presence of co-occurring maternal psychiatric problems such as anxiety, ASB or problem drinking. The current study utilised a longitudinal high-risk sample of offspring of mothers with recurrent depression and

considered prospective associations between additional parent clinical problems (anxiety, ASB, and harmful drinking) and new-onset offspring psychiatric disorder.

Co-occurring psychopathology in mothers was common and was associated with increased severity of adults' own depression symptoms, consistent with previous research (Coryell et al., 2012; Kessler et al., 1999; Kim-Cohen et al., 2005; Moffitt et al., 2007). Co-occurring psychopathology in mothers was a strong predictor of future disorders in offspring; in this sample more than half of new-onset disorders in offspring occurred for the subgroup of depressed mothers with other clinical problems. This association remained even when mothers' baseline depression severity was controlled for.

Age at onset, chronicity, and past severity of parent depression have been found to be associated with child outcomes in this sample (Mars et al., 2012) and previous studies (Hammen & Brennan, 2003). We therefore considered whether these other characteristics of maternal depression accounted for the increased risk for offspring psychopathology among mothers with co-occurring psychopathology. Age at onset was associated with maternal co-occurring psychopathology, but age at onset did not account for the association between maternal co-occurring psychopathology and the increased risk for offspring new-onset psychopathology. Similarly, differences in reported financial hardship also failed to account for this association.

One possible mechanism is that depression occurring with additional clinical problems indexes higher genetic loading. There is evidence of a shared genetic liability between depression and anxiety, and to a lesser extent depression and alcohol abuse, and depression and ASB (Kendler et al., 1997; Merikangas et al., 1994; O'Connor et al., 1998). Additional clinical problems in the mother may also have detrimental environmentally-mediated effects on children's mental health, for example, through impaired parenting. Previous research has shown that parent depression is associated with impairments in parenting which may, in part, mediate the effect of maternal depression

on child outcome (Goodman & Gotlib, 1999) although findings are not entirely consistent, with other studies suggesting that this link might represent passive gene-environment correlation (Rice, Harold, Shelton, & Thapar, 2006).

Additional clinical problems in parents with depression are associated with increased impairment (Kessler et al., 1999; Kim-Cohen et al., 2005; Moffitt et al., 2007), and this increased impairment may well manifest itself in different ways that have a negative impact on the offspring. There is some evidence that recurrent maternal depression accompanied by other psychopathology is associated with less optimal parenting compared to depression alone, at least in mothers of infants (Carter, Garrity-Rokous, Chazan-Cohen, Little, & Briggs-Gowan, 2001). ASB with depression in mothers has also been found to be associated with less warmth and more hostility compared to mothers with depression alone (Kim-Cohen et al., 2006). How other clinical problems affect parenting is not clearly understood. Future research should consider the mechanisms that may account for the association between comorbid clinical problems in parents with recurrent depression and child psychopathology as this has important implications for prevention and intervention. Intervention studies that target co-occurring mental health problems in parents as well as the treatment of depression would help to identify if this results in benefits to offspring as well as parents.

Strengths

A major strength of the current study is the use of longitudinal data with excellent retention to assess the development of psychopathology in high-risk offspring over time, and thus identify risk markers that are associated with the onset of psychopathology in adolescent offspring. To our knowledge, no previous study has assessed the cumulative burden of clinical problems in mothers with recurrent depression, and the impact on child disorder over time.

Limitations

This study should be considered in light of several limitations. First, the CAPA assesses offspring psychopathology in the preceding three months. We were unable to comprehensively assess lifetime diagnoses for the offspring and thus any diagnoses prior to the baseline assessment, or between baseline and follow-up that subsequently remitted, may have been missed. This may be a particular concern in relation to depression given its episodic course. Additional sensitivity tests did show that findings were unchanged when we excluded a small number of children who at baseline reported high levels of prior depression symptoms or when we included two additional children as new-onset cases based on retrospective reports of symptoms at follow-up. Second, a wide age range of children were included in the study. Not all had passed fully through the period of risk for onset of depression and other disorders, and may go on to develop problems in the future. The study may thus represent an underestimate of the intergenerational risk for psychopathology in this population. Third, only two follow-up assessments were conducted and this combined with variation in follow-up intervals meant it was not feasible to undertake more sophisticated methods such as survival analysis. Fourth, given the already significant burden of interview assessments, it was only possible to assess maternal anxiety, ASB and alcohol misuse using questionnaires rather than diagnostic interviews. Again, it seems likely that findings are somewhat conservative, as co-occurring disorders meeting stringent diagnostic criteria would be expected to be even more strongly associated with offspring disorder. However, self-report measures of mental health are commonly used in primary care and thus the findings of this study are relevant to the contexts where most depressed adults are assessed and treated. The current study did not assess maternal drug misuse, another common co-occurring problem in adults with depression (Swendsen & Merikangas, 2000). Fifth, co-occurring

psychopathology in mothers was independently associated with concurrent depression severity (as measured by the BDI) and an earlier age at depression onset. Analyses suggest that these factors do not account for the observed differences in risk for offspring. However, despite these controls it remains possible that the study has not fully accounted for residual variation in parental depression illness course, severity and impairment. Sixth, The EPAD study consists predominantly of depressed mothers and we were unable to consider whether or not findings extended to offspring of depressed fathers; patterns of co-occurring psychopathology are likely to differ by parent gender. Recent evidence has highlighted the importance of considering paternal depression as a risk for offspring psychopathology in its own right (Ramchandani, Stein, et al., 2008). A related point is that where one parent has depression, psychopathology in the co-parent may further increase risk to offspring (Marmorstein, Malone, & Iacono, 2004). Alternatively, if the co-parent presents with no psychopathology this may act as a protective factor for offspring (Brennan et al., 2002). Finally, many of the children in the current study developed psychiatric disorders other than depression; notably anxiety and disruptive behaviour disorders. It was not possible to delineate and compare risk for specific new-onset disorder types in this study. Further research should consider whether specific co-occurring problems in mothers with recurrent depression can help explain this heterogeneity in risk in offspring. Future research should also consider whether findings are the same or different for children of depressed fathers, the role of the co-parent, as well as address possible mechanisms involved in the link between parent and child psychopathology.

Clinical Implications

Intervention studies suggest that effective treatment of parental depression can reduce child symptomatology (Pilowsky et al., 2008). The current findings highlight the

importance of clinicians also recognising additional psychopathology in mothers with depression as these offspring are at especially high risk of developing psychopathology. These families should be prioritised for prevention and early intervention (Garber et al., 2009).

Tables and figures

Table 3.1: Baseline rates of disorder in offspring of depressed mothers, and new onset of any psychiatric disorder at each follow-up

	Baseline		New onset wave 2		New onset wave 3	
	%	N	%	n	%	n
Any disorder	23.2%	73/315	16.7%	33/198	5.6%	11/197
Depressive disorder	4.8%	15	5.6%	11	1.5%	3
Anxiety disorder	10.8%	34	10.1%	20	4.1%	8
Disruptive behaviour disorder	7.0%	22	6.1%	12	3.0%	6
Bipolar spectrum disorders	0.3%	1	0%	0	0%	0
ADHD	6.3%	20	0%	0	0%	0
Eating disorders	1.0%	3	0%	0	0%	0

Table 3.2: Parent demographics and clinical profile at baseline assessment

	Baseline	
Sample N (mothers)	223 ^a	
Parent age in years (mean, standard deviation)	41.42	(5.56)
	N	%
Financial hardship	59	26.6
University degree	68	30.8
Single parent family	58	26.0
	N	%
Current depression severity		
Minimal (BDI score 0-9)	71	32.1
Mild (BDI score 10 - 18)	80	36.2
Moderate (BDI score 19 - 29)	43	19.5
Severe (BDI score 30 - 63)	27	12.2
Co-occurring maternal clinical problems ^b		
Anxiety problems (HADS \geq 11)	71	31.8
Antisocial Behaviour (ASR $>$ +1SD)	31	14.0
Harmful Drinking (AUDIT $>$ 13)	16	7.2
Number of co-occurring clinical problems		
0	133	59.6
1	64	28.7
2+	26	11.7

^a excluding families where the child had a diagnosis at baseline.

^b All mothers had a diagnosis of recurrent major depression.

Table 3.3: New-onset disorder by child age and gender at baseline in offspring of depressed mothers

Offspring age at baseline	Total		Females		Males	
	n	%	n	%	n	%
9-11	11/80	13.8%	8/49	16.3%	3/31	9.7%
12-14	26/95	27.4%	16/53	30.2%	10/42	23.8%
15-16	7/34	20.6%	4/21	19.0%	3/13	23.1%
Total	44/209	21.1%	28/123	22.8%	16/86	18.6%

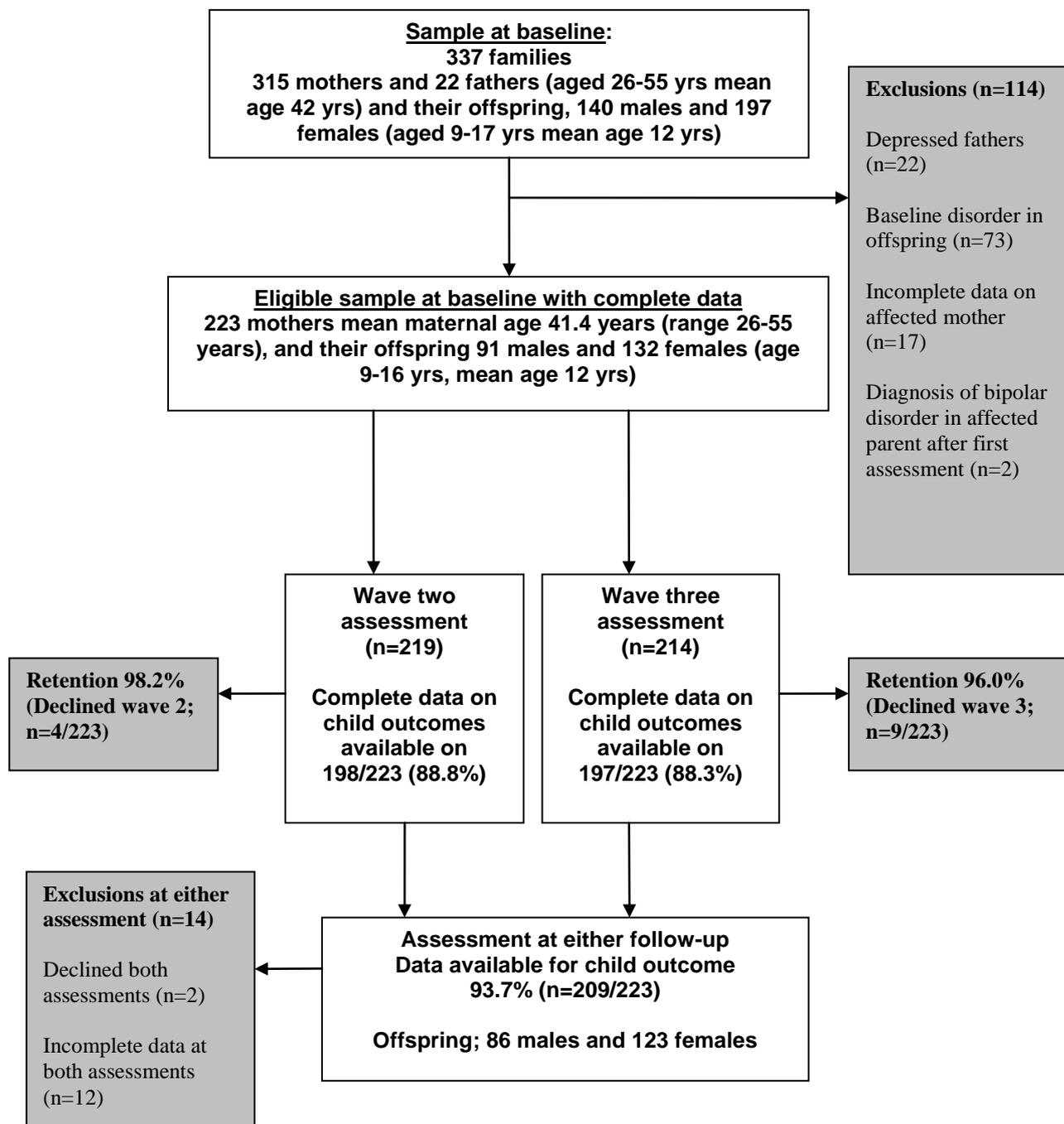


Figure 3.1: Flow chart showing retention at each assessment in the current study

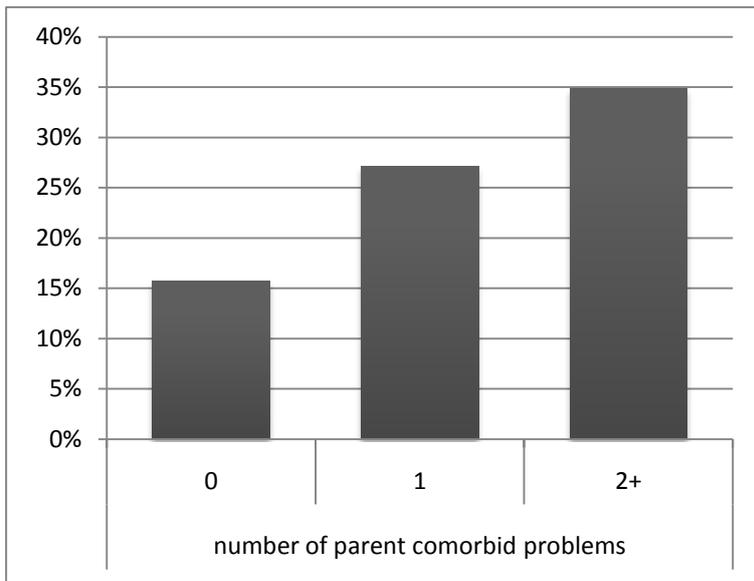


Figure 3.2: Rates of new-onset child psychiatric disorder across follow-up by maternal co-occurring psychopathology

Link section: Co-occurring psychopathology in mothers with recurrent depression and risk of psychopathology to adolescent offspring

The results from the previous chapter highlight that mothers with depression often present with additional psychopathology including anxiety, antisocial behaviour (ASB) and alcohol misuse. The burden of the number of co-occurring psychopathology in mothers with recurrent depression was associated with increased risk for new-onset psychiatric disorder in offspring over and above maternal depression severity, suggesting that it is a risk marker for offspring psychopathology in its own right, rather than simply a marker of maternal depression severity.

The previous chapter focused on risk for new onset of any psychiatric disorder. Offspring of depressed parents are at risk of developing a range of problems including depression, anxiety, and disruptive behaviours (Lieb, Isensee, Höfler, Pfister, et al., 2002; Weissman et al., 1984) and it is important to understand what may account for these heterogeneous outcomes. Co-occurring psychopathology in mothers with recurrent depression may explain, at least in part, the heterogeneous outcomes observed in offspring. However, this has rarely been considered.

Therefore the following chapter examined each maternal co-occurring problem (anxiety, ASB, and alcohol misuse) on risk for offspring symptoms of depression, anxiety and DBD to examine how co-occurring maternal psychopathology was associated with offspring symptomatology. The aim of the following chapter was to test whether specific co-occurring problems in mothers with recurrent depression demonstrated any specificity of risk to offspring, thereby in part, explaining the heterogeneity of outcome in offspring over and above the effect of maternal depression severity.

Chapter 4

Co-occurring symptomatology in mothers with recurrent depression: examining the specificity of risk to offspring

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Chapter 4: Co-occurring symptomatology in mothers with recurrent depression: examining the specificity of risk to offspring

Abstract

Background: Offspring of mothers with depression, especially when maternal depression is accompanied by comorbid problems, are at heightened risk of developing a range of psychopathologies, including depression, anxiety, and disruptive behaviours. Reasons for this heterogeneity in offspring are poorly understood.

Aims: To consider whether co-occurring symptoms of maternal anxiety, antisocial behaviour and alcohol use in mothers with recurrent depression explain the heterogeneity in offspring mental health outcomes after adjusting for maternal depression severity.

Methods: Mothers with recurrent depression and their adolescent offspring (9-17 years at baseline) were assessed three times between 2007 and 2010. Mothers completed questionnaires assessing their own depression severity, anxiety, alcohol problems and antisocial behaviour at Time 1 (T1). Offspring symptoms of depression, anxiety, and disruptive behaviours were assessed using the Child and Adolescent Psychiatric Assessment at Time 3 (T3).

Results: Maternal depression severity at T1 was associated with all child outcomes at T3, but only showed unique association with child depression when co-occurring parent and child problems were taken into account. Maternal antisocial behaviour predicted child disruptive symptoms but not child depression or anxiety when adjusting for maternal

depression severity. Neither maternal alcohol use nor maternal anxiety predicted future offspring symptomatology.

Conclusion: This study highlights that additional clinical problems in mothers may be related to specific maladaptive outcomes in offspring; risk for offspring disruptive behaviours were better explained by co-occurring maternal antisocial behaviour than by variation in severity of maternal depression severity. This has implications for the targeting of intervention and prevention strategies.

Introduction

Children of depressed mothers are at an increased risk of developing a range of psychopathologies including depression, anxiety and disruptive behaviours (Brennan et al., 2002; Lieb et al., 2000; Wickramaratne & Weissman, 1998). What accounts for these heterogeneous outcomes is not well understood.

One possibility is that shared genetic and environmental risk factors associated with maternal depression have an impact on multiple types of offspring psychopathology (Silberg et al., 2010; Tully et al., 2008). Alternatively, mothers with depression may themselves represent a heterogeneous group (Goodman & Gotlib, 1999; Kendler et al., 1999; Weissman et al., 1986); it may be possible to identify subgroups of mothers with varying degrees of risk for specific forms of child psychopathology. Patients with recurrent depression often present with additional psychopathology notably anxiety (Pini et al., 1997), antisocial behaviour (Kim-Cohen et al., 2006; Zoccolillo, 1992), or alcohol misuse (Grant & Harford, 1995; Merikangas et al., 1998; Swendsen & Merikangas, 2000).

One recent study reported that the overall burden of comorbidity in mothers with recurrent depression (anxiety, antisocial behaviour, or alcohol misuse) was associated with increased risk of offspring psychopathology independently of maternal severity of depression (Sellers et al., 2012), but it is not clear whether specific types of co-occurring psychopathology in mothers contributes to the heterogeneity of outcomes in offspring of depressed mothers.

Three possibilities need to be considered. First, co-occurring psychopathology in mothers with recurrent depression may act as a nonspecific risk for offspring mental health with little or no specificity in risk transmission for particular types of psychopathology. For example, co-occurring psychopathology in adults with depression

is associated with increased severity of depression symptoms (Grant & Harford, 1995; Kessler et al., 1999; Kim-Cohen et al., 2005; Moffitt et al., 2007), and increased illness severity is associated with increased risk of offspring psychopathology (Hammen & Brennan, 2003; Janzing et al., 2009). However, our previous research suggests that the burden of co-occurring problems (anxiety, antisocial behaviour, or substance misuse) in mothers with recurrent depression are associated with increased risk for the development of psychopathology in offspring, over and above maternal depression severity (Sellers et al., 2012). This suggests that co-occurring psychopathology in mothers with recurrent depression may not act as a non-specific risk for offspring mental health problems.

Second, intergenerational transmission of risk may show some degree of specificity for broad categories of mental health; for example, ‘internalising’ problems (such as depression or anxiety) in parents may increase risk for similar problems in offspring (Merikangas et al., 1994; Warner et al., 1995), with externalising problems in parents (antisocial behaviour) increasing risk for offspring externalising problems (such as conduct disorder and oppositional defiant disorder) (Kendler et al., 1997). Finally, a third possibility is that specific types of problems in mothers may be associated with the same types of disturbance in offspring (Beidel & Turner, 1997; Biederman et al., 2001; Biederman et al., 2006; Hirschfeld-Becker et al., 2008; Kim-Cohen et al., 2005; Weissman et al., 1993). There is some evidence in support of each of these possibilities but firm conclusions are not possible at present.

A recent cross-sectional community World Health Organisation mental health survey (McLaughlin et al., 2012) found that parent psychopathology of any sort increased offspring risk for psychopathology, with little evidence of specificity of intergenerational risk transmission. However this study did not use a high-risk design and mechanisms may not be the same in offspring of depressed parents.

In contrast, other community studies suggest a distinction in familial risk for two broad dimensions of ‘internalising’ and ‘externalising’ problems (Kendler et al., 2011; Kendler et al., 1997; Kendler, Prescott, Myers, & Neale, 2003; Lahey, Van Hulle, Singh, Waldman, & Rathouz, 2011). High-risk studies have also suggested that there is some degree of specificity for broad categories of mental health in the transmission of risk of psychiatric disorders. Parental depression has been shown to predict both offspring depression and anxiety (Warner et al., 1995), and anxiety problems have also been found to be elevated among relatives of depressed probands compared to controls (Merikangas et al., 1994). These findings highlight the likely overlap in the aetiology and intergenerational transmission of anxiety and depression (Merikangas et al., 1994).

Other family studies have identified a strong degree of specificity, and found that depression and anxiety in parents are more strongly associated with depression and anxiety in children respectively. For example, studies comparing offspring of parents with anxiety, depression, or both (Avenevoli et al., 2001; Beidel & Turner, 1997; Biederman et al., 2001; Biederman et al., 2006) have found that maternal anxiety increased risk for offspring anxiety (regardless of the presence of maternal depression), and that maternal depression increased risk for offspring depression (regardless of the presence of maternal anxiety). The majority of these studies focused on panic disorder as an indicator of parent anxiety (Biederman et al., 2001; Biederman et al., 2006; Weissman et al., 1993), but did not account for anxiety symptoms outside of this diagnostic category.

Two family studies examining the impact of antisocial behaviour (ASB) in mothers with depression are also relevant. These found that disruptive behaviour problems (conduct or oppositional defiant symptoms) were especially elevated in children of mothers with both depression and ASB relative to mothers with depression only (Hirschfeld-Becker et al., 2008; Kim-Cohen et al., 2005). However, these studies

focused only on disorder-specific risk transmission (i.e. the link between parent comorbid antisocial behaviour and offspring disruptive behaviours). It is not clear whether co-occurring ASB in mothers with depression also increases risk for other forms of child psychopathology.

Parent alcohol misuse has also been associated with an elevated risk for disruptive behaviours in offspring (Hussong et al., 2007; Kuperman, Schlosser, Lidral, & Reich, 1999; Reich, Earls, Frankel, & Shayka, 1993) suggesting that there may be a degree of specificity for offspring psychopathology. However, findings are not consistent with associations being found between parent alcohol misuse and offspring anxiety and depression (Kuperman et al., 1999), albeit to a lesser extent. Furthermore, studies have not tested whether problem drinking contributes to risk for child psychopathology observed in parents with recurrent depression.

Previous research findings vary, with relatively little evidence regarding the specificity of the intergenerational transmission of risk for psychopathology to children of depressed parents, and it is therefore difficult to draw firm conclusions as to whether transmission for psychopathology is disorder-specific or disorder-general for offspring of depressed parents. One possible reason for the inconsistency in findings is that there is also often comorbidity in adolescents between depression and other internalising problems, and between depression and behavioural problems (Angold et al., 1999; Avenevoli et al., 2001). Correlations between different disorders in children and adolescents are typically moderate to high, with the association between disruptive behaviours and depression being almost as strongly related as depression with anxiety (Angold et al., 1999). Although this co-occurring psychopathology in children and adolescents is considered to be the rule rather than the exception, it is rarely taken into account in studies of familial risk transmission. Thus, associations found between

specific maternal and child symptoms could reflect other co-occurring offspring psychopathology.

Overall most studies have focused on the transmission of one disorder at a time, making it difficult to detect patterns of transmission of various disorders from parents to offspring. Studies that have assessed several disorders at a time and tested patterns of familial transmission are largely population-based (Kendler et al., 1997; Kendler et al., 2003; Klein et al., 2001; McLaughlin et al., 2012; Merikangas et al., 1994). Therefore, it has been difficult to draw conclusions about the pattern of transmission of psychopathology in offspring of depressed parents. Prospective longitudinal designs allow for the examination of the processes for the inter-generational transmission of risk across time, as well as being able to assess temporal associations to understand risk markers for the development of psychopathology in offspring.

We employed data from a longitudinal study of children of depressed parents to investigate whether specific co-occurring problems (anxiety, ASB, alcohol problems) in mothers with recurrent depression were associated with future risk of specific child symptoms of depression, anxiety, and disruptive behaviour disorder (DBD). The study accounted for the co-occurrence of child symptoms, and for correlated variation in maternal depression severity.

We hypothesized that maternal anxiety symptoms and maternal depression severity would be highly correlated (Merikangas et al., 1994) and that variation in both anxiety symptoms and depression severity in the mother would predict offspring anxiety and depression, but not disruptive behaviours. We also hypothesized that maternal ASB would be associated with a specific risk for offspring disruptive behaviour disorder (DBD) symptoms, and that this would remain significant after adjusting for maternal depression severity. There was insufficient research on the role of alcohol problems in depressed parents to make specific predictions.

Methods

Participants

The current study utilised data from the ‘Early Prediction of Adolescent Depression’ (EPAD) study, a three wave longitudinal study of the offspring of parents with recurrent depression. Parents were recruited predominantly from primary care practices in South Wales, UK. A history of recurrent depression in the parent (2 or more episodes of DSM-IV major depression) was confirmed at interview using the ‘life history calendar’ approach whereby retrospective information is collected, using life events as markers to aid recall (Belli, 1998; Caspi et al., 1996). Families were excluded if the depressed parent was diagnosed with bipolar disorder throughout the course of the study, was not biologically related to the child, or the child had moderate to severe intellectual disability ($IQ < 50$). Children were aged 9 to 17 years old at first assessment.

The sample at baseline consisted of 337 parents with recurrent depression (315 mothers, 22 fathers; age 26-55 years, mean 41.7 years). Because a very small percentage of parents were fathers, depressed fathers were excluded from the current analyses ($n = 22$). Two families were excluded due to a diagnosis of bipolar disorder in the affected parent. The eligible sample in the current study therefore consisted of 313 mothers at baseline (mean age 41.26, range 26 - 55 years) and their children (mean age 12.35 at baseline, range 9-17 years; 58.4% females).

Two follow-up assessments were conducted approximately 16 months ($SD = 2.70$) and 29 months ($SD = 3.59$) after the baseline assessment. The current study utilised data from Time 1 (T1) and Time 3 (T3), with 23 families declining to participate in the final assessment (retention = 92.7%; $n = 290/313$).

Families who declined to participate at T3 were more likely to have higher offspring depression and DBD symptoms at T1, and higher maternal depression severity and ASB scores. Of those who participated at T3, complete data (i.e. no missing data for

any items on child symptomatology at T3) was available for 90% of families (260/290). The Little's test of missing data indicated that the data were not missing completely at random (MCAR). Multiple imputation with data augmentation was used to generate values for missing data across relevant theoretical variables within the proposed model using NORM 2.03 (Schafer, 1997, 1999) which is regarded as the most robust method for multiple imputation (Allison, 2001). Subsequently generated datasets were then tested with Mplus (Muthén & Muthén, 1998). Therefore the current analyses were conducted on the full sample of 313 mothers and their offspring.

Procedure

Assessments were completed in the family home for the majority of cases (99.6%). Parent and child assessments were conducted by different interviewers and in separate rooms where possible. Participants were given a description of the study and provided written informed consent/assent as appropriate. The duration of assessments was approximately 3 hours, and families were compensated for their time. Interviewers were blind to any co-occurring problems in the parents, and to child psychopathology. Interviews were conducted by trained psychology graduates and supervised by psychiatrists at weekly meetings. Ethical approval was provided by the Multi-Regional Ethics Committee.

Measures

Maternal symptomatology at T1: Measures of index parent psychopathology have been described in detail elsewhere (Sellers et al., 2012). Maternal depression severity at baseline was assessed using the Beck Depression Inventory (BDI) (Beck et al., 1979). The BDI is a 21 item questionnaire with each item scored 0 to 3 according to severity of symptoms (e.g. 'I do not feel sad', 'I feel sad much of the time', 'I am sad all the time', 'I am so sad or unhappy that I can't stand it'), with a maximum score of 63 (observed range

= 0 - 49; $\alpha = .91$). Additional clinical problems assessed were anxiety, antisocial behaviour (ASB), and alcohol use.

Maternal anxiety symptoms were assessed using the Hospital Anxiety and Depression 'HADS' anxiety subscale (Zigmond & Snaith, 1983). Seven items (e.g. 'I feel tense or wound up') were scored from 0 to 3 according to severity of anxiety symptoms ('most of the time', 'a lot of the time', 'time to time or occasionally', 'not at all'). A total anxiety symptom score was calculated (observed range = 0 - 20; $\alpha = .82$).

Maternal antisocial behaviour was assessed using 33 items of the 34-item Adult Self Report (ASR) questionnaire the Adult Self Report (ASR) (Achenbach & Rescorla, 2003) with items coded 0 (absent), 1 (somewhat/sometimes true) or 2 (very true). The item 'I have never been arrested' was excluded as this item referred to lifetime behaviour. A total ASB score was calculated (observed range = 0 - 23; $\alpha = .75$).

Maternal alcohol use was assessed using the Alcohol Use Disorders Identification Test (AUDIT) questionnaire (Saunders et al., 1993), a 10-item questionnaire assessing harmful drinking (e.g. How often do you have a drink containing alcohol? 'never', 'monthly or less', '2 - 4 times a month', '2 - 3 times a week', '4 or more times a week'). Each item is scored 0 to 4 and a total AUDIT score was calculated (observed range = 0 - 25; $\alpha = .78$). Higher scores indicated increased severity of symptoms on all measures.

Child symptomatology at T3: Parent and child versions of the Child and Adolescent Psychiatric Assessment (Angold & Costello, 2000), a semi-structured interview, were used to assess child symptoms of depression, DBD and generalised anxiety in the preceding three months.

Child depression symptoms were defined as the presence of DSM-IV depression symptoms (for example low mood/irritability; loss of interest; weight/appetite change) with a possible range of 0 - 9. Child anxiety symptoms were defined as the presence of DSM-IV symptoms of generalised anxiety disorder (for example: excessive worry,

feeling restless or on edge, fatigue, and concentration difficulties) with a possible range of 0 - 15. Child DBD symptoms were defined as the presence of DSM-IV symptoms of oppositional defiant disorder or conduct disorder (for example: bullies, initiates physical fights, defies rules, is angry and resentful, and deliberately annoys others) with a possible range of 0 – 22.

Inter-rater reliability was assessed for offspring symptoms of depression and DBD with excellent agreement for child reports of depression (average $\kappa = .90$) and DBD (average $\kappa = .93$) and for parent reports of offspring depression (average $\kappa = .96$) and DBD (average $\kappa = .95$). Where a symptom was reported by either mother *or* child, the symptom was considered to be present.

Analysis Strategy

Path analysis was employed to examine the relationship between specific indices of maternal psychopathology and offspring symptomatology. Path analysis allows the simultaneous estimation of multiple exogenous (independent) and endogenous (dependent) constructs to be assessed within the context of a single theoretically guided analytic model. The co-occurrence of offspring psychopathology could therefore be modelled, and thus the *unique* effect of each parent predictor on each child outcome (symptoms of depression, anxiety, and DBD) could be estimated simultaneously. The analyses were conducted in several stages.

First, four separate path models were specified and examined to estimate the effects of maternal depression severity, anxiety, ASB, and alcohol use respectively at T1 on child depression, anxiety and DBD at T3, taking into account the correlation between child symptomatology at T3.

Second, path analysis was conducted to estimate the effects of all assessed maternal co-morbid symptoms (anxiety, ASB, alcohol use) at T1 simultaneously on risk

for offspring symptoms of depression, anxiety, and DBD at T3, again taking into account the correlation between child symptoms at this time point. This allowed the estimate of the *unique* effect of each co-occurring problems on risk for specific child outcomes.

Finally, path analyses estimated the effects of maternal co-occurring symptoms on risk for offspring symptomatology after adjusting for maternal depression severity. Only significant co-occurring symptoms in mothers at T1 were considered in this model. Where maternal co-occurring problems did not significantly predict child outcomes, paths from these co-occurring problems were set to zero. To test the model fit, indices used were Chi-square test (χ^2), Root Mean Square Error Approximation (RMSEA), and Standardised Root Mean Square Residual (SRMR). Good model fit was indicated by a non-significant χ^2 statistic, an RMSEA fit statistic of less than .05, and an SRMR close to zero (Kline, 2005). Child symptoms (depression, anxiety, DBD) were not normally distributed and were therefore all transformed using a natural log transformation prior to analyses.

Results

Correlational Analyses

Means, standard deviations, and inter-correlations for all study variables are presented in Table 4.1. Maternal depression severity at baseline was highly correlated with co-occurring maternal anxiety symptoms and moderately correlated with co-occurring maternal ASB symptoms. Maternal depression severity and co-occurring alcohol use showed a small but significant correlation. Co-occurring maternal symptoms were also correlated; there were moderate correlations between maternal symptoms of anxiety and ASB, and ASB and alcohol use, and a small but significant correlation between maternal anxiety and alcohol use.

Maternal depression severity at T1 was correlated with T3 symptoms of depression, anxiety, and DBD in offspring. Maternal anxiety symptoms at T1 were correlated with child symptoms of DBD but not depression or anxiety at T3. Parent ASB symptoms at T1 were correlated with offspring DBD symptoms at T3, but not offspring depression or anxiety. Parent alcohol use symptoms at T1 were not associated with child symptoms at T3. Child symptoms of depression and anxiety were highly correlated. Child DBD symptoms were moderately correlated with child symptoms of both depression and anxiety.

Path analyses

Path analyses first tested the unique associations between each form of maternal psychopathology and child outcomes when accounting for the correlation between child symptoms. Maternal depression severity was associated with all child outcomes (Figure 4.1 panel a). Maternal anxiety symptoms showed no unique association with any child outcomes (Figure 4.1 panel b). Maternal ASB was associated with child DBD symptoms only (Figure 4.1 panel c). Maternal alcohol use was not associated with child symptoms of depression, anxiety, or DBD (Figure 4.1 panel d).

Path analysis then considered the *unique* effect of each maternal co-occurring problem (symptoms of anxiety, ASB and alcohol use) at T1 on child symptoms of depression, anxiety, and DBD at T3 simultaneously. As shown in Figure 4.2, of the co-occurring problems in mothers assessed, only co-occurring maternal ASB was associated with offspring psychopathology; maternal ASB predicted offspring DBD symptoms ($\beta = .15, p = .018$), but not offspring symptoms of depression ($\beta = .03, p = .357$) or anxiety ($\beta = .04, p = .199$). Neither symptoms of maternal anxiety or alcohol misuse (T1) were associated with offspring symptoms of depression, anxiety, or DBD (T3). Therefore, only maternal co-occurring symptoms of maternal ASB were considered for further analyses.

A final model considered whether maternal co-occurring ASB at T1 remained associated with offspring DBD symptoms at T3 after adjusting for T1 maternal depression severity (and the correlation between child outcomes). Paths from maternal anxiety at T1 to child symptoms at T3 were fixed to zero, as were paths from maternal alcohol use at T1 to child symptoms at T3 (i.e. paths from parent anxiety and alcohol misuse to child symptoms were dropped from further analyses and therefore are not shown in Figure 4.3). As shown in Figure 4.3, maternal co-occurring ASB symptoms remained significantly associated with future DBD symptoms in offspring ($\beta = .14, p = .033$), whereas the association between maternal depression severity and offspring DBD was attenuated ($\beta = .10, p = .086$). Maternal depression severity remained associated with offspring depression symptoms ($\beta = .13, p = .037$). This model showed a good fit to the data (model fit statistics: $\chi^2(6) = 5.04, p = >.05$; RMSEA = .01; SRMR = .003).

Discussion

The current study examined whether variation in psychopathology experienced by offspring of depressed mothers could be explained by the additional problems experienced by mothers with recurrent depression. The effect of multiple co-occurring problems in depressed mothers on offspring has rarely been considered. With some notable exceptions (e.g. Merikangas et al 1994; Kendler et al 1997) most previous family studies have focussed on assessing the specificity of transmission of ‘internalising problems’ (anxiety and depression) in offspring of parents with anxiety, depression, or both, or assessed only one disorder at a time in offspring (Avenevoli et al., 2001; Biederman et al., 2001; Biederman et al., 2006).

Findings in this study provide partial support for the hypothesis that specific co-occurring problems in mothers are associated with unique risk effects for specific problem outcomes in offspring. In line with previous family studies of ASB in mothers

with depression, maternal ASB was associated with increased risk for offspring DBD over and above parent depression severity (Hirschfeld-Becker et al., 2008; Kim-Cohen et al., 2005). In the current study we identified that the risk for offspring DBD symptoms was better accounted for by maternal co-occurring ASB, rather than maternal depression severity, highlighting the importance of considering co-occurring ASB in mothers with depression. In addition, although maternal depression severity when considered in isolation was significantly associated with all child outcomes, the association between maternal depression severity and offspring DBD symptoms was attenuated when maternal co-occurring ASB was considered, and maternal depression severity was only significantly associated with offspring symptoms of depression. These findings show support of the specificity of transmission of ASB and depression respectively. However, this interpretation must be considered with caution, given that the associations between maternal depression severity and both offspring anxiety and DBD symptoms were significant at the level of a trend (i.e. they just fall short of significance).

In contrast, maternal anxiety was not uniquely associated with any child outcome. This differs from previous studies suggesting that maternal anxiety and depression may specifically predict anxiety and depression respectively. However, these studies assessed panic disorder rather than a broad measure of anxiety severity (Biederman et al., 2001; Biederman et al., 2006; Warner et al., 1995). Patterns of transmission may differ by different types of anxiety disorders (Cooper, Fearn, Willetts, Seabrook, & Parkinson, 2006; Rutter et al., 2006). In the current study, a high correlation between anxiety and depression was observed, but maternal depression severity and anxiety did not index equivalent risk effects in offspring.

In the current study we found no associations between maternal alcohol use and offspring symptoms of depression, anxiety or DBD. Mothers reported low rates of alcohol use overall which may explain the lack of associations found. This might have

been due to mothers under-reporting drinking or heavy drinkers not electing to participate in a research study. Nevertheless, the proportion of mothers reporting alcohol dependence is in line with estimates from epidemiological studies (Merikangas et al., 1998). Research suggests that alcohol problems are strongly and uniquely transmitted within families (Merikangas et al., 1994). However, in the current study we were unable to include measures of child alcohol use to test this possibility.

Limitations

The current study should be considered in light of some limitations. First, although retention rates were high (over 90%) there was partial missing data across maternal and child assessments. The current study used multiple imputation (Schafer, 1999) to minimize any resulting biases. Second, there were too few fathers in the current study to assess the effects of co-occurring psychopathology in the depressed fathers, and it is important to note that risk to offspring associated with parental depression may vary by parent gender (Connell & Goodman, 2002). Third, a related issue is that variation in depression and other psychopathology in partners of depressed mothers may also have an influence on the heterogeneity of outcomes observed in offspring, especially given that there is some evidence of ‘assortative mating’, a non-random pattern whereby adults with depression partner with others with psychopathology (particularly ASB) greater than by chance (Marmorstein et al., 2004). However, in the present study, additional exploratory analyses on a subsample with relevant data showed no significant associations between maternal depression severity and paternal symptoms of depression, anxiety, alcohol use, or ASB (Appendix 5). Fourth, the current study used questionnaires rather than diagnostic interviewers to assess maternal symptoms. Dimensional symptom scores can be an informative measure of severity, and intergenerational risk for psychopathology is likely to behave in a continuous fashion with increased symptoms of psychopathology in

mothers increasing risk for offspring symptoms (Fergusson, Horwood, & Lynskey, 1995). Nevertheless, it is possible that greater specificity of risk would be observed if more closely matched diagnostic categories in mothers and offspring were compared. Finally, even a prospective longitudinal study such as this does not allow us to draw conclusions about whether maternal psychopathology has causal effects on offspring psychopathology. It is also unclear whether these findings would apply to non-clinical samples of mothers without recurrent depression. However, it highlights markers of risk for offspring psychopathology in a high-risk group, which may improve the identification of children who are at greatest risk and who could benefit from targeted intervention.

Future directions

Mechanisms by which risk for offspring psychopathology is transmitted need to be clarified. Evidence from genetically informed family-based designs (children of twins, IVF design) illustrate that there is shared genetic liability for parental depression and offspring disruptive behaviour problems (Silberg et al., 2010; Singh et al., 2011; Tully et al., 2008) but that predominately environmental processes underlie the association between parental depression and child depression and internalising problems (Harold et al., 2010; Lewis et al., 2011; Silberg et al., 2010; Singh et al., 2011; Tully et al., 2008). It is possible that problems that co-occur with parent depression may exert different risk effects on children and that this may partly account for differences in the presentation of offspring psychopathology within this high risk group. For instance, previous research suggests that maternal ASB may be a particularly important risk factor for parenting problems (Kim-Cohen et al., 2006) and further exploration of the impact of comorbid problems in parents with recurrent depression on family processes is therefore necessary.

Summary

Offspring of depressed parents are at increased risk of developing a range of psychiatric problems, and there is a need to understand these heterogeneous outcomes. Overall these findings are in accordance with previous research suggesting that there is some degree of specificity. ASB symptoms in mothers with recurrent depression demonstrated specificity of risk for offspring DBD symptoms. Maternal depression severity also showed a unique association with offspring symptoms of depression once co-occurring maternal and child problems were taken into account.

Clinicians need to be aware of additional psychopathology in mothers with recurrent depression; co-occurring psychopathology in mothers with recurrent depression is common and has been associated with greater maternal depression severity and increased risk to offspring (Sellers et al., 2012). The current study highlights that risk for offspring DBD is better explained by co-occurring maternal ASB than by variation in severity of maternal depression. This has implications for the targeting of intervention and prevention strategies, particularly as different disorders are likely to require different interventions (Weisz, Thurber, Sweeney, Proffitt, & LeGagnoux, 1997; Wood, Harrington, & Moore, 1996; Woolfenden, Williams, & Peat, 2001). Furthermore, DBD is an important predictor of future problems, including depression, substance misuse, and ASB (Combs-Ronto et al., 2009; Costello et al., 2011; Costello et al., 2003; Kim-Cohen et al., 2003; McGee et al., 2011), therefore effective targeting of DBD problems could help to reduce the burden of adult psychopathology.

Tables and figures

Table 4.1: Inter-correlations, and Means for all study variables

	1	2	3	4	5	6	7
1. Maternal depression severity T1	--						
2. Maternal anxiety T1	.68**	--					
3. Maternal ASB T1	.43**	.30**	--				
4. Maternal alcohol use T1	.14*	.14*	.25**	--			
5. Child depression symptoms T3	.14*	.03	.04	.01	--		
6. Child GAD symptoms T3	.12*	.03	.11	.02	.72**	--	
7. Child DBD symptoms T3	.19**	.11*	.15*	.04	.39**	.28**	--
Mean	16.53	9.25	7.75	5.38	1.99	1.76	2.93
SD	11.21	4.52	4.99	5.06	2.04	2.55	2.65

N.B. * $p < .05$; ** $p < .001$

Figure 1a

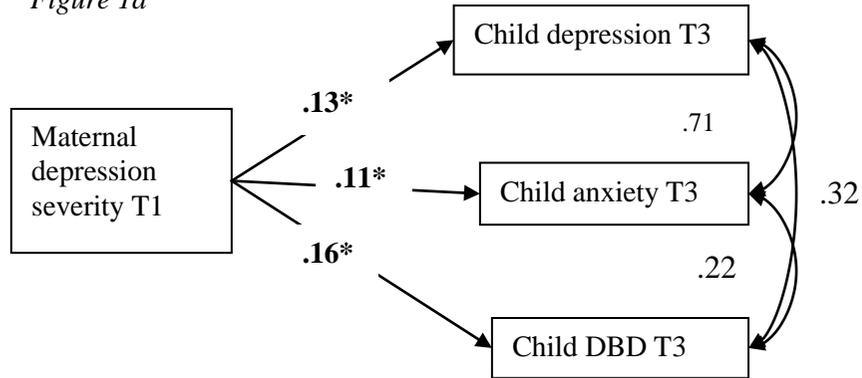


Figure 1b

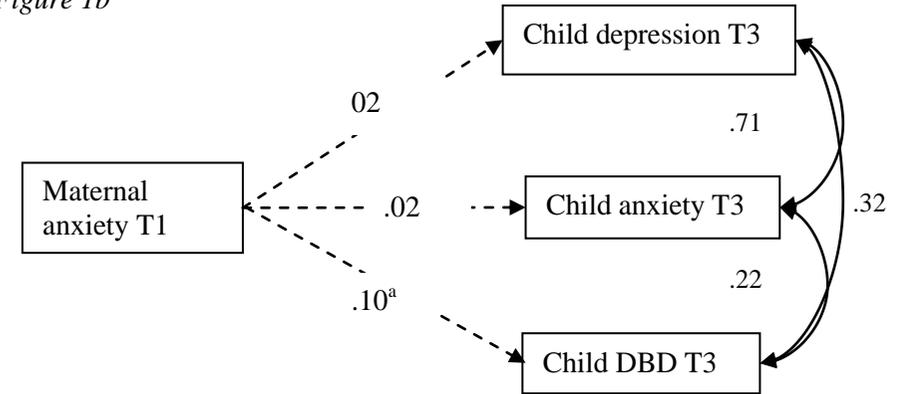


Figure 1c

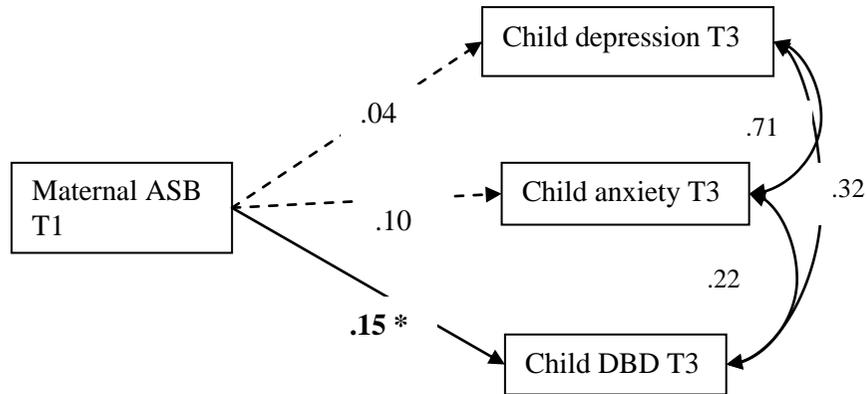


Figure 1d

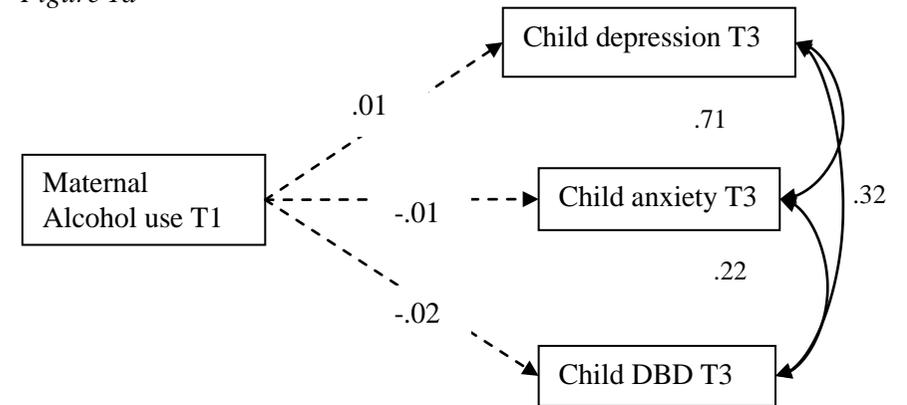


Figure 4.1: Associations between maternal depression severity, and child symptoms of depression, anxiety and DBD

Pathways show standardised coefficients obtained using MPLUS. * $p \leq .05$; ^a $p < .10$.

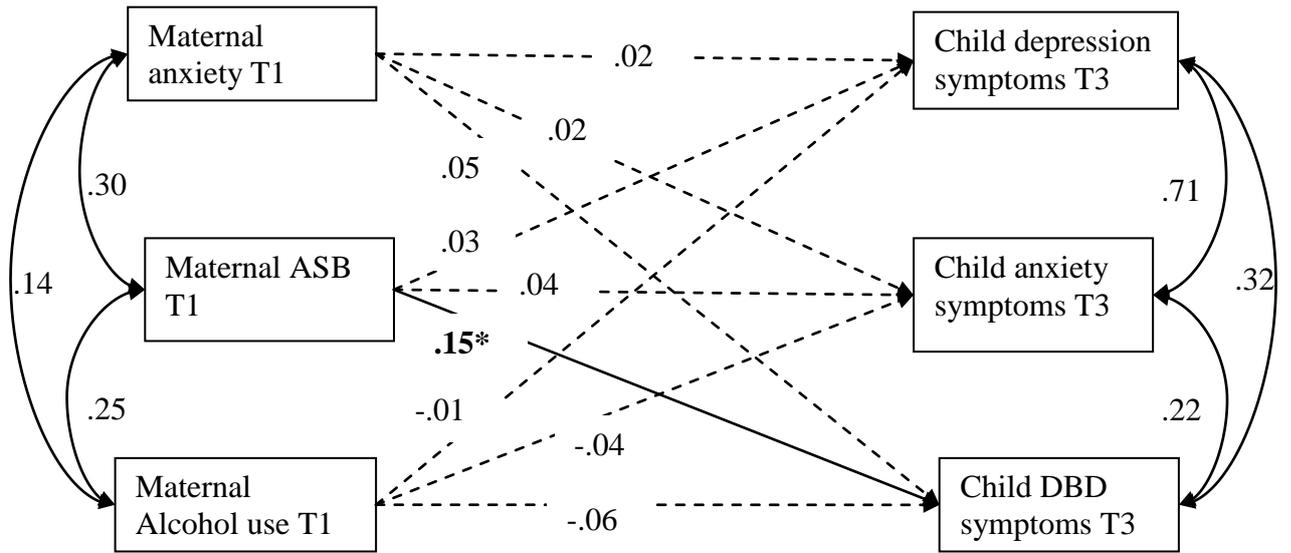


Figure 4.2: Associations between maternal co-occurring symptoms of maternal anxiety, ASB and alcohol use, and child symptoms of depression, anxiety and DBD.

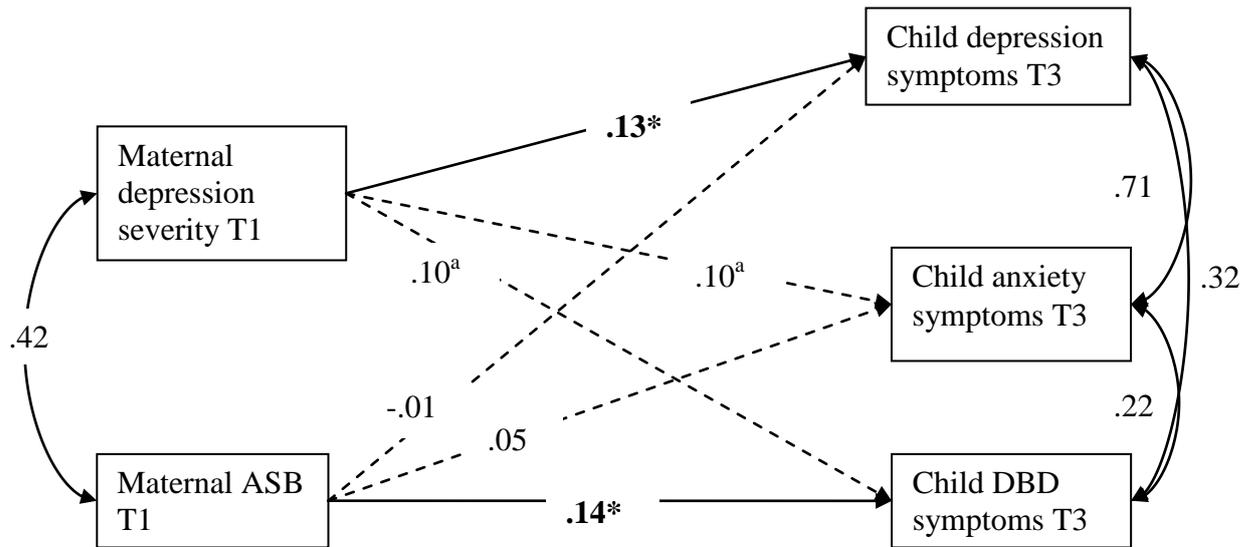


Figure 4.3: Associations between maternal depression severity and co-occurring symptoms of ASB and child symptoms of depression, anxiety and DBD.

Pathways show standardised coefficients obtained using MPLUS. * $p \leq .05$; ^a $p < .10$.

Model fit statistics: $\chi^2(6) = 5.04$; CFI = .99; RMSEA = .01; SRMR = .003.

Link section: Co-occurring symptomatology in mothers with recurrent depression: examining the specificity of risk to offspring

Chapter 4 explored the association between maternal co-occurring psychopathology and risk for offspring psychopathology. Having identified some degree of specificity of risk from maternal ASB to offspring DBD symptoms, and from maternal depression to offspring depression symptoms, the current thesis then considered potential mechanisms that may explain these associations.

Impairments in parenting were examined as potential mediators that may explain the association between maternal symptomatology and offspring symptomatology. Specifically, the constructs of warmth and hostility directed towards the study child were examined to test whether warmth or hostility mediated any effect of maternal depression severity on risk for offspring psychopathology, after adjusting for co-occurring maternal psychopathology.

As demonstrated in chapter 4, in this study, neither co-occurring symptoms of maternal alcohol misuse nor anxiety at Time 1 were associated with any child outcomes (depression, anxiety, or DBD) at Time 3. Therefore co-occurring symptoms of anxiety and alcohol misuse were not taken forward in further analyses.

The next chapter considered whether disruptions in the parent-child relationship mediated the effects of maternal psychopathology on risk for offspring psychopathology using all three assessments points in the EPAD study.

Chapter 5

Maternal depression and co-occurring antisocial behaviour: testing maternal hostility and warmth as mediators of risk for offspring psychopathology

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second review

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Chapter 5: Maternal depression and co-occurring antisocial behaviour: testing maternal hostility and warmth as mediators of risk for offspring psychopathology

Abstract

Background: Disruption in the parent-child relationship is a recognised risk factor through which maternal depression increases risk for offspring psychopathology. However, depression is commonly accompanied by other psychopathology. Few studies have examined the role of co-occurring psychopathology in depressed mothers in relation to offspring outcomes. Using a longitudinal study of offspring of mothers with recurrent depression, the study aimed to test whether maternal warmth/hostility mediated links between maternal depression severity on child outcomes when controlling for co-occurring maternal antisocial behaviour.

Methods: Mothers with a history of recurrent major depressive disorder and their adolescent offspring (9-17 years at baseline) were assessed three times between 2007 and 2011. Mothers completed questionnaires assessing their own depression severity and antisocial behaviour at Time 1 (T1). The parent-child relationship was assessed using parent-rated questionnaire and interviewer-rated five-minute speech sample at Time 2 (T2). Offspring symptoms of depression and disruptive behaviours were assessed using the Child and Adolescent Psychiatric Assessment at Time 3 (T3).

Results: Maternal hostility and warmth respectively mediated the association between maternal depression severity and risk for offspring psychopathology. However, the effects were attenuated when maternal antisocial behaviour was included in the analysis. In tests of the full theoretical model, maternal antisocial behaviour predicted both

maternal hostility and low warmth, maternal hostility predicted offspring disruptive behaviour disorder symptoms but not depression, and maternal warmth was not associated with either child outcome.

Conclusions: Parenting interventions aimed at reducing hostility may be beneficial for preventing or reducing adolescent disruptive behaviours in offspring of depressed mothers, when depressed mothers report co-occurring antisocial behaviour.

Key words: Hostility; warmth; mediation; depression; antisocial behaviour; disruptive behaviour.

Abbreviations: ASB: Antisocial Behaviour; DBD: Disruptive Behaviour Disorder

Introduction

Maternal depression is a well-established risk for offspring depression and disruptive behaviour disorder (DBD) (Brennan et al., 2002; Lieb et al., 2000; Wickramaratne & Weissman, 1998). Genetically sensitive designs suggest heritable factors only partially account for the intergenerational transmission of risk, and that non-inherited factors also have an important role (Asbury, Dunn, Pike, & Plomin, 2003; Silberg et al., 2010; Tully et al., 2008). Mothers who suffer from depression are reported to show more hostility and less warmth compared to healthy controls; such difficulties might be one mechanism through which maternal depression exerts effects on offspring (Goodman & Gotlib, 1999; Keenan-Miller et al., 2010; Kim-Cohen et al., 2005; Marmorstein & Iacono, 2004; McCarty & McMahon, 2003).

Warmth and hostility are distinct constructs of the mother-child relationship, with hostility being defined as maternal anger, criticism, and negativity directed towards the child. In addition mothers may be disapproving of the child. In contrast, warmth is defined as supportive parenting and positive parental affect whereby parents demonstrate affection and interest in their child (Connor & Rueter, 2006; Rueter & Conger, 1998). Although they are distinct constructs of the mother-child relationship, they are also correlated (Rueter & Conger, 1998). Because these disruptions to the parent-child relationship are potentially modifiable, a greater understanding of the impact of difficulties in the parent-child relationship in mothers with depression on offspring could inform intervention and prevention strategies.

Disruptions in the parent-child relationship have been found to mediate the association between maternal depression severity and offspring depression (Davies & Windle, 1997) and externalizing problems (McCarty & McMahon, 2003). Recent research examining the effects of the parent-child relationship on offspring depression

and conduct symptoms found that although current maternal depression was associated with both increased negativity and less positivity towards the child, neither aspect of the parent-child relationship were related to offspring internalizing symptoms; maternal positivity mediated the association between maternal depression and child externalizing symptoms (Elgar et al., 2007; McCarty & McMahon, 2003; Nelson et al., 2003), although not all studies support the mediating role of parenting on risk for child psychopathology (Foster, Garber, et al., 2008; Frye & Garber, 2005; Keenan-Miller et al., 2010).

Maternal depression often co-occurs with additional psychopathology, including antisocial behaviour (ASB), which is rarely taken into account even though the presence of multiple forms of psychopathology in parents with depression confers heightened risk of psychiatric disorder in offspring (Sellers et al., 2012). Additional psychopathology in mothers with recurrent depression may explain, at least in part, the association between maternal depression and attributes of the parent-child relationship. Family risk factors, such as disruptions in parent-child relationships, are common across families experiencing different types of psychopathology; thus effects on the parent-child relationship may not be specific to depression (Fendrich et al., 1990; Jaffee et al., 2006). There is preliminary evidence that depressed mothers with co-occurring ASB provide poorer quality care-giving environments compared to mothers with depression alone (Kim-Cohen et al., 2006). Therefore co-occurring ASB in mothers with recurrent depression may account for the association between maternal depression and parent-child relationship difficulties. The unique effect of maternal depression on child outcomes via the parent-child relationship independent of maternal ASB has not been previously assessed.

To address these issues, the current study employed data from a high-risk longitudinal study of adolescent offspring of mothers with recurrent depression using a multi-informant design to consider the role of maternal warmth and hostility. We aimed

to test whether maternal hostility and /or warmth mediated any effect of maternal depression severity on child symptoms of depression and DBD when accounting for maternal co-occurring ASB. We hypothesized that constructs of the parent-child relationship (hostility/warmth) would mediate the effects of maternal depression severity on child symptomatology, particularly offspring DBD; and that direct and indirect effects of maternal depression severity would be attenuated when adjusting for co-occurring maternal ASB.

Methods

Participants

The current analyses utilized data from the three-wave 'Early Prediction of Adolescent Depression' (EPAD) study, a study of the offspring of parents with recurrent depression. The sample and procedure have been described in detail elsewhere (Mars et al., 2012; Sellers et al., 2012), and are therefore summarised briefly.

Parents were recruited predominantly from primary care in South Wales, UK on the basis of treatment for at least two episodes of depression (confirmed at interview). Families were excluded if the depressed parent was not biologically related to the child, or the child had moderate to severe intellectual disability ($IQ < 50$). Children were aged 9 to 17 years old at first assessment.

The sample at baseline consisted of 337 parents with recurrent depression, and their adolescent offspring. Two families were excluded due to a diagnosis of bipolar disorder in the affected parent after the first assessment. Fourteen families were excluded as the child was not living at home throughout the course of the study. Depressed fathers were also excluded ($n = 22$).

The eligible sample in the current study thus consisted of 299 mothers at baseline (age $M = 41.2$ years, range 26-55 years) and their children (age $M = 12.3$, range 9-17 years; 58.5% females). T2 assessment was conducted approximately 16 months later (SD

= 2.64). Thirteen families declined to participate (retention = 95.6%, $n = 286/299$). T3 took place a further 12 months later ($SD = 1.48$). Twenty-three families declined to participate (retention = 93.3% $n = 276/299$). The majority of families participated at all three assessments (91.3%, $n = 273/299$). Families were interviewed at their home (99.6%) or University Hospital of Wales, and provided informed consent (assent if child under 16 years). Ethical approval was provided by the Multi-Regional Ethics Committee.

Measures

Maternal depression. Maternal diagnoses of recurrent depression were confirmed at baseline using a life history calendar approach (Belli, 1998; Caspi et al., 1996) and the Schedule for Clinical Assessment in Neuropsychiatry (Wing et al., 1990). In addition, mothers completed the Beck Depression Inventory (BDI) (Beck et al., 1979) to assess the severity of depression symptoms at T1 ($\alpha = .91$).

Maternal antisocial behaviour. Mothers reported on their own current ASB at T1 using the 34-item Adult Self Report (ASR) questionnaire (Achenbach & Rescorla, 2003) with items coded 0 (absent), 1 (somewhat or sometimes true) or 2 (very true). The item 'I have never been arrested' was excluded as it was the only item that referred to lifetime behaviour ($\alpha = 0.75$).

Child psychopathology. Parent and child versions of the Child and Adolescent Psychiatric Assessment (Angold & Costello, 2000) were used to assess child symptoms of depression and DBD (Oppositional Deviant Disorder/Conduct Disorder) in the preceding three months. The total number of DSM-IV symptoms (for each disorder) in the child at T3 was calculated by combining mother and child reports; where a symptom was reported by mother *or* child, the symptom was considered to be present. Symptom totals were created for child depression and child DBD. Inter-rater reliabilities for child symptoms were excellent (average $\kappa = .94$).

Maternal warmth and hostility. Maternal warmth and hostility were assessed at T2 by two different methods; a self-report questionnaire measure (Iowa Youth and Families project (IYFP) family interaction rating scales) (Melby et al., 1993) and an interviewer-rated five minute speech sample of expressed emotion (EE) (Caspi et al., 2004). Complete data on both measures of the parent-child relationship was required ($n = 207$). As described below, information from the two was combined to create a robust measurement of the parent-child relationship.

A 10-item questionnaire (IYFP) was completed by the mother. It contained two subscales assessing hostility (4-items) and lack of warmth (6-items) directed towards the child. Each item was coded 1-7 with higher scores indicating increased hostility or low warmth (hostility: $M = 12.42$, $SD = 4.20$, $\alpha = .89$. Warmth: $M = 12.61$; $SD = 6.80$ $\alpha = .93$). Warmth items were then reverse coded so that higher scores were indicative of higher warmth.

In addition, the measure EE in the current study used a five-minute speech sample (described in detail by Caspi et al, 2004). Mothers were asked to describe their child and were encouraged to speak freely. A series of prompt questions were utilized to elicit responses. In the current study, two additional prompts were included ('What are your child's strengths and good points?' and 'what is it like being their mum; what are the good things?'). Interviews were recorded and coded by the researchers who had all undergone in-house training supervised by a consultant child psychiatrist. The current study utilized the global measures of warmth and hostility (each coded 0-5). High scores indicated high hostility or high warmth (hostility: $M = .78$, $SD = .90$. Warmth: $M = 3.49$; $SD = .98$). Thirty interviews were randomly selected to assess inter-rater reliability and were coded by a second interviewer, blind to the initial coding of the interviews. Ratings were compared between the first and second rater. Inter-rater reliability for warmth and

hostility both showed substantial levels of agreement (warmth at Time 2 $ICC = 0.69$; hostility at Time 2 $ICC = 0.79$).

The two measures of warmth (EE and IYFP) were moderately correlated ($r = .30$, $p < .001$), as were the two measures of hostility ($r = .36$, $p < .001$). A composite score of maternal warmth, and a composite score of maternal hostility were created from the IYFP and EE. The subscales of hostility and warmth from each measure of the parent-child relationship were first standardized using z -score transformations and then combined: the z -scores of hostility from each measure of the parent-child relationship were added together to create a composite measure of maternal hostility as were the z -scores of warmth.

Analysis strategy

To test whether the parent-child relationship mediated the relation between psychopathology and offspring symptoms of depression and DBD, the direct effects between maternal depression severity or ASB at T1 and offspring psychopathology (symptoms of depression and DBD) at T3 were tested. Mediation analyses then tested whether maternal hostility/warmth at T2 mediated the association between maternal depression severity and offspring symptoms of DBD and depression, after adjusting for maternal ASB. Indirect effects were estimated with bias-corrected bootstrapping and were considered significant if the 95% confidence intervals did not include zero (MacKinnon et al., 2002).

Families with missing data at each follow-up were more likely to have higher offspring depression and DBD symptoms at baseline, and higher maternal depression severity and ASB scores (supplementary Table 5.1). The Little's test of missing data indicated that the data were not missing completely at random (MCAR). Multiple imputation with data augmentation was used to generate values for missing data across

relevant theoretical variables within the proposed model using NORM 2.03 (Schafer, 1997, 1999), regarded as the most robust method for multiple imputation (Allison, 2001). Subsequently generated datasets were then tested within Mplus 6.12 (Muthén & Muthén, 1998).

Results

Correlational analysis

Means, standard deviations and inter-correlations of the study variables are presented in Table 5.1. Mothers' depression severity at baseline was associated with co-occurring symptoms of ASB ($r = .43, p = <.001$). Maternal hostility and child symptomatology were related to each other when examined longitudinally. Correlations between constructs *across* time evidenced fair to moderate relations for offspring depression and DBD symptoms (maternal hostility and offspring depression $r = .18, p = .01$, DBD $r = .51, p = <.001$). Maternal warmth showed a different pattern of association with offspring symptomatology. Correlations between maternal warmth and offspring DBD symptoms were low to moderate ($r = -.24, p = <.001$), but there was not a significant correlation between maternal warmth and offspring depression ($r = -.13, p = .10$).

Mediation analyses

Parent hostility and warmth as mediators of associations between parent psychopathology and child DBD: A significant direct effect was observed between maternal depression severity at T1 and child symptoms of DBD at T3 ($\beta = .17, p = .01$). A significant direct effect was also observed between maternal ASB at T1 and child DBD symptoms at T3 ($\beta = .15, p = .02$).

Tests of mediation revealed that the association between maternal depression severity and child DBD symptoms was fully mediated by maternal hostility (Figure 5.1,

panel a), with a significant indirect effect of depression severity on child DBD via hostility (unstandardized 95% bias-corrected bootstrapped CI = .01, .02). However, after adjusting for maternal ASB, there was no longer a significant direct effect of maternal depression severity on child DBD, nor any significant indirect pathway (via maternal hostility; unstandardized 95% bias-corrected bootstrapped CI = -.02, .01). Instead, maternal hostility mediated the effect of maternal ASB on offspring DBD (Figure 5.1, panel b; unstandardized 95% bias-corrected bootstrapped CI = .01, .05).

When considering the effect of maternal warmth, results revealed that the association between maternal depression severity and child DBD symptoms was reduced (from $\beta = .17$ to $\beta = .13$) when maternal warmth was considered (Figure 5.2, panel a), although the indirect effect via warmth was not significant (unstandardized 95% bias-corrected bootstrapped CI = .00, .01). When adjusting for maternal ASB, there was no direct or indirect effect of maternal depression severity (unstandardized 95% bias-corrected bootstrapped CI = -.001, .01). Maternal warmth fully mediated the effect of maternal ASB on offspring DBD (Figure 5.2, panel b), with a significant indirect path (unstandardized 95% bias-corrected bootstrapped CI = .001, .02).

Offspring depression: A significant direct effect was observed between maternal depression severity at T1 and child symptoms of depression at T3 ($\beta = .14, p = .04$). However, a significant direct effect was not observed between maternal ASB at T1 and child depression at T3 ($\beta = .04, p = .59$). Tests of mediation revealed that the association between maternal depression severity and child depression symptoms was attenuated when maternal hostility was considered (Figure 5.3 panel a), although the indirect effect via hostility was not significant (unstandardized 95% bias-corrected bootstrapped CI = .00, .08). When adjusting for maternal ASB, there was no direct or indirect effect of maternal depression severity (unstandardized 95% bias-corrected bootstrapped CI = -.01, .01). There was a significant indirect path from maternal ASB to offspring depression via

maternal hostility (unstandardized 95% bias-corrected bootstrapped CI = .001, .03; Figure 5.3, panel b).

Maternal depression and ASB, and child depression and DBD symptoms: the role of maternal warmth and hostility. Given significant associations between parental warmth and hostility and between child depression and DBD (Table 5.1), a final model assessed unique influences of each construct of the parent-child relationship (hostility and warmth) on each child outcome when considered simultaneously (Figure 5.4). As shown, maternal depression severity did not significantly predict either warmth or hostility, nor were there any significant direct effects from maternal depression severity to child symptoms of depression or DBD. Maternal ASB symptoms were associated with both warmth and hostility. Maternal hostility in turn was a significant predictor of child symptoms of DBD but not depression.

Given findings of non-significant paths from maternal warmth to either child outcome when maternal hostility was included in the model, a competing model constrained pathways from maternal warmth to child symptomatology to zero. Model fit statistics indicated a good fit to the data ($\chi^2(2) = 1.87, p = .393$; CFI = .99; RMSEA = .05). In the context of maternal hostility, maternal warmth did not have a strong influence on offspring symptoms of depression or DBD in this sample.

Discussion

Consistent with previous research (Goodman & Gotlib, 1999; Keenan-Miller et al., 2010; Marmorstein et al., 2004; McCarty & McMahon, 2003), variation in maternal depression severity in this high risk sample was associated with offspring depression and DBD symptoms, and these associations were mediated via differences in parental warmth and hostility. Many of these mothers with recurrent depression also experienced additional psychopathology including ASB (Sellers et al., 2012), and mothers with

increased depression severity had higher levels of ASB. When co-occurring ASB was taken into account direct and indirect effects (via parent-child relationships) of depression severity on child outcomes were attenuated. These findings are consistent with prior evidence that depressed mothers with co-occurring ASB symptoms may provide especially poor quality care-giving environments (Kim-Cohen et al., 2006), but provides additional evidence that depression severity alone may have less influence on child outcomes via parent-child relationships than previously thought (at least within this high-risk clinical sample).

The final model considered both maternal hostility and warmth and child symptoms of depression and DBD simultaneously to take into account the association between these constructs, given evidence that comorbid psychopathology is more the rule than the exception in adolescents (Angold et al., 1999). Findings here indicate that maternal ASB was especially predictive of offspring DBD symptoms and that associations were particularly mediated via parental hostility. Low maternal warmth appeared to represent less of a risk for offspring DBD symptoms when hostility was taken into account. Influences of maternal antisocial behaviour and hostility on child depression appeared less robust when child DBD was taken into account. These findings build on previous research suggesting that negative (rather than positive) aspects of parenting have a stronger effect on risk for offspring psychopathology (Lovejoy et al., 2000), and that effects are likely to be stronger for offspring conduct disorder than internalizing problems (Combs-Ronto et al., 2009; Gershoff, 2002; McCarty & Weisz, 2002; Psychogiou et al., 2007; Stubbe et al., 1993).

It is important to consider alternative explanations for the current findings. The transmission of risk from maternal psychopathology to offspring symptoms via the parent-child relationship may represent a gene-environment correlation whereby parent's genes are not only inherited by the offspring, but also shape the family environment (Rice

et al., 2006). Previous genetically sensitive research, however, suggests that influences of parent ASB on the risk for offspring DBD symptoms is *environmentally* mediated including via maternal hostility (Harold et al., 2010; O'Connor et al., 1998).

The findings should also be considered in light of certain limitations. First, families with missing data reported higher maternal ASB and depression severity scores, as well as higher child depression and DBD symptoms at baseline compared to those with complete data. The study may therefore represent an underestimate of the risk for offspring psychopathology. Additionally, although retention rates were high (over 90% at each follow-up assessment), partial missing data across assessments further reduced available numbers. However the current study used Multiple Imputation (Schafer, 1997, 1999) to minimize any influence of non-response biases. Second, although the current study was able to investigate risk factors for offspring psychopathology across adolescence, firm conclusions about effects at particular points during this developmental period are not possible due to the wide age range of children included in the study. Third, it should be noted that the reliability estimate for the EE measure of warmth was lower than estimates of hostility. However, reliability still demonstrated substantial levels of agreement. Finally, there were too few fathers in the current study to consider the effects of paternal depression on the parent-child relationship and child outcomes. Research suggests that depression in fathers has a significant and deleterious effect on relationships and child psychopathology (Connell & Goodman, 2002; Kane & Garber, 2004; Wilson & Durbin, 2010) and future research should test effects of paternal depression and co-occurring ASB on parent-child relationships. Future research should also consider that mothers with depression often present with other clinical problems including anxiety and substance misuse (Swendsen & Merikangas, 2000) that could potentially also influence maternal hostility and warmth and offspring psychopathology.

Evidence on mechanisms of risk transmission in high-risk families affected by recurrent maternal depression is important so that intervention and prevention programs can be effectively targeted. Some previous research has recognized that there is significant heterogeneity in risk for depression in children of depressed mothers, linked to course and severity of mothers' illness (Brennan et al., 2000; Campbell et al., 2009; Mars et al., 2012). The current study adds to the evidence that co-occurring psychopathology such as ASB is also important to take into account (Jaffee et al., 2006; Sellers et al., 2012).

The current study highlights that there is an excess risk for DBD symptoms associated with greater maternal depression severity but that this may be explained in part by co-occurring maternal ASB and associated disruptions to the parent-child relationship. DBD is one of the most common reasons for referral of children to mental health services; furthermore offspring DBD is also an important a risk factor for future depressive disorders (Silberg et al., 2010). Therefore, interventions for children of depressed mothers need to focus on DBD symptoms not just depression. Parenting interventions aimed at reducing maternal hostility in mothers with depression may be especially beneficial for preventing or reducing disruptive behaviour problems in offspring, especially when depressed mothers also exhibit ASB. There is strong evidence that parenting interventions can be effective at reducing disruptive behaviour problems in children and adolescents (Woolfenden et al., 2001). These interventions may be of particular importance for families where a mother suffers from depression and also exhibits ASB.

Key points

- Maternal depression is associated with disruptions in the parent-child relationship which may negatively impact on child symptomatology. Mothers with recurrent depression often present with additional psychopathology, including antisocial behaviours which could explain this association.
- Disruptions in the parent-child relationship mediated the association between maternal depression severity and risk for offspring symptomatology. However, maternal depression severity no longer predicted warmth or hostility after adjusting for maternal antisocial behaviour.
- In the final model maternal antisocial behaviour predicted both maternal hostility and warmth. Maternal hostility predicted offspring disruptive behaviours.
- Interventions aimed at reducing maternal hostility may hold some promise for reducing risk for offspring disruptive behaviours, particularly where mothers also present with additional antisocial behaviour.

Tables and figures

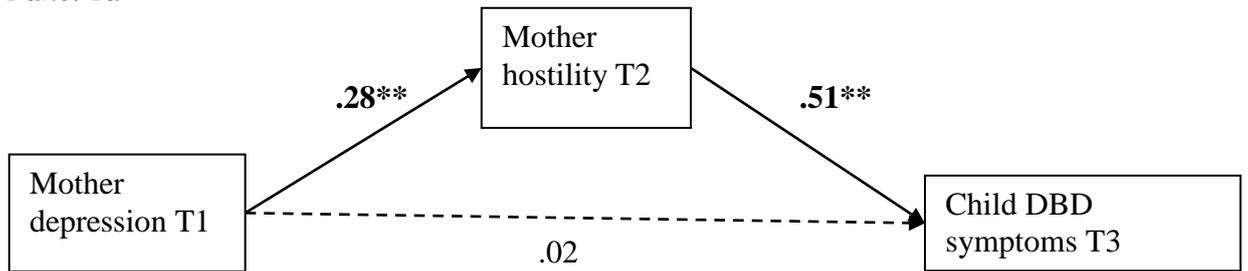
Table 5.1: Inter-correlations, Means, and Standard Deviations for all study variables

	1	2	3	4	5	6
1. Time 1 maternal depression severity	--					
2. Time 1 maternal antisocial behaviour	.43**	--				
3. Time 2 maternal hostility ^a	.26**	.37**	--			
4. Time 2 maternal warmth ^a	-.17*	-.27**	-.41**	--		
5. Time 3 child depression symptoms	.14*	.04	.18*	-.13	--	
6. Time 3 child disruptive behaviour symptoms	.19**	.15*	.51**	-.24**	.39**	--
Mean	16.41	7.70	-.01	.04	1.99	3.01
Standard deviation	(11.19)	(4.98)	(1.63)	(1.57)	(2.11)	(2.66)

N.B. * $p < .05$; ** $p < .001$

^a Standardized z-scores of five minute speech sample and IYPF questionnaire measures of the parent-child relationship

Panel 1a



Panel 1b

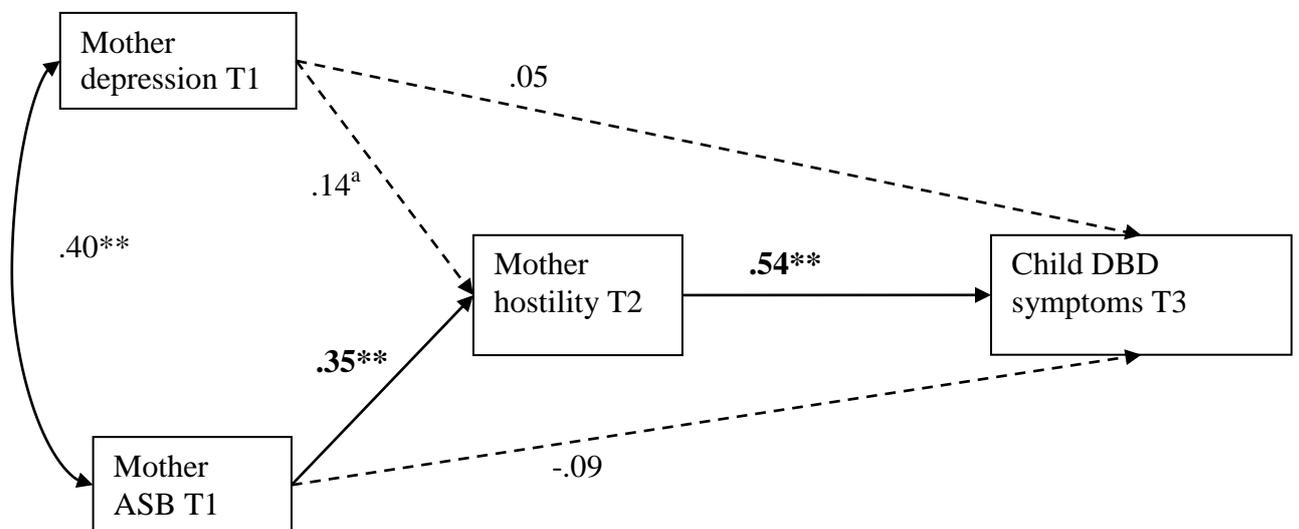
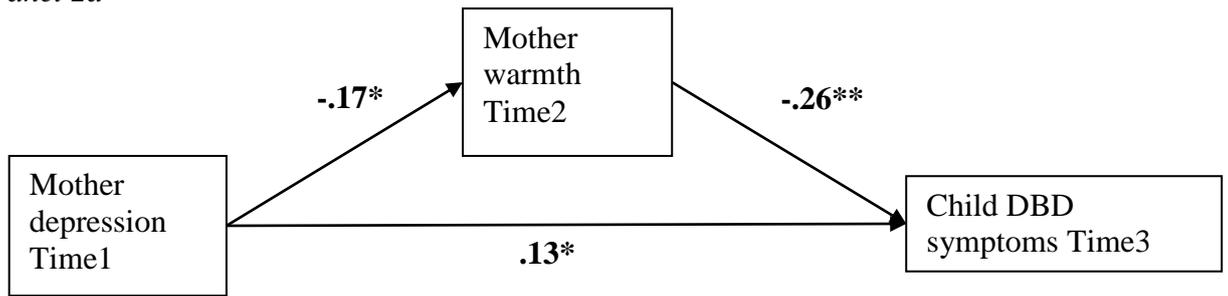


Figure 5.1: Mediating model showing the effect of maternal depression severity on offspring DBD via maternal hostility (panel a) after adjusting for maternal ASB (panel b).

** $p = <.001$; * $p = <.05$; a $p = <.10$

Panel 2a



Panel 2b

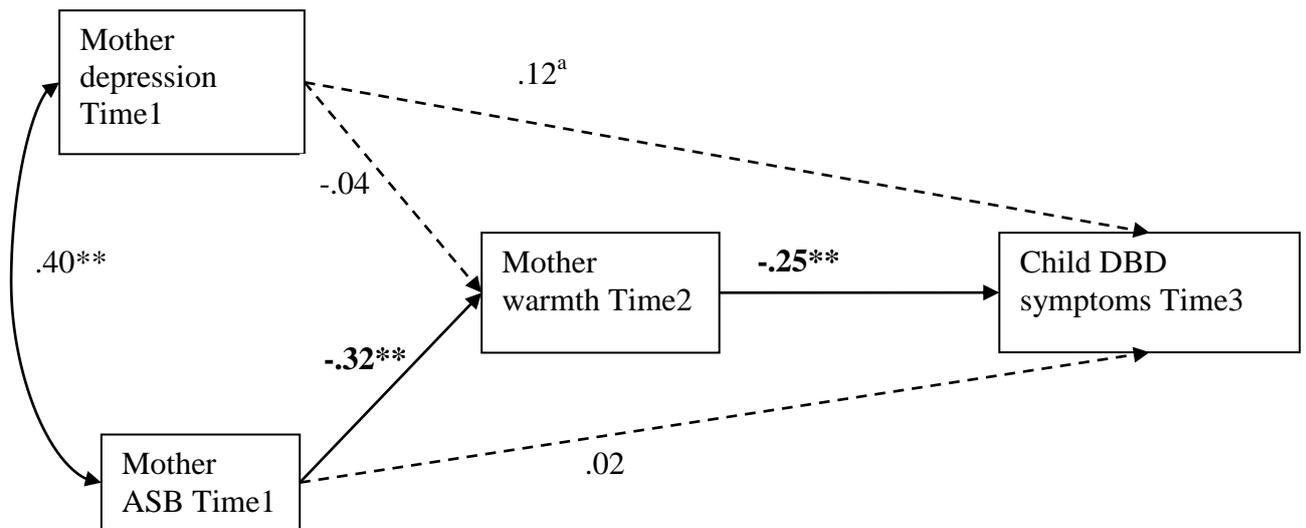


Figure 5.2: Mediating model showing the effect of maternal depression severity on offspring DBD via maternal warmth (panel a) after adjusting for maternal ASB (panel b).

** $p = <.001$; * $p = <.05$; a $p = <.10$

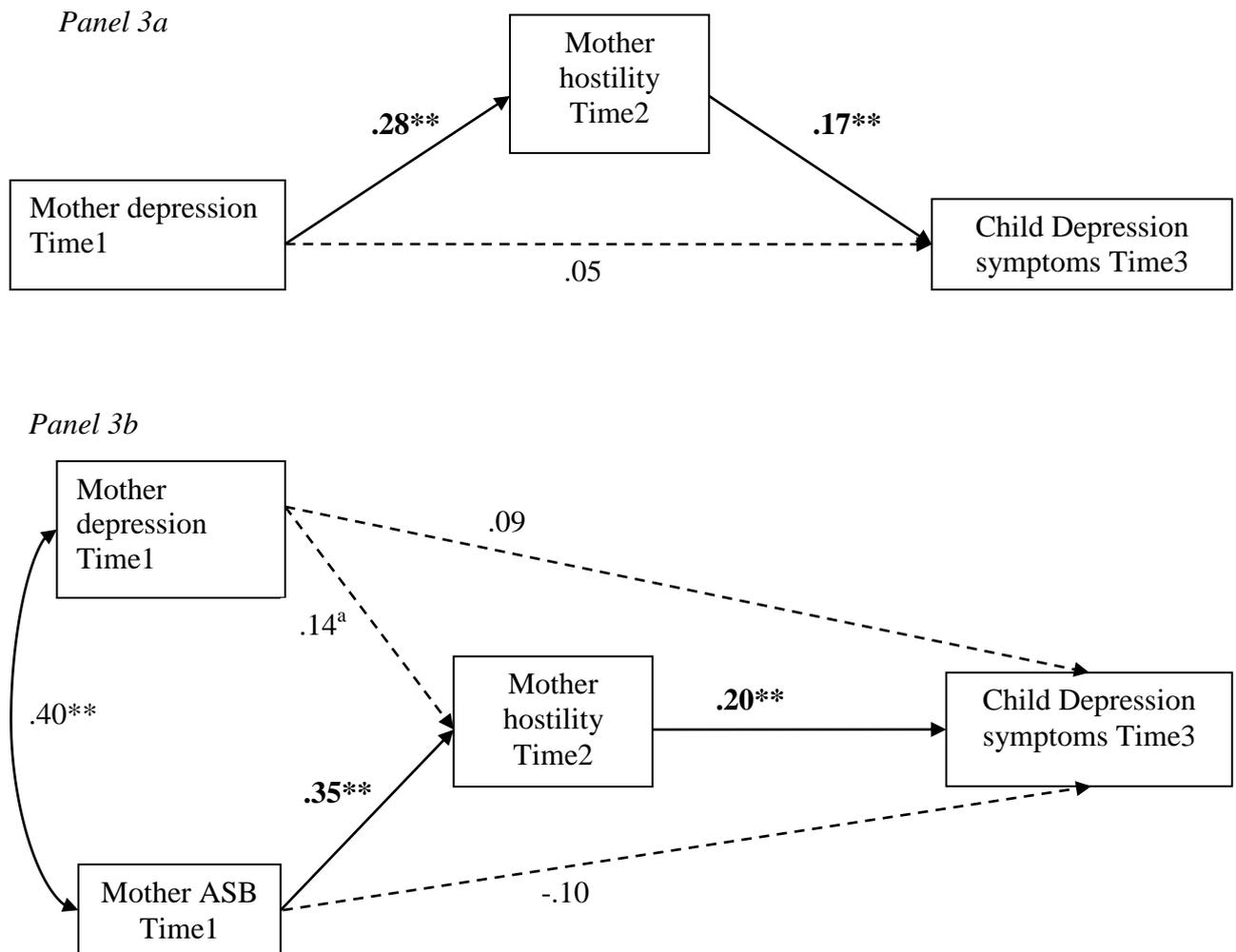


Figure 5.3: Mediating model showing the effect of maternal depression severity on offspring depression via maternal hostility (panel a) after adjusting for maternal ASB (panel b).

** $p = <.001$; * $p = <.05$; a $p = <.10$

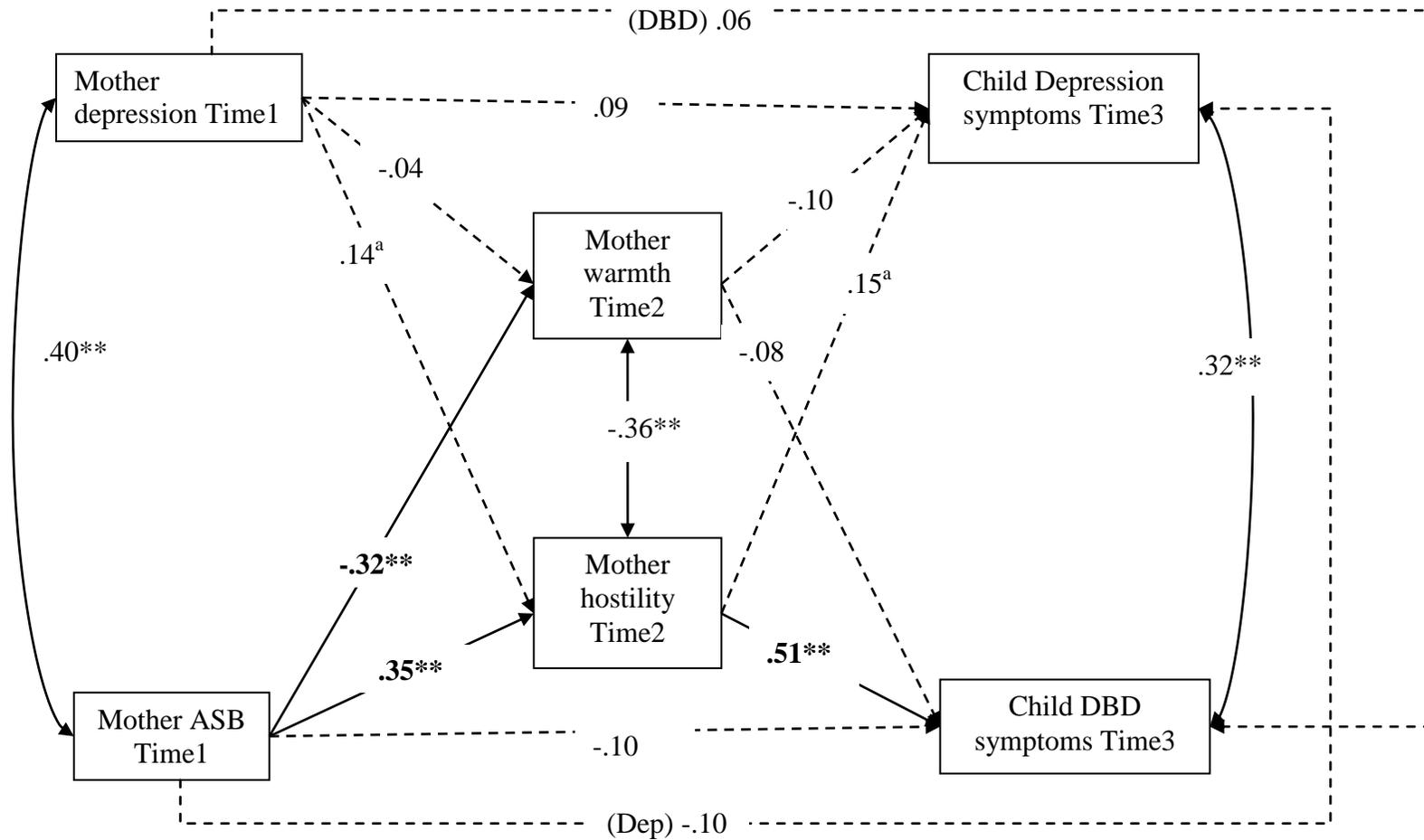


Figure 5.4: Estimated pathways between maternal depression and ASB, constructs of the parent-child relationship (warmth and hostility) and child symptoms of depression and DBD. ** $p < .001$; * $p < .05$; a $p < .10$

Supplementary material

Supplementary Table 5.1: Sample Descriptive of Complete and Missing Data at each Follow-up by Baseline Predictors

	Time 2			Time 3		
	Complete (n=203/299)	Missing (n=96/299)	<i>p</i>	Complete (n=219/299)	Missing (n=80/299)	<i>p</i>
Maternal symptoms						
Depression severity, mean (SD)	15.50 (10.84)	18.65 (11.78)	.033	15.18 (10.81)	20.23 (11.56)	.001
ASB score, mean (SD)	7.17 (4.61)	8.78 (5.54)	.010	7.27 (4.64)	8.90 (5.66)	.013
Maternal parenting						
Hostility, mean (SD)	-.12 (1.64)	.09 (1.61)	.368	-.17 (1.57)	.27 (1.77)	.069
Warmth, mean (SD)	.08 (1.61)	-.14 (1.82)	.349	.12 (1.51)	-.27 (1.77)	.127
Child symptoms						
Child depression, mean (SD)	1.60 (1.80)	1.80 (1.89)	.305	1.54 (1.80)	2.01 (1.88)	.034
Child DBD, mean (SD)	2.86 (2.31)	3.37 (2.62)	.176	2.88 (2.48)	3.42 (2.23)	.035

Link section: Maternal hostility and warmth: risk for psychopathology in offspring of depressed mothers

The findings in the previous chapter highlight that impairments in parenting are important mediators of risk from parent depression severity to child symptomatology. Maternal antisocial behaviour (ASB) accounted for the association between maternal depression severity and parenting impairments (increased hostility and lower levels of warmth). Maternal ASB predicted impairments in parenting, which in turn predicted offspring symptomatology.

Subsidiary analyses were conducted to extend these findings; disruptions in the mother-child relationship were examined as putative mediating mechanisms explaining the association between maternal depression severity and offspring new-onset psychiatric disorder (Appendix 6). Maternal hostility, but not maternal warmth, predicted new-onset psychiatric disorder. Maternal hostility mediated the effect of maternal depression severity on risk for child new-onset psychiatric disorder. Maternal ASB accounted for the association between maternal depression severity and maternal hostility. This pattern of results was similar to those observed in chapter 5, and supports previous evidence that mothers with depression and co-occurring ASB provide especially poor care-giving environments compared to mothers with depression alone (Jaffee et al., 2006; Kim-Cohen et al., 2006). Furthermore, these results suggest that the effects of maternal ASB may be particularly important for the *development* of psychiatric disorder in adolescent offspring of mothers with recurrent depression.

However, it is important to test for the possibility of reverse causation; exposure to offspring symptomatology may increase maternal hostility or decrease warmth. Alternatively effects may be bidirectional with hostility/warmth affecting child psychopathology and vice

versa (Bell, 1968). The following chapter examined the direction of effects between hostility and warmth in the mother-child relationship, and offspring symptoms of DBD and depression.

Although in the final model of the previous chapter effects were observed suggesting that impairments in parenting may be specific to offspring DBD, analyses in the subsequent chapter also tested the direction of effects between parenting and offspring depression symptoms; these analyses were conducted for completeness. Furthermore, in chapter 5, when mediation models were conducted with each parenting construct and child outcome separately, maternal hostility was found to mediate the effect of maternal psychopathology on risk for offspring depression symptoms (Chapter 5, Figure 5.3). Although this effect was reduced to marginal significance in the full theoretical model (Chapter 5, Figure 5.4), it suggests that each child construct and each parenting construct should be examined.

Chapter 6

Maternal hostility and child disruptive behaviour in adolescents of depressed mothers

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review

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Chapter 6. Maternal hostility and child disruptive behaviour in adolescents of depressed mothers

Abstract

Objective: Disruptions in the parent-child relationship have been postulated as a mediator through which maternal depression may exert effects on risk for offspring psychopathology. The direction of effects are rarely tested and few studies consider transactional effects for different types of child symptomatology. This study tested the direction of effects between mother-child hostility and warmth and child symptoms of depression and disruptive behaviour in a high-risk group of adolescent offspring of mothers with recurrent depression.

Methods: Mothers and their offspring (<18 years at baseline) were assessed on three occasions between 2007 and 2011. The majority of families participated at all three assessments (91.3%; 273/299). At assessments two and three mother hostility/warmth towards the child was assessed using a maternal self-report questionnaire and interviewer-rated five-minute speech sample. Offspring symptomatology was assessed using the Child and Adolescent Psychiatric Assessment.

Results: Bidirectional relationships between maternal hostility and child disruptive behaviour symptoms were observed. Maternal warmth was related to changes in offspring disruptive behaviours but not vice versa. Maternal hostility and warmth were not related to change in offspring depression symptoms or vice versa.

Conclusions: Maternal hostility may be a specific risk factor for disruptive behaviours in adolescent offspring of depressed mothers. Additionally, child disruptive behaviours influenced hostility in mothers, highlighting the importance of considering bidirectional effects. Interventions aimed at reducing maternal hostility may hold promise for preventing/reducing offspring disruptive behaviours. Interventions that reduce offspring disruptive behaviours may show benefits for parent-child relationships.

Key words: hostility; warmth; depression; disruptive behaviour; direction of effect

Introduction

It is well established that offspring of depressed parents are at increased risk of developing depression and disruptive behaviour disorders (Brennan et al., 2002; Lieb et al., 2000; Wickramaratne & Weissman, 1998). Disruptions in the parent-child relationship are well-established, robust and modifiable risk factors for childhood antisocial behaviour/conduct disorder. Aspects of the mother-child relationship have been considered as possible mediators through which maternal depression is linked to offspring psychopathology (Goodman & Gotlib, 1999; Keenan-Miller et al., 2010; Kim-Cohen et al., 2005; Marmorstein & Iacono, 2004; McCarty & McMahon, 2003). However, it is also recognised that children's behaviour may increase maternal hostility or decrease warmth; or effects may be bidirectional with hostility or warmth affecting child psychopathology and vice versa (Bell, 1968).

Although much research has examined the effects of the parent-child relationship on risk for offspring psychopathology, fewer studies have examined the effects of child-driven processes. Much research is cross-sectional, or does not assess the parent-child relationship at multiple time points; thus the direction of effects are rarely directly tested (Asarnow et al., 2001; Caspi et al., 2004; Foster, Garber, et al., 2008; Nelson et al., 2003; Peris & Baker, 2000; Silk et al., 2009). Possible child effects of child psychopathology on parenting in families where one or both parents suffer from recurrent depression, to our knowledge, have not been previously examined.

Research assessing the direction of effects between the parent-child relationship and child adjustment has focused primarily on risk for offspring conduct problems in high-risk groups of young children, with strong evidence of bidirectional influences (Combs-Ronto et al., 2009; Gross et al., 2008; Miner & Clarke-Stewart, 2008). There is less evidence on the association between the parent-child relationship and risk for offspring conduct problems in

adolescent offspring, a period of transition when the parent-child relationship is subject to change (McGue et al., 2005; Steinberg, 2001). Only very few studies have utilised samples of mothers with recurrent depression; those that have, identified that family risk factors were associated with conduct disorder in offspring (Fendrich et al., 1990), but possible child effects of conduct problems on parenting mothers with recurrent depression have not been tested.

In contrast to research on child conduct problems, the reciprocal relationships between the parent-child relationship and child symptoms of depression are less well examined. Most research has focused broadly on ‘internalising’ problems rather than symptoms of depressive disorders, and where the direction of effects has been tested, evidence has been inconsistent. Some studies have found that adolescent internalising symptoms predicted change in the parent-child relationship across time (Hale III et al., 2011; Loukas, 2009), whereas other studies have found effects of the parent-child relationship on offspring emotional adjustment (Chen, Liu, & Li, 2000; Rueter et al., 1999). Yet other studies have found evidence of bidirectional effects between the parent-child relationship and offspring internalising symptoms (Branje et al., 2010; Hipwell et al., 2008). However, few studies have examined whether the risk of depression problems in offspring of parents with depression are mediated via parent-child relationships, and these have mainly focused on non-clinical samples of parents. A study using a clinical sample identified that although parental depression was a risk factor for offspring depression, rates of offspring depression increased in the presence of family discord (Pilowsky, Wickramaratne, Nomura, & Weissman, 2006). Additionally, a treatment trial of mothers with recurrent depression identified that changes in maternal warmth partially mediated the relationship between maternal depression remission and offspring internalising symptoms (Foster, Webster, Weissman, Pilowsky, Wickramaratne, Talatj, et al., 2008). However, additional studies

suggest that parent depression may be more important than family risk factors when predicting offspring depression (Fendrich et al., 1990; Nomura, Wickramaratne, Warner, Mufson, & Weissman, 2002). The extent to which the parent-child relationship mediates links between parent depression and offspring psychopathology is not well understood, nor is it clear if there are any child-effects on the parent-child relationship in clinical samples of parents with recurrent depression.

To address these issues, the current study employed data from a prospective longitudinal study. The aim was to test the direction of effects between two constructs of the mother-child relationship (maternal hostility and warmth), and child symptoms of depression and disruptive behaviour disorder (DBD) in a high-risk group of adolescent offspring of depressed mothers. We hypothesised that there would be bidirectional effects between the mother-child relationship and offspring symptoms of DBD. Research has been much less consistent regarding the direction of effects between the parent-child relationship and offspring depression. However, given findings that improvements in maternal depression severity are related to improvements in both the mother-child relationship and child depression, we hypothesised that the mother-child relationship may predict change in offspring depression symptoms.

Methods

Participants

The current analyses utilised data from a three-wave longitudinal study of adolescent offspring of parents with recurrent depression; the ‘Early Prediction of Adolescent Depression’ (EPAD) study. The sample and procedure have been set out in detail elsewhere (Mars et al., 2012; Sellers et al., 2012) and are described briefly.

Parents were recruited predominantly from primary care in South Wales, UK. A history of recurrent depression in the parent (2 or more episodes of DSM-IV major depression) was confirmed at interview. Families were excluded if the depressed parent was diagnosed with bipolar disorder throughout the course of the study, was not biologically related to the child, or the child had moderate to severe intellectual disability ($IQ < 50$). Children were aged 9 to 17 years old at first assessment. The sample at baseline consisted of 337 parents with recurrent depression, and their adolescent offspring. Depressed fathers were excluded from the current analyses ($n = 22$). Two families were excluded due to a diagnosis of bipolar disorder in the affected parent. Fourteen families were excluded as the child was not living at home throughout the course of the study. The eligible sample in the current study therefore consisted of 299 mothers at baseline (mean age 41.2 years, range 26-55 years) and their children (mean age 12.3 years range 9-17 years; 58.5% females).

A first follow-up assessment was conducted approximately 16 months later ($SD = 2.64$) with 13 families declining to participate (retention = 95.6%, $n = 286/299$). A second follow-up took place a further 12 months later ($SD = 1.48$) with 23 families declining to participate in the final assessment (retention = 93.3% $n = 276/299$). Families were interviewed at their home (99.6%) or University Hospital of Wales, and provided informed consent (assent if child under 16 years). Ethical approval was provided by the Multi-Regional Ethics Committee.

The majority of families participated at all three assessments (91.3%, $n = 273/299$). Families with missing data at either follow-up were more likely to have offspring with higher depression and DBD symptoms at baseline. The Little's test of missing data indicated that the data were not missing completely at random (MCAR). Multiple imputation with data augmentation was used to generate values for missing data across relevant theoretical variables within the proposed model using NORM 2.03 (Schafer, 1997, 1999), regarded as

the most robust method for multiple imputation (Allison, 2001). Subsequently generated datasets were then tested within Mplus 6.12 using maximum likelihood estimation (Muthén & Muthén, 1998).

Measures

Child symptoms of depression and disruptive behaviour disorders: A semi-structured interview, the Child and Adolescent Psychiatric Assessment (Angold & Costello, 2000) was completed at Time two (T2) and Time three (T3) by the mother and the child to assess the presence of symptoms of depression and conduct disorder/oppositional defiant disorder in the preceding three months. Child DBD symptoms were defined as the presence of DSM-IV symptoms of oppositional defiant disorder or conduct disorder. The total number of DSM-IV symptoms (for depression and DBD) in the child at T2 and T3 were calculated by combining mother and child reports; a symptom was considered to be present where it was reported by either mother *or* child. Inter-rater reliabilities for child symptoms were excellent (average $\kappa = .94$).

Maternal warmth and hostility: Maternal warmth and hostility were assessed at T2 and T3 by two methods; a maternal self-report questionnaire measure (Iowa Youth and Families Project (IYFP) family interaction rating scales)(Melby et al., 1993) and an interviewer-rated five minute maternal speech sample of expressed emotion (EE) (Caspi et al., 2004) to create a robust measure of the parent-child relationship.

The 10-item IYFP questionnaire was completed by the mother. It contained two subscales assessing hostility (4-items) and lack of warmth (6-items) directed towards the child. Each item was coded 1-7 with higher scores indicating increased hostility or low warmth. Warmth items were reverse coded so that higher scores indicated higher warmth (hostility: T2 $\alpha = .89$, T3 $\alpha = .84$; warmth: T2 $\alpha = .93$, T3 $\alpha = .94$).

The EE measure has been described in detail by Caspi and colleagues (Caspi et al., 2004). Briefly, mothers were asked to describe their child and were encouraged to speak freely. A series of prompt questions were utilized to elicit responses (Caspi et al., 2004). Two additional prompts were included (e.g. ‘What are your child’s strengths and good points?’). Interviews were recorded and coded by the researchers who had undergone in-house training supervised by a consultant child psychiatrist. The current study utilized the global measures of warmth and hostility (each coded 0-5). High scores indicated high hostility or warmth. Thirty interviews were randomly selected to assess inter-rater reliability and were coded by a second interviewer, blind to the initial coding of the interviews. Inter-rater reliability showed substantial levels of agreement (warmth T2 $ICC = 0.69$; T3 $ICC = .68$; hostility T2 $ICC = 0.79$, T3 $ICC = .85$). A composite score of maternal warmth, and a composite score of maternal hostility were created from the IYFP and EE. The subscales of hostility and warmth from the IYFP and EE were standardized using z-score transformations and then combined: the z-scores of hostility from each measure of the mother-child relationship were added together to create a composite measure of maternal hostility, and the z-scores of warmth from the IYFP and EE were also added together to create a composite measure of maternal warmth.

Results

Correlational analysis

Means, standard deviations, and inter-correlations for all study variables are presented in Table 6.1. Measures of the mother-child relationship and offspring symptomatology were stable across the 13-month period (maternal hostility $r = .67$, $p = <.001$; warmth $r = .70$, $p = <.001$; offspring depression $r = .58$, $p = <.001$; offspring DBD $r = .67$, $p = <.001$). In addition, maternal hostility and child symptomatology were related to each other when

examined either concurrently or longitudinally. Correlations between constructs *within* time were fair to moderate (T2 maternal hostility and offspring depression $r = .28, p = <.001$, DBD $r = .54, p = <.001$; T3 maternal hostility and offspring depression $r = .25, p = <.001$, DBD $r = .54, p = <.001$) with correlations between constructs *across* time evidencing fair to moderate relations for offspring depression and DBD symptoms (T2 maternal hostility and T3 offspring depression $r = .18, p = .014$, DBD $r = .51, p = <.001$; T3 maternal hostility and T2 offspring depression $r = .23, p = <.001$, DBD $r = .45, p = <.001$).

Maternal warmth showed a different pattern of association with offspring symptomatology. Maternal warmth and child symptoms of DBD were related to each other when examined either concurrently or longitudinally, but maternal warmth was not consistently associated with offspring symptoms of depression (T2 maternal warmth and offspring depression $r = -.13, p = .069$, DBD $r = -.28, p = <.001$; T3 maternal warmth and offspring depression $r = -.16, p = .015$, DBD $r = -.32, p = <.001$) with correlations between constructs *across* time evidencing fair relations between maternal warmth and offspring DBD symptoms, but not offspring depression (T2 warmth and T3 offspring depression $r = -.13, p = .080$; DBD $r = -.24, p = <.001$; T3 maternal warmth and T2 offspring depression $r = -.07, p = .330$, DBD $r = -.21, p = <.001$). Thus, it can be seen that associations with both measures of the mother-child relationship were consistently stronger for offspring DBD symptoms than offspring depression symptoms.

Cross-lagged and reciprocal effects analyses

Cross-lagged models utilise longitudinal data to test the direction of effects where associations have been observed between variables. Pathways simultaneously estimate the contribution of each construct at one time point in accounting for the other construct at a subsequent time point whilst controlling for the previous levels of the constructs. Reciprocal

effects models are used to test the direction of effects that exist within time, again controlling for the stability of each construct across time. In this study, cross-lagged and reciprocal effects models tested links between child symptomatology (depression and DBD) and maternal hostility and warmth. Offspring depression symptoms were not significantly correlated with warmth within or across time (Table 6.1) and therefore these associations were not considered in cross-lagged or reciprocal effects analyses.

Offspring DBD: Figure 6.1a shows results for the cross-lagged model linking child DBD symptoms and mother-child hostility. The stability coefficients for both maternal-child hostility and child's DBD symptoms were strong ($\beta = .63, p = <.001$; $\beta = .56, p = <.001$ respectively). Longitudinal cross-lagged effects were statistically significant between children's DBD symptoms and maternal hostility ($\beta = .11, p = <.05$), as were effects between maternal hostility and children's DBD symptoms ($\beta = .21, p = <.001$), demonstrating bidirectional effects whereby child's DBD symptoms affect maternal hostility over time and vice versa. Tests of reciprocal effects models are shown in Figure 6.1 panel b. The reciprocal effect model again showed strong stability across time ($\beta = .57, p = <.001$ for child DBD symptoms; $\beta = .65, p = <.001$ for maternal hostility). Maternal hostility exerted effects on offspring DBD symptoms within time, but not the other way around.

Figure 6.2a shows results for the cross-lagged model linking child DBD symptoms and maternal warmth. The stability coefficients across time for maternal warmth ($\beta = .70, p = <.001$) and children's DBD symptoms ($\beta = .65, p = <.001$) were strong. No longitudinal cross-lagged effects were observed between children's DBD symptoms and maternal warmth ($\beta = -.04, p = >.05$), or between maternal warmth and children's DBD symptoms ($\beta = -.08, p = >.05$). Tests of reciprocal effects models (Figure 6.2 panel b) again demonstrated stability of offspring DBD $\beta = .64, p = <.001$ and maternal warmth ($\beta = .69, p = <.001$) across time.

Maternal warmth exerted effects on offspring DBD symptoms within time, but not the other way around.

Offspring depression: Figure 6.3 (panel a) shows results for the cross-lagged models linking offspring depression to parent hostility. The stability coefficients of maternal hostility ($\beta = .68, p = <.001$) and children's depression symptoms across time ($\beta = .54, p = <.001$) were strong. There were no significant cross-lagged effects; child symptoms of depression were not related to maternal hostility across time (depression T2 to hostility T3 $\beta = .03, p = .576$), nor was maternal hostility related to child symptoms of depression ($\beta = .04, p = .506$) across time. Tests of reciprocal effects models confirmed the pattern of results observed in the cross-lagged model (Figures 6.3 panel b). Reciprocal effects models again showed strong within construct stability across time (offspring depression $\beta = .53, p = <.001$; maternal hostility $\beta = .67, p = <.001$). No significant reciprocal effects were observed between maternal hostility and offspring depression symptoms.

Discussion

Research of parents with depression has primarily assessed the effects of the parent-child relationship on risk for offspring psychopathology. However, very little previous research has directly tested the direction of effects between the parent-child relationship and offspring symptomatology nor considered if these effects vary for different forms of child psychopathology.

In the current study we observed that although maternal hostility was correlated with offspring depression symptoms both within and across time, hostility did not predict change in offspring depression symptoms; nor did offspring depression symptoms predict change in maternal hostility. This is in contrast to two previous studies that identified child effects (child internalising symptoms) on the parent-child relationship (Branje et al., 2010; Hale III

et al., 2011) and vice versa (Branje et al., 2010). However, both these studies used general population samples and mechanisms may not be equivalent in a high-risk group of offspring of mothers with recurrent depression that have met diagnostic criteria.

When examining the direction of effects between the mother-child relationship and offspring DBD symptoms, maternal warmth predicted change in offspring DBD symptoms within time. DBD symptoms did not have an effect on maternal warmth within or across time. We found evidence of bidirectional effects for offspring DBD symptoms and maternal hostility. Offspring DBD symptoms predicted change in maternal hostility over time. In addition, the converse was also true; maternal hostility predicted change in offspring DBD symptoms. Reciprocal effects models also demonstrated that maternal hostility predicted change in offspring DBD symptoms. These findings are consistent with previous research of offspring at high-risk of developing conduct problems, finding bi-directional effects between mother-child hostility and risk for offspring DBD (Combs-Ronto et al., 2009; Gross et al., 2008), and negative associations between maternal warmth and child antisocial behaviour (Boeldt et al., 2012; Caspi et al., 2004; Pettit, Bates, & Dodge, 1997). However, we extend understanding by showing that a similar pattern is observed between the mother-child relationship and risk for offspring DBD among depressed mothers, and that such effects continue to operate in adolescence. Both warmth and hostility in the mother-child relationship were associated with offspring DBD, with maternal warmth having a protective effect on risk for offspring within time, whereas maternal hostility increased risk for offspring DBD both within and across time. Furthermore, such effects appear specific to offspring DBD problems; neither warmth nor hostility had an effect on risk for offspring depression in the current study. Mechanisms for intergenerational transmission of risk may differ for offspring depression. This finding builds on previous research suggesting that the effects of disruptions to the mother-child relationship are likely to be stronger for offspring DBD than

depression (Combs-Ronto et al., 2009; Gershoff, 2002; McCarty & Weisz, 2002; Psychogiou et al., 2007; Stubbe et al., 1993).

It is important to consider the possibility that bidirectional effects observed between maternal hostility and offspring DBD symptoms may be due to gene-environment correlations where identified environmental risk factors may in fact be markers of genetic risk (Boeldt et al., 2012; Rice et al., 2006). However, Caspi et al (2004) found that differences in maternal hostility predicted differences between monozygotic twins (who share 100% of their genes in common), indicating that the effects of maternal hostility on offspring antisocial behaviour are unlikely to be due solely to genetic mediation. Two longitudinal genetically sensitive studies assessing the direction of effects between hostility and child antisocial behaviour also found that negative feelings towards offspring were an environmentally mediated risk for offspring antisocial behaviour, whereas child effects on maternal hostility were partly genetically mediated by offspring antisocial behaviours evoking parent negativity (Ge et al., 1996; Larsson, Viding, Rijdsdijk, & Plomin, 2008).

These findings should be considered in light of study limitations. First, although retention rates were high, data was not missing completely at random; families who declined to participate at follow-up assessments reported higher baseline child depression and DBD symptoms compared to those who participated. The study may therefore underestimate the association between maternal hostility and offspring psychopathology across time. Furthermore, missing data across assessments reduced available numbers in the analysis. The current study used multiple imputation to address these issues. Second, a wide age range of children was included in the study; however the focus of the current study was to investigate the direction of effects between the parent-child relationship and offspring psychopathology across the course of adolescence. Third, the study focused on maternal perceptions of the mother-child relationship and did not include information from fathers or from the

perspective of the child. However, a robust measure of the mother-child relationship was obtained through the use of multiple methods (questionnaire and speech sample).

DBD is one of the most common reasons for referral of children to mental health services, and has also been identified as a risk factor for future depressive disorders (Silberg et al., 2010) and other difficulties including substance misuse, academic difficulties and future antisocial behaviour (Combs-Ronto et al., 2009; Costello et al., 2011; Costello et al., 2003; Kim-Cohen et al., 2003; McGee et al., 2011). Understanding risks for the development of disruptive behaviours may help inform future intervention and prevention strategies and thus reduce the risk for future psychopathology. The current study suggests that maternal warmth may be a protective factor for offspring disruptive behaviours symptoms. Furthermore, adolescent disruptive and aggressive behaviours may develop through negative reinforcement of hostile relationships, with aggressive behaviours also provoking maternal hostility. It is important to consider that hostility may be a 'normal' reaction to difficulties associated with DBD symptoms (Anderson, Lytton, & Romney, 1986). A better understanding amongst professionals, parents, and society about DBD and its underlying causes may be needed to reduce negative or hostile reactions. Interventions aimed at reducing maternal hostility, and increasing maternal warmth may prevent or reduce disruptive behaviours in childhood (Scott, 2005; Scott, Spender, Doolan, Jacobs, & Aspland, 2001) and adolescence (Woolfenden et al., 2001).

Given evidence of bidirectional effects found here, where children with DBD symptoms present to services, the effect on parents also needs to be considered. Interventions that reduce offspring DBD may show benefits for mother-child relationships. This may be of particular importance in high-risk families affected by maternal depression. At present child and adolescent services are independent of adult services; however communication between different services may assist with early intervention and prevention strategies. In addition to

these health services, these findings are also of interest and have implications for other services (such as Social Services, Youth Offending Services and Education) where DBD might present and raise concern. Therefore information and interventions should be made available to services for families.

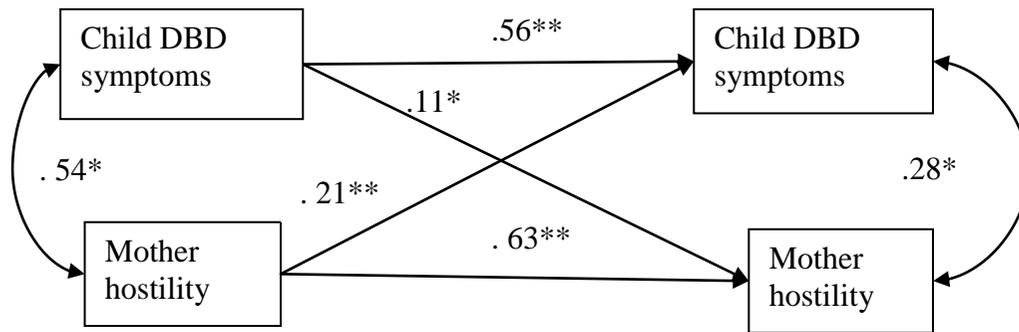
Tables and figures

Table 6.1: Inter-correlations among study variables

	1	2	3	4	5	6	7	8
1. Time 2 maternal hostility ^a	--							
2. Time 2 maternal warmth ^a	-.41**	--						
3. Time 2 child depression symptoms	.28**	-.13	--					
4. Time 2 child disruptive behaviour symptoms	.54**	-.28**	.46**	--				
5. Time 3 maternal hostility ^a	.67**	-.46**	.23**	.45**	--			
6. Time 3 maternal warmth ^a	-.44**	.70**	-.07	-.21**	-.63**	--		
7. Time 3 child depression symptoms	.18*	-.13	.58**	.37**	.25**	-.16*	--	
8. Time 3 child disruptive behaviour symptoms	.51**	-.24**	.34**	.67**	.54**	-.32**	.39**	--
Mean	-.01	.04	1.94	2.98	-.02	-.01	1.99	3.01
Standard Deviation	(1.63)	(1.57)	(1.97)	(2.55)	(1.69)	(1.61)	(2.11)	(2.66)

N.B. *p<.05 **p<.001. ^a Standardised z-scores of five minute speech sample and IYPF questionnaire measures of the parent-child relationship

Panel 1a



Panel 1b

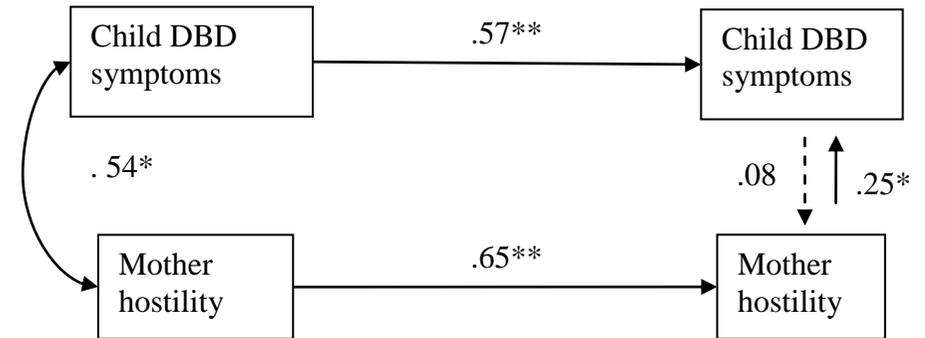
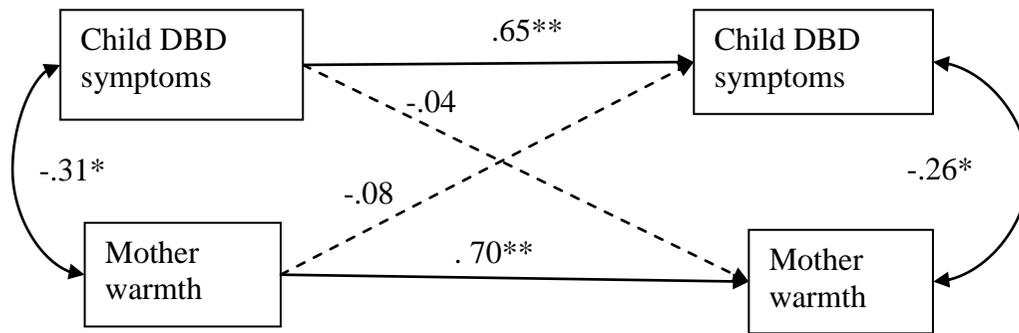


Figure 6.1: Maximum likelihood estimation of cross lagged (panel a) and reciprocal (panel b) effects of offspring DBD symptoms and maternal hostility.

Notes: * $p < .05$, ** $p < .01$. Cross-lagged model saturated no goodness of fit statistics generated.

Panel 2a



Panel 2b

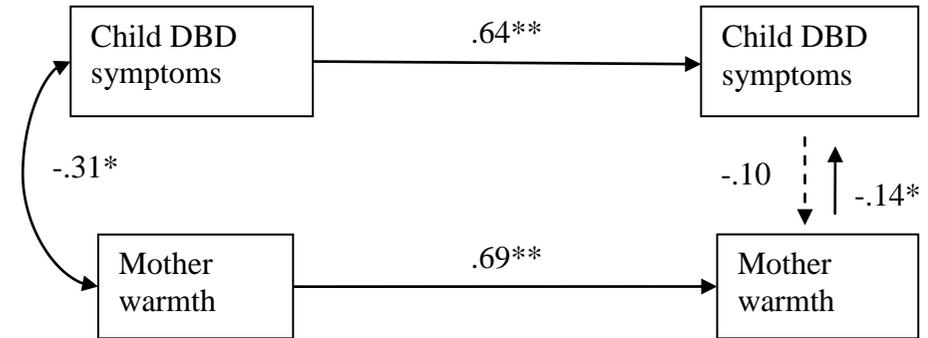
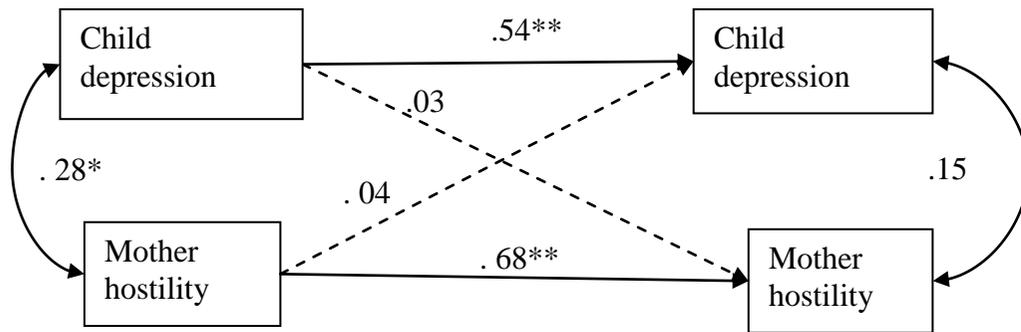


Figure 6.2: Maximum likelihood estimation of cross lagged (panel a) and reciprocal (panel b) effects of offspring DBD symptoms and maternal warmth

Notes: * $p < .05$, ** $p < .01$. Cross-lagged model saturated no goodness of fit statistics generated.

Panel 3a



Panel 3b

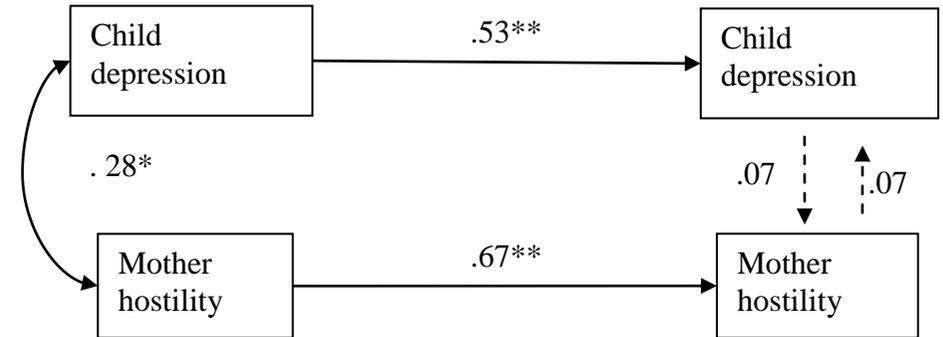


Figure 6.3: Maximum likelihood estimation of cross lagged (panel a) and reciprocal (panel b) effects of offspring depression symptoms and maternal hostility

Notes: * $p < .05$, ** $p < .01$. Cross-lagged model saturated no goodness of fit statistics generated.

Chapter 7. Overall Discussion

It is well established that parent depression is associated with an increased risk of psychopathology in offspring. However, outcomes are heterogeneous, with not all children going on to develop psychiatric disorders. Furthermore, offspring are at increased risk of developing a range of disorders, not just depression, but reasons for these heterogeneous outcomes are not well understood. Mechanisms for different disorders are likely to be complex and multi-factorial, involving genetic and environmental factors.

The presentation of depression is complex, and can co-occur with additional psychopathology. Given this complexity, the current thesis examined whether and how co-occurring psychopathology in mothers with recurrent depression increased risk for offspring psychopathology. A brief discussion of the findings will be presented followed by a discussion of the strengths and limitations of the study. Implications for practice will also be suggested, and areas for future work.

1. Summary of findings

Prior research suggests that anxiety, ASB, or alcohol use co-occur with adult depression, and are *each* associated with increased depression severity (Kessler et al., 1999; Kim-Cohen et al., 2005; Moffitt et al., 2007); this was observed in the current study. Furthermore, when examining the cumulative burden of co-occurring psychopathology in mothers with recurrent depression, the number of co-occurring problems was also associated with more severe maternal depression symptoms.

In the current study, the number of co-occurring problems in mothers predicted new-onset psychiatric disorder in offspring over and above maternal depression severity. This suggests that the burden of co-occurring problems in mothers with recurrent depression is a

risk factor for the development of psychopathology in offspring, rather than simply a marker of depression severity. This is in accord with a prior regionally representative study (McLaughlin et al., 2012). However, findings are extended in the current thesis, identifying that the burden of co-occurring psychopathology in mothers is associated with risk of psychopathology in high-risk adolescent offspring of mothers with recurrent depression.

Analyses considered whether specific co-occurring problems in mothers with recurrent depression were associated with specific offspring psychopathology, thus explaining, at least in part, the heterogeneous outcomes in adolescent offspring. Analyses accounted for the co-occurrence of offspring psychopathology (Angold et al., 1999; Avenevoli et al., 2001). By considering multiple domains of symptomatology in the mothers with recurrent depression, and multiple domains of offspring symptomatology simultaneously, it was possible to test specificity of inter-generational risk of particular dimensions of psychopathology. There was some degree of specificity of risk from maternal psychopathology to offspring symptomatology. Maternal depression severity predicted child depression symptoms, whereas maternal co-occurring ASB predicted offspring DBD. This is consistent with previous family studies of mothers with recurrent depression which have found that co-occurring maternal antisocial behaviour accounted for some of the association between parent depression and child conduct problems (Hirschfeld-Becker et al., 2008; Kim-Cohen et al., 2005).

Maternal hostility and warmth were then examined as potential mediating mechanisms. Both hostility and warmth were better-explained by mothers' co-occurring symptoms of ASB than by maternal depression severity. This is in accord with previous research examining parenting in depressed mothers with or without co-occurring ASB (Kim-Cohen et al., 2006). Additionally, maternal hostility predicted offspring symptoms of disruptive behaviour but not depression. This suggests that maternal hostility may be a

specific risk factor for offspring DBD symptoms, mediating effects of maternal ASB on risk for offspring DBD.

When examining the direction of effects between parenting and offspring symptomatology, warmth was not consistently associated with offspring depression symptoms within and across time, and therefore cross-lagged and reciprocal effects models were not conducted between maternal warmth and offspring depression symptoms. The construct of hostility was correlated with offspring depression symptoms within and across time. However, maternal hostility demonstrated no significant cross-lagged or reciprocal effects with offspring depression. However, maternal warmth predicted offspring DBD symptoms within time. Furthermore, bidirectional effects were observed between maternal hostility and offspring DBD symptoms across time; offspring DBD symptoms were predicted by maternal hostility, and maternal hostility was also predicted by offspring DBD symptoms across time; again suggesting that maternal hostility may especially important for the development of offspring DBD.

Overall, the current findings highlight that additional psychopathology in mothers with recurrent depression is common, is associated with increased depression severity, disruptions in parenting, and consequently with risk for the development of offspring psychopathology, especially DBD. Furthermore, findings of the current thesis suggest that, in the context of maternal depression, the co-occurrence of maternal ASB is a particularly important risk factor for the development of disruptive behaviours in offspring, and that this is mediated by impairments in parenting, particularly hostility.

2. Coercion theory and the development of antisocial behaviour

Coercion theory is a developmental perspective of antisocial behaviour that considers the course of antisocial behaviour from childhood to adolescence (Patterson, DeBaryshe, &

Ramsey, 1989). This theory states that bidirectional coercion between the parent and the child escalates over time, and thereby impact upon whether the child or adolescent will engage in deviant or antisocial behaviours (Dishion, Eddy, Haas, Fuzhong, & Spracklen, 1997; Granic & Patterson, 2006; Patterson & Stouthamer-Loeber, 1984; Reid, Patterson, & Snyder, 2002). Behaviours will persist when reinforced, whereas behaviours that do not have the desired effect will diminish. More specifically, the child's negative behaviours are an attempt to 'coerce' a parent into stopping any undesired request. Increasingly difficult behaviours follow further attempts to gain offspring compliance. This process may lead to parent withdrawal of requests. The coercive behaviour in offspring is then likely to generalize to other social settings such as school (Akers & Jensen, 2009).

The findings from the current thesis support this theory; bidirectional effects were observed between maternal hostility and offspring disruptive behaviours. This effect was specific to offspring disruptive behaviours, and suggests that parenting and child symptomatology impact upon each other across time. Furthermore, maternal hostility was found to mediate the effect of maternal ASB in mothers with recurrent depression on risk for offspring DBD symptoms. A number of well-validated evidence-based parenting interventions exist (Gardner, Burton, & Klimes, 2006; Hutchings et al., 2007; Sanders, 1999; Scott, 2005; Scott et al., 2001; Woolfenden et al., 2001). These may be especially beneficial in families where a parent presents with depression and co-occurring ASB and associated disruptions in the parent-child relationship.

3. The association between maternal hostility and child psychopathology

In the current thesis, maternal hostility was identified as a risk factor for offspring psychopathology, particularly DBD symptoms. It is important to consider what mechanisms may account for this association. Child perceptions, interpretations, and appraisals of events

may be particularly important. For example, it is important to consider whether the child perceives threat, or that they are to blame for conflict or hostile interactions (Harold & Conger, 1997; Shelton & Harold, 2008).

The meaning attached to parenting may be particularly important for the development of offspring psychopathology. The level of hostility in family interactions has been found to be related to child perceptions of events; a recent study suggested that parent hostility predicted adolescents' child perceptions of emotional security within the parent-child relationship (Cook, Buehler, & Fletcher, 2012). Parent-adolescent hostility has also been found to predict adolescent's representations of their parents' one year later, with increased parent-adolescent hostility predicting decreased levels of perceived emotional support, and levels of trust (Paley, Conger, & Harold, 2000). Furthermore, perceptions and appraisals of parent-child hostility have been associated with poorer outcomes in offspring, including anxiety and aggressive behaviours (Buschgens et al., 2010; Davies, Cummings, & Winter, 2004; Lansford et al., 2010; Yahav, 2006), suggesting that the meaning and appraisals offspring attach to the parent-child relationship may be an important consideration when examining risk for the development of offspring psychopathology.

4. Parenting as an environmental or genetic risk factor

In the current thesis, maternal ASB was found to be an important risk factor for offspring DBD symptoms, mediated by maternal parenting. The constructs of maternal hostility and warmth were posed as environmentally mediated mechanisms that may explain the risk for offspring psychopathology. However, it is important to consider whether gene-environment correlations might also account for these findings. Passive gene-environment correlations arise because parental genes are correlated with the environments they provide for their children (Rutter, 2007a). Active gene-environment correlations arise because the children's genetically influenced behaviours are correlated with the environments they select

(Rutter, 2007a). Evocative gene-environment correlations occur because child's genetically influenced characteristics are correlated with the behaviours they evoke in others (Boeldt et al., 2012; Rice et al., 2006). The parent's genotype may therefore be confounded with their own parenting and their child's behaviour. Children's own behaviour may also evoke differences in parenting. Both considerations highlight the possibility that identified environmental risk factors are markers for shared genetic risk factors

Although these issues cannot be addressed with the sample used in the current thesis, other genetically sensitive designs have been utilised to consider this issue, with results suggesting that the influences of parent antisocial behaviour on the risk for offspring disruptive behaviours reflect (at least in part) *environmental* mediation via parenting. Caspi et al (2004) ruled out the possibility that effects of maternal hostility on risk for child DBD problems were solely genetically mediated; differences in maternal hostility predicted differences in offspring DBD problems between genetically identical monozygotic twins. Furthermore, a genetically sensitive study of children born via assisted conception examined the role of warmth and hostility in explaining links between parent psychopathology and child psychopathology in genetically related or unrelated parent-child pairs (Harold et al., 2010). Mother-child hostility mediated the association between maternal antisocial behaviour and offspring antisocial behaviour in both genetically related and unrelated groups, providing evidence for environmental mediation. In contrast, maternal warmth and hostility mediated the effect between maternal depression and child depression in genetically related but not genetically unrelated groups, suggesting here a possible passive gene-environment correlation (Harold et al., 2010).

Two longitudinal population-based studies have assessed the direction of effects between parenting and child externalising problems in pre-adolescent (Larsson et al., 2008) and early adolescent (Burt et al., 2005) offspring using genetically sensitive designs. Bi-

directional effects were observed between parent negativity and offspring externalising problems. Parent effects on offspring (negative feelings towards offspring predicting child externalising problems) were found to be primarily a function of environmental effects. In contrast, child effects on parenting (child externalising problems predicting parent negativity) were largely explained by genetic factors, with offspring externalising problems evoking parent negativity (Burt et al., 2005; Larsson et al., 2008). Together these studies suggest that parent hostility towards offspring represents, at least in part, an *environmentally* mediated risk factor for offspring disruptive behaviour in parents with ASB. However, future research should extend these findings by examining whether these mechanisms are similar in *adolescents* of mothers with *recurrent depression* and co-occurring antisocial behaviour.

5. Strengths

Most previous studies have compared offspring of depressed mothers and non-depressed mothers. One of the main strengths of the current thesis is that it assessed within-group variation in mothers with recurrent depression and risk for offspring. This provided the requisite power to address the issue of how heterogeneity among parents with depression is related to heterogeneity in offspring risk.

Second, the current thesis utilised longitudinal data with excellent retention rates to assess the development of psychopathology over time. This allowed the testing of key questions, such as identifying risk factors that predict new-onset psychopathology, using three time points to test mediation, and test the direction of effects between key constructs. Furthermore, the current thesis focused on these issues across the course of adolescence. Evidence suggests that risk for psychopathology increases markedly during adolescence (Costello et al., 2011; Costello et al., 2003), and that the parent-child relationship is subject to change (McGue et al., 2005).

Third, the sample was a large and well characterised clinical sample of parents with recurrent depression and their adolescent offspring. Therefore, throughout the current thesis, the relations between co-occurring psychopathology in mothers with recurrent depression and offspring psychopathology could be assessed. This has rarely been considered; few studies have assessed the burden of co-occurring psychopathology in mothers with recurrent depression and the impact on offspring psychopathology. Furthermore, studies that have considered the specificity of risk from parent to offspring in these high-risk groups have focused primarily on homotypic transmission.

Fourth, the current thesis used standardised semi-structured assessments to assess offspring mental health. Such interviews are the ‘gold standard’, being detailed and rigorous. Reliability of assessments was assessed and in the current study was high. Furthermore, the semi-structured interview allowed both diagnoses and symptom counts to be derived. This allowed for the analysis of clinically relevant categories, and dimensional measures of symptoms. Multiple informants were used to assess child psychopathology. This has been found to have higher validity than using single informants; parents may not be aware of some symptoms that their offspring report, in addition some symptoms have been found to be under-reported by children (Angold & Costello, 1995; Angold et al., 1995). Therefore, using multiple informants to assess behaviour is the ‘gold standard’ for research as well as clinical practice. Furthermore, utilising multiple informants reduces shared method variance (for example where mothers report on their own and their offspring’s mental health, the association between these two constructs may be inflated).

6. Limitations

The findings in the current thesis should also be considered in light of some limitations. First, although potential risk factors and mechanisms were identified, conclusions

about causality would be premature. Randomised control trials would be needed to test, for example, whether interventions targeting such risk factors did indeed have an impact on offspring psychopathology. However, the use of longitudinal data utilised here allowed the formal testing of the direction of effect to assess the temporal associations between key constructs. Furthermore, the findings do highlight important risk factors associated with risk for offspring psychopathology which may improve the targeting of interventions. In particular, children of depressed mothers with other co-occurring psychopathology represent an especially high-risk subgroup.

Second, despite excellent retention rates, attrition is inevitable in longitudinal research. Mothers who did not participate at either follow-up (Time 2 or Time 3) were found to have higher baseline depression severity scores and ASB scores. In addition, where families did not take part at Time 3, their offspring had higher depression and DBD symptoms at baseline. Therefore, the data were not missing completely at random. The current thesis made use of multiple imputation techniques to address this issue.

Third, there was variation in child age at each assessment (offspring aged 9 to 17 years at the baseline assessment). Not all children had passed through the age of risk for the development of some disorders by the final assessment. Therefore the adolescents may go on to develop additional psychopathology in the future. In addition, different risk factors may be associated with child psychopathology at different developmental stages (Copeland et al., 2009; Costello et al., 2011). However, insufficient power for analyses stratified by child age prevented this from being tested in the current study.

Fourth, EPAD does not include enough depressed fathers to consider whether findings are similar or different in offspring of depressed fathers. Depression is relatively common in men, with the lifetime prevalence estimated to be 12.7% (Blazer et al., 1994) but is under-represented in the EPAD study. This may be due, in part, to the method of recruitment of

families; the majority of families were recruited via primary care, and there is evidence to suggest that females are better at accessing help than men (Mackenzie, Gekoskia, & Knoxa, 2006). It is important to consider paternal depression as a risk for offspring psychopathology in its own right. Paternal depression has been related to offspring internalising and externalising psychopathology after controlling for maternal depression (Kane & Garber, 2004; Ramchandani, Stein, et al., 2008), suggesting that there may be a unique contribution of paternal depression. However, more research is needed here, particularly with clinical samples.

Fifth, the current study used questionnaires rather than diagnostic interviews to assess maternal comorbid psychopathology due to the burden of other assessments conducted as part of the study. Mothers completed interviews regarding their depression history, and current depression symptoms, as well as lengthy interviews about offspring psychopathology. However, questionnaire screens are commonly used in primary care, where most depressed adults are assessed and treated. It is also important to consider that other forms of psychopathology also co-occur with depression, including drug misuse and eating disorders. These additional problems were not assessed in the EPAD study. How these additional problems are associated with risk for offspring psychopathology in children of mothers with recurrent depression also needs to be considered.

Sixth, it is important to consider that there was a relatively small overlap between measures of the mother-child relationship (EE and IYFP), which could have impacted on the pattern of results observed in the current thesis. However, this is often the case when information is obtained from different sources, with evidence suggesting that parent reports of parenting do not correlate highly with other family members, or outside observers; using a single reporter is unlikely to provide sufficient information for understanding complex processes (Bogenschneider & Pallock, 2008; Tein, Roosa, & Michaels, 1994; Winsler et al.,

2005). The two measures were therefore combined to create a robust multi-informant measure of the parent-child relationship. Future research could examine how measures of the parent-child relationship from different sources are associated with child outcomes. Some previous research suggests that it is the level of disagreement between reporters, rather than overall levels of parenting *per se* that may be associated with negative child outcomes (Gaylord, Kitzmann, & Coleman, 2003; Pelton & Forehand, 2001; Pelton, Steele, Watts Chance, & Forehand, 2001).

Finally, the EPAD study was not designed to test whether associations reflected shared genes, environmental factors, or the interplay between the two. However, as noted, previous literature suggests that effects of maternal antisocial behaviour on offspring disruptive behaviour are *environmentally* mediated, including via maternal hostility (Harold et al., 2010; Larsson et al., 2008).

7. Future directions

7.1. The role of fathers

Assortative mating is a process whereby particular traits or characteristics are observed in partners at frequencies greater than would be expected by chance. Previous studies have suggested that depressed mothers are more likely than non-depressed mothers to have partners with some form of psychopathology, particularly depression or antisocial behaviour (Marmorstein & Iacono, 2004). Therefore, further research should consider the role of fathers in families where a mother has recurrent depression. If the father presents with no psychopathology this may act as a protective factor for offspring (Brennan et al., 2002). Alternatively, if the father also has depression, risk for offspring psychopathology may increase either through genetic or environmental mechanisms (Goodman & Gotlib, 1999;

Klein et al., 2005; Marmorstein et al., 2004). Evidence suggests that children with two depressed parents are at significantly greater risk of developing psychopathology (Lieb, Isensee, Höfler, Pfister, et al., 2002; Weissman et al., 1984), particularly externalising disorders (Brennan et al., 2002; Ramchandani, O'Connor, et al., 2008; Ramchandani, Stein, et al., 2008) compared to children with one parent with depression.

Paternal ASB may also exacerbate the association between maternal depression severity and offspring DBD, although effects of paternal psychopathology on risk for offspring may be moderated by the presence of the father (Blazei et al., 2008; Jaffee, Moffitt, Caspi, & Taylor, 2003; Thornberry, Freeman-Gallant, & Lovegrove, 2009). Exploratory preliminary analyses (Appendix 5) considered this possibility in the EPAD sample. Maternal symptoms of depression severity, anxiety, and ASB were not associated with paternal self-rated symptoms of depression severity, anxiety, ASB, or alcohol use. Therefore, the associations observed between maternal co-occurring psychopathology and child psychopathology are unlikely to be explained by assortative mating in this sample. However, the analyses conducted were preliminary; in-depth associations were not available for the majority of many partners.

Paternal depression may have a negative effect on parenting; paternal depression has been associated with increased father-child hostility and decreased positive parenting behaviours compared to fathers without depression (Kane & Garber, 2004; Wilson & Durbin, 2010), and these impairments in parenting may mediate the effect of paternal depression symptoms on risk for offspring internalising and externalising problems (Hanington, Heron, Stein, & Ramchandani, 2011; Kane & Garber, 2009). Furthermore, evidence suggests this effect may be independent of the effects of maternal depression symptoms (Kane & Garber, 2009); the interpersonal effects of depression may therefore not be restricted to mothers.

However, the effect of paternal depression on risk for offspring psychopathology has, until recently, largely been neglected.

7.2. Inter-parental conflict

It is important to consider that the parenting constructs addressed in the current thesis (particularly maternal hostility) are likely part of a wider family context. The findings in the current thesis could therefore be further developed to move beyond the dyad of the mother-child relationship and consider other likely important factors; individuals should be considered in the context of the whole family system (Cox & Paley, 2003). Family processes such as marital discord may be particularly important. For example, parent depression has been associated with higher levels of marital conflict (Cummings, Keller, & Davies, 2005; Downey & Coyne, 1990). Marital discord has also been associated with offspring risk for future internalising and externalising problems (Cummings & Davies, 1994, 2002; Hanington et al., 2011; Schoppe-Sullivan, Schermerhorn, & Cummings, 2007; Shelton & Harold, 2008), with some studies suggesting stronger links between marital conflict and internalising problems than between marital conflict and externalising problems (Davies & Windle, 1997; Harold & Conger, 1997; Kouros, Merrilees, & Cummings, 2008). Therefore, these findings may go some way to help explain the mechanisms of risk for different outcomes in offspring.

Marital discord has also been found to be associated with offspring's own appraisals of parent rejection (Shelton & Harold, 2008). In a sample of adolescents, youth-rated parent warmth and rejection were found to mediate the relationship between inter-parental conflict and offspring depression (O'Donnell, Moreau, Cardemil, & Pollastri, 2010). However, additional research suggests that poor marital relations (e.g. marital conflict, less secure marital attachment), but not impaired parenting, may mediate the effect of parent depression on child outcomes (internalising or externalising symptoms) in a low risk community sample

of young children (Cummings et al., 2005). Future research is warranted to further clarify mechanisms of inter-generational transmission of risk for offspring psychopathology, and these studies highlight the importance of considering additional family processes when examining the risk for offspring psychopathology in adolescents of depressed parents.

7.3. Parent Responsivity

It is important to consider that there are additional constructs of parenting that may be associated with both maternal psychopathology and child outcomes. Parent responsivity is a construct of parenting that refers to how a parent responds to cues from their child, and how parents provide input and support for their offspring (Warren & Brady, 2007). Hostile mother-child relationships are likely to be associated with responsive parenting (Sturge-Apple, Davies, Boker, & Cummings, 2004; Sturge-Apple, Davies, & Cummings, 2006).

Maternal depression has been associated with impairments in responsive parenting (Cox, Puckering, Pound, & Mills, 1987; Cummings & Davies, 1994; Lovejoy et al., 2000), although there is some evidence to suggest that this may be better accounted for by maternal co-occurring psychopathology (Carter et al., 2001). Furthermore, maternal responsiveness has been associated with child outcomes. Maternal responsiveness during infancy has been found to predict offspring behaviour problems in early and middle childhood (Goldberg, Gotowiec, & Simmons, 1995; Johnston, Murray, Hinshaw, Pelham Jr., & Hoza, 2002; Wakschlag & Sydney, 1999). Maternal responsiveness has also been shown to predict child emotional development (Davidov & Grusec, 2006; Shipman & Zeman, 2001). In addition, children whose mothers display more responsive behaviours have fewer emotional and behaviour problems by early childhood (Beckwith, Rodning, & Cohen, 1992). This research suggests that maternal responsiveness may be important to construct for the development of psychopathology in offspring.

A limitation of these findings, however, is that in much previous literature, maternal responsiveness has been assessed in infancy, defining maternal responsiveness as responses to crying, sensitivity or intrusiveness in play. This is unlikely to be a valid measure of maternal responsiveness in adolescence. To assess the effect of maternal responsiveness in adolescence, it is necessary to have a developmentally-appropriate measure of maternal responsiveness. Questionnaire measures of parental responsiveness and assessment of support during homework tasks may be alternative age-appropriate measures. Research that has assessed parent responsiveness towards adolescent offspring has focused on achievement, and found that parent responsivity is associated with higher academic achievement and mathematics ability in adolescents (Bogenschneider & Pallock, 2008; Paulson, 1994; Pratt, Green, & MacVicar, 1992). Whether parent responsiveness is associated with adolescent mental health problems is less certain, although some evidence suggests lower levels of parent responsiveness may be important to the development of externalising problems in adolescents (Bogenschneider & Pallock, 2008; Reitz, Deković, & Meijer, 2006).

7.4. Peer relationships and parental monitoring

It may also be important to consider processes outside the family context in high-risk adolescents. As children develop across the course of adolescence and into early adulthood, the relative importance of family factors versus peer influences may change (Tully et al., 2008). Ideally, peer processes need to be considered alongside aspects of the mother-child relationship. Previous research has suggested that the quality of the parent-child relationship (including hostility) and peer relationships (including rejection, support, and peer deviance) are important risk factors for future adolescent aggression and conduct problems (Benson & Buehler, 2012; Trudeau, Mason, Randall, Spoth, & Ralston, 2012), and that family and peer influences may show important interactive effects. For example, effective parenting (e.g.

through greater monitoring of out-of-home activities) may protect against the effects of deviant peers across adolescence (Trudeau et al., 2012). Many studies have suggested that parent monitoring is associated with better outcomes in offspring (Amato & Fowler, 2002; Dishion & McMahon, 1998; Kilgore, Snyder, & Lentz, 2000; Pettit, Bates, Dodge, & Meece, 1999). Parent monitoring may change over the course of adolescence, with evidence suggesting that parents may disengage from monitoring as disruptive or deviant behaviours continue (Kerr, Stattin, & Burk, 2010).

7.5. Parent monitoring versus Parent Knowledge

Recent evidence suggests that adolescents' self-disclosure of activities, rather than parental monitoring/surveillance per se, are more likely to predict positive child outcomes (Stattin & Kerr, 2000). Relationships that facilitate communication and bonds between parents are likely to be important for spontaneous child disclosure (Kerr & Stattin, 2000). Hostile mother-child relationships are unlikely to foster such disclosure. Future research should therefore consider the effect of parent monitoring, the effect of child disclosure of activities, as well as the effect of deviant peers, on risk for offspring conduct problems, and how these processes are influenced by parental depression.

7.6. Variation by child gender

Although beyond the scope of the current thesis, previous research demonstrates that the effects of dysfunctional parent-child relationships on risk for offspring psychopathology may vary by child gender. Male offspring may be more likely to respond with aggression whereas female offspring may be more likely to respond with distress (Cummings, Iannotti, & Zahn-Waxler, 1986). Other research suggests that female offspring may be more sensitive to the negative effects of maternal depression symptoms than boys (Lewis et al., 2011).

Opposite sex parenting effects may also be important for child adjustment (Blatt-Eisengart et al., 2009; Davies & Windle, 1997; Leinonen, Solantaus, & Punamäki, 2003). These effects need to be clarified in high-risk groups of adolescent offspring of parents with recurrent depression.

7.7 The moderating role of socio-economic factors

It has long been recognised that there is an association between socioeconomic factors and depression (Gilman, Kawachi, Fitzmaurice, & Buka, 2003; Lorant et al., 2007; Lorant et al., 2003; Newland, Crnic, & Mills-Koonce, 2013). Depression is over-represented among adults with lower socio-economic status (SES) or education attainment (Bradley & Corwyn, 2002). Low parent SES has also been associated with an increased risk for offspring psychiatric problems in children including anxiety, depressive disorders and disruptive disorders (Bolger, Patterson, Thompson, & Kupersmidt, 1995; Bradley & Corwyn, 2002; Brooks-Gunn & Duncan, 1997; Gilman et al., 2003; Johnson et al., 1999; McLeod & Shanahan, 1993).

Socio-economic factors have been also been found to moderate the association between maternal psychopathology and child outcomes; evidence suggests that offspring of parents from higher SES may be less affected by parent depression, whereas offspring of parents from low SES may be more vulnerable to the negative effects of parent depression. This may be due, in part, to SES having an impact on material and social resources, including positive parenting (Bradley & Corwyn, 2002).

A range of measures of SES have been found to be associated with parenting and the family environment, supporting the notion that SES impacts on such resources. Mothers with lower income and educational attainment are less positive in their parenting practices, and use less discipline (Fox, Platz, & Bentley, 1995). Adolescents experiencing economic

disadvantage report lower levels of positive family interactions and perceived parenting (Shek & Tsui, 2013). In contrast, high SES parents have been found to engage children more in conversation, read to them, and provide teaching experiences (Bradley & Corwyn, 2002).

This evidence is of particular relevance to the findings in the current thesis; specifically, SES may moderate the association between maternal depression and parenting factors. The effects of maternal depression on parenting may be stronger in more disadvantaged groups (Bradley & Corwyn, 2002; Stein, Malmberg, Sylva, Barnes, & Leach, 2008), in contrast, high parental SES (and in turn, the association with positive parenting) may act as a protective factor for offspring at high risk of developing psychopathology (Lovejoy et al., 2000). This research highlights the importance of considering the moderating effect of SES on the association between maternal depression and child outcomes.

7.8. Genetically sensitive designs

Finally, future research should consider utilising genetically sensitive designs in high-risk groups of adolescents to clarify whether the effects of parenting represent environmental risk factors. As highlighted above, previous research suggests that it is likely that parent hostility is an environmental risk factor for offspring DBD symptoms. However, these studies were not conducted with adolescent offspring or high-risk groups, and therefore further evidence is needed. In addition, the majority of genetically sensitive designs (twin studies, adoption studies) are typically community based and few would have the required power to undertake the types of analyses considered here.

8. Implications

The current thesis provided additional evidence that the burden of co-occurring psychopathology in adults was associated with more severe concurrent depression, which has implications for the monitoring and treatment of adult depression. Additional psychopathology in mothers with recurrent depression also predicted increased risk for the development of a psychiatric disorder in offspring, and this has implications for these children who are already at increased risk of developing psychopathology by virtue of have a parent diagnosed with recurrent depression. In particular, monitoring co-occurring psychopathology in mothers with recurrent depression in general practice may improve identification of children at greatest risk of developing psychiatric disorders. This is particularly important as evidence from this sample suggests that, even in a high-risk group of offspring whose parents are known to services, the children with psychiatric disorders largely do not access services, often even in the presence of suicidal risk (Potter et al., 2012). Results from the present thesis suggest that there is some specificity of risk to offspring. This finding is particularly relevant to the targeting of intervention strategies, particularly as different disorders are likely to require different interventions. The findings suggest that although maternal depression is considered to be a risk factor for the development of offspring DBD symptoms, this association may be better accounted for by maternal co-occurring ASB. Maternal depression per se may have a less important role in the development of offspring DBD than previously thought. This highlights the need for primary care workers to assess co-occurring maternal ASB in mothers with recurrent depression to better aid the targeting of prevention strategies to offspring at risk of developing disruptive behaviours. This is particularly important as DBD symptoms in adolescence are associated with a wide range of negative outcomes, and are strong predictors of future psychopathology (Combs-Ronto et al., 2009; Costello et al., 2011; Costello et al., 2003; Kim-Cohen et al.,

2003; McGee et al., 2011; Silberg et al., 2010). Identifying those at risk of developing DBD, and preventing the development of such problems, may reduce the burden of adult psychopathology.

The current thesis has demonstrated that maternal hostility may be a specific risk factor for offspring disruptive behaviours. Parenting interventions aimed at reducing maternal hostility may be beneficial for preventing or reducing disruptive behaviour problems in offspring of depressed mothers, particularly where mothers present with additional co-occurring antisocial problems. Indeed, parenting programmes have shown some sustained benefits for the management of conduct problems in young children, with both parenting skills and conduct problems showing improvements (Posthumus, Raaijmakers, Maassen, van Engeland, & Matthys, 2012). These interventions aimed at preventing disruptive behaviours also provide an opportunity for reducing the burden associated with many adult psychiatric disorders.

Given the bidirectional effects observed in the current thesis between maternal hostility and offspring disruptive behaviours, interventions that are aimed at reducing offspring disruptive behaviours may also be useful for improving outcomes for both child and parent. Child training may be an important component of intervention programmes. Current interventions that have combined parent training and child training have shown positive results in young children (Webster-Stratton & Hammond, 1997; Webster-Stratton, Reid, & Hammond, 2004). A recent Cochrane review concluded that, overall, family and parenting interventions were beneficial for the management of conduct problems in children and adolescents aged between 10-17 years (Woolfenden et al., 2001). However, effects were diverse and it is necessary to understand which aspects of family intervention programmes are the most relevant for the prevention of disruptive behaviours in this age group.

Finally, it is important to consider the association between maternal depression and parenting interventions; some research suggests that parenting interventions aimed at reducing maternal hostility may also be beneficial for reducing maternal depression symptoms (Barlow & Coren, 2000; Barlow, Coren, & Stewart-Brown, 2003; Gross, Fogg, & Tucker, 1995). Additional evidence also suggests that maternal depression may moderate the response to parenting interventions, with the most beneficial response being observed among parents with lower depression scores (Beauchaine, Webster-Stratton, & Reid, 2005).

9. Conclusion

Comorbid psychopathology in adults with depression is common and explains some of the risk to adolescent offspring; comorbid psychopathology in mothers with recurrent depression was an important risk factor for new onset psychiatric disorder in offspring over and above maternal depression severity. Maternal psychopathology demonstrated some specificity of risk, with maternal depression severity predicting offspring depression symptoms, and maternal co-occurring ASB predicting offspring symptoms of disruptive behaviour disorder. Furthermore, offspring disruptive behaviours developed through hostile parenting, with offspring disruptive behaviours also provoking hostile parenting. The current thesis therefore demonstrates the importance of considering co-occurring psychopathology in mothers with recurrent depression, particularly ASB, when examining risk for offspring psychopathology.

Appendices

Appendix 1: Table 1.1. Rates of child disorder at baseline assessments and follow-up assessments

	Wave 1		Wave 2		Wave 3	
	% of sample (n = 337)		% of sample (n = 286)		% of sample (n = 283)	
Any DSM-IV disorder	23.7%	(80)	27.9%	(80)	25.4%	(72)
Any Depressive disorder	4.5%	(15)	7.7%	(22)	7.1%	(20)
MDD ^a	3.6%	(12)	5.9%	(17)	5.3%	(15)
Dysthymia	0.3%	(1)	0.3%	(1)	0.7%	(2)
Depressive disorder NOS ^b	0.6%	(2)	1.4%	(4)	1.1%	(3)
Adjustment with depressed mood		(0)	0.3%	(1)	1.4%	(4)
Bipolar Spectrum Disorder	0.3%	(1)	1.0%	(3)	1.4%	(4)
Cyclothymia		(0)	0.7%	(2)		(0)
Any Anxiety Disorder	11.6%	(39)	13.2%	(38)	13.4%	(38)
GAD ^c	3.3%	(11)	5.6%	(16)	7.4%	(21)
Separation anxiety	3.6%	(12)	3.1%	(9)	1.8%	(5)
OCD ^d	1.2%	(4)	1.5%	(4)	2.5%	(7)
Panic disorder	0.3%	(1)		(0)		(0)
Agoraphobia	0.6%	(2)		(0)		(0)
Social Phobia	4.5%	(15)	5.9%	(17)	5.3%	(15)
Anxiety NOS	1.2%	(4)	1.4%	(4)	1.4%	(4)
Adjustment with Anxiety		(0)		(0)	0.4%	(1)
Simple phobia	2.7%	(9)	7.3%	(21)	7.4%	(21)
Any DBD^e	7.1%	(24)	10.1%	(29)	8.1%	(23)
ODD ^f	5.3%	(18)	6.3%	(18)	6.7%	(19)
CD ^g	0.3%	(1)		(0)	0.4%	(1)
Disruptive NOS	1.5%	(5)	3.8%	(11)	1.1%	(3)
ADHD ^h (wave 1 or wave 2)	6.2%	(21)	6.6%	(19)	6.4%	(18)
Bulimia	0.6%	(2)		(0)		(0)
Eating Disorder NOS	0.3%	(1)	1.0%	(3)	0.4%	(1)

^a Major Depressive Disorder; ^b Not Otherwise Specified; ^c Generalised Anxiety Disorder;

^d Obsessive Compulsive Disorder; ^e Disruptive Behaviour Disorder; ^f Oppositional Defiant Disorder; ^g Conduct Disorder; ^h Attention Deficit Hyperactivity Disorder.

Appendix 2: Expressed emotion

The measure of Expressed Emotion (EE) does not have a clear theoretical foundation and this had led to concerns that research may be carried out without a clear rationale as to why EE should be related to the disorder under investigation, or how different aspects of EE may affect outcome. It is therefore described in some detail in this section; examining EE components and its relationship with other variables may improve our understanding.

The five minute speech sample (FMSS) has been primarily composed of two components: criticism and emotional over-involvement (EOI; a measure of self-sacrificing behaviours). Most previous studies have categorised overall EE as 'high' or 'low' according to overall high criticism or emotional over-involvement. High EE is considered present if either high criticism (the parent expresses a negative initial statement, a negative relationship, one or more criticism, or the tone of the interview is critical), or EOI (parents express excessive emotion such as crying, state strong statements of affection, or excessive detail about the past) are present.

More recently EE has been applied to child and adolescent populations and EE is assumed to measure a parent's attitudes towards their child, thus assessing the parent-child relationship. It may be difficult to get parents to reveal how they feel about their children through questionnaire measures because of factors including social desirability; the measure of EE may be a less obtrusive measure of the relationship between parent and child (Caspi et al., 2004). High EE has been associated with poorer child outcomes; it has been associated with increased impairment, slower recovery, and is predictive of relapse (McCleary & Sanford, 2002). However, how it operates is unclear.

Limitations of the previous research assessing EE

Warmth has historically not been included as a separate component of EE. This was largely because low warmth was found to be associated with high criticism. This led to the assumption that warmth and criticism were opposites of the same construct, and to a neglect of the assessment of the role of warmth within families (Hooley & Parker, 2006).

EE has often been categorised as ‘high’ or ‘low’ and this may be inappropriate for several reasons. First, EE is unlikely to operate in a dichotomous fashion, furthermore there is a lack of consensus about how to categorise relatives as ‘high EE’, and which cut points to use. However cut-points remain despite losing information from a continuous variable (Kuipers, 1994; Wearden, Tarrier, Barrowclough, Zastowny, & Rahill, 2000). Second, different components of EE may be differentially associated with other risk factors and outcomes. Categorising parents as ‘high’ or ‘low’ EE would obscure such findings. Research assessing this is inconsistent, with studies suggesting that EE criticism may be associated specifically with DBD (Nelson et al., 2003; Peris & Baker, 2000; Vostanis et al., 1994), or depression (Asarnow, Tompson, Hamilton, Goldstein, & Guthrie, 1994; Asarnow et al., 2001), or that low warmth may be specifically associated with internalising problems (Stubbe et al., 1993), or with both internalising and externalising (Vostanis et al., 1994). These findings underscore the need to assess components of EE separately to gain a better understanding of EE and its effects.

A further limitation of the measure of EE is that it was originally developed for relatives of adults with schizophrenia. The EE construct of EOI may be developmentally inappropriate to apply to children and adolescents. The distinction between supportive parenting and over-involvement becomes less clear in child and adolescent groups compared to adult groups. Furthermore, EOI has been found to be virtually absent in clinical and non-clinical groups of children (Kershner, Cohen, & Coyne, 1996) or it has not been associated

with child outcomes, or observational measures of parenting (McCarty, Lau, Valeri, & Weisz, 2004). The construct of EOI may therefore be less pertinent to children and adolescents.

Finally, it is unclear whether EE is a response to a patient's behaviour or is a causal risk factor. Although EE is associated with child psychopathology it is possible that high EE is a consequence of the difficulties and distress associated with child behaviours, rather than a cause of child psychopathology. Therefore, whether EE has a causal role in the development of child psychopathology has not been established. It is likely that there are bidirectional effects, with parent EE predicting offspring psychopathology and vice versa.

Maternal warmth and hostility (EE): methodology

To improve understanding of the measure of EE in mothers with recurrent depression, the following section will assess the constructs of warmth and hostility with regards to:

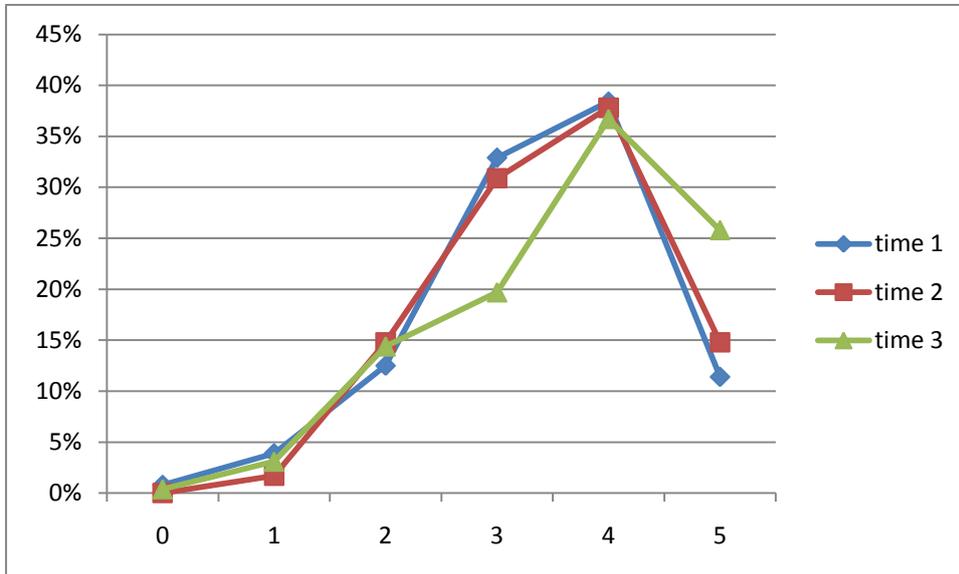
- (1) Frequency of the constructs
- (2) Stability of the constructs
- (3) Construct validity
- (4) Associations with well-known risk factors
- (5) Inter-rater reliability

For the purposes of these analyses the child was required to be living at home throughout the entirety of the study period.

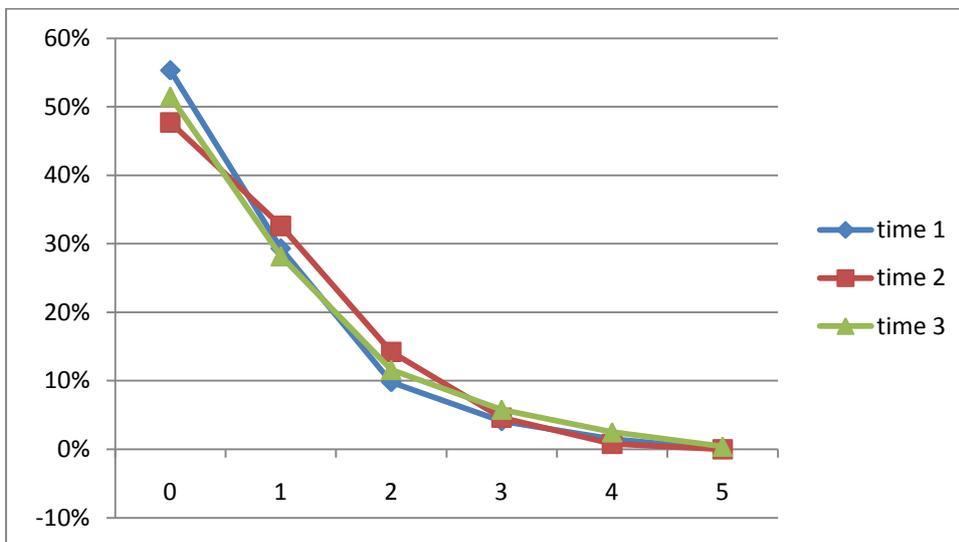
1. Frequency of the constructs of warmth and hostility

There are no established cut-points for EE, particularly for this age group (adolescent offspring), therefore rather than assessing 'high' or 'low' maternal warmth/hostility, a continuous approach was used to assess the frequency of hostility and warmth at each assessment. The majority of mothers in the sample had high moderate to high warmth

(Appendix Figure 1.1 panel a) and low hostility towards the child (Figure 1, panel b) at each assessment.



Panel a: Maternal warmth at each assessment



Panel b: maternal hostility at each assessment

Appendix Figure 1.1: Rates of maternal warmth, and hostility (EE) at each assessment

2. Stability over time

Parent attitudes towards their children, and thus the measure of EE, is considered to be both a stable and dynamic process (Barrowclough & Hooley, 2003), with the measure of EE showing some stability, as well as change over time (Peris & Baker, 2000; Sandberg, Rutter, & Jarvi, 2003). There were moderate but significant associations across time for maternal warmth (time 1 with time 2 $r = .47$, $p = <.001$; time 2 with time 3 $r = .43$, $p = <.001$) and hostility (time 1 with time 2 $r = .39$, $p = <.001$; time 2 with time 3 $r = .44$, $p = <.001$), supporting this theory.

3. Construct validity

It remains unclear whether EE measures the parent-child relationship specifically, or is a more general measure of the family environment. There has been limited research investigating factors that contribute to EE. Therefore, baseline cross-sectional correlations were conducted to assess the relationship between maternal warmth/hostility assessed by the EE, and by a self-report questionnaire completed by the mother (the IOWA). Correlations were also conducted with baseline maternal EE warmth/hostility and the family environment scale (FES) subscales of conflict and cohesion (parent and child reports).

3.1. Family interaction rating scale (warmth/hostility)

3.1.1. The parent-child relationship (parent rated)

Baseline maternal EE hostility ratings were positively correlated with the hostility subscale of the IOWA questionnaire ($r = .34$, $p = <.001$). Baseline EE warmth was positively correlated with the IOWA warmth subscale ($r = .35$, $p = <.001$). As expected, EE hostility and IOWA warmth were negatively correlated ($r = -.28$, $p = <.001$), as was EE warmth and IOWA hostility ($r = -.30$, $p = <.001$).

3.1.2. Inter-parental conflict (parent rated)

Baseline maternal EE hostility towards the child was not significantly correlated with baseline maternal reports of hostility towards their partner ($r = .12, p = .099$), but was negatively associated with warmth towards the partner ($r = -.18, p = .009$). Baseline EE warmth towards the child was not correlated with baseline self-reports of hostility towards the partner ($r = -.12, p = .107$), but was negatively correlated with the IOWA warmth towards partner subscale ($r = -.26, p = <.001$).

3.2. Family Environment Scale

The Family Environment Scale (FES; (Moos & Moos, 1994)) was developed to measure social and environmental characteristics of families. It is a self report questionnaire rated by both the parent and the child. It is an 18-item questionnaire, with two subscales (each with 9 items) of ‘conflict’ and family ‘cohesion’. Higher scores indicated increased impairment. Internal consistency acceptable for mother (conflict $\alpha = .82$, cohesion $\alpha = .81$) child reports (conflict $\alpha = .77$, cohesion $\alpha = .75$).

3.2.1. Family Environment Scale (parent rated)

Baseline maternal EE hostility was correlated with mother-rated FES conflict subscale ($r = 0.25, p = <0.001$), and lack of cohesion ($r = .24, p = <.001$). EE warmth was negatively correlated with mother-rated FES conflict ($r = -.25, p = <0.001$) and lack of cohesion ($r = -.28, p = <0.001$) subscales.

3.2.2. Family Environment Scale (child rated)

Baseline maternal EE hostility was correlated with child-rated FES conflict subscale ($r = 0.22, p = 0.001$), and lack of cohesion ($r = .22, p = .001$). Maternal EE warmth was also correlated with child-rated FES conflict ($r = -.16, p = .014$) and lack of cohesion ($r = -.22, p = .001$) subscales.

4. Associations between EE and risk factors

Maternal age was not correlated with warmth ($r = -.004$, $p = .947$) or hostility ($r = .06$, $p = .331$) at baseline. EE warmth ($r = .15$, $p = .017$) but not hostility ($r = -.08$, $p = .203$) was associated with household income. Single mothers had lower warmth ($M = 3.28$ $SD = 1.05$) and increased hostility ($M = .84$, $SD = 1.01$) compared to those with two parent household; mothers and fathers (M warmth = 3.48, $SD = .1.06$; M hostility = .62, $SD = .81$) and mothers and step-fathers (M warmth = 3.52, $SD = .78$; M hostility = .51, $SD = .78$). However, there were no statistically significant differences in maternal EE warmth and hostility by family structure.

5. Inter-rater reliability

All interviews were recorded later coded by the researchers who all had in-house training and were supervised by a consultant child psychiatrist. The task took approximately 5-10 minutes to administer and approximately 30 minutes to code. Coding of interviews was conducted according guidelines specified by Caspi et al (2004).

Fifty-six interviews were missing at the baseline assessment, 79 recordings of EE were missing at time two and 74 were missing at time three (due to technical errors, or refusal to be recorded, declining to participate, or not fully completing assessments).

For inter-rater reliability 30 randomly selected interviews (at each assessment) were re-coded by a trained interviewer, blind to the initial coding of the interviews. Ratings were compared between the first and second rater. Kappa statistics were computed for categorical variables (initial statement), and the intra-class correlations were conducted to assess inter-rater reliability for continuous variables (number of comments, warmth, hostility). Weighted kappa for EE initial statement indicated substantial agreement between raters (baseline $\kappa = 0.75$; time 2 $\kappa = .88$; time three $\kappa = .78$). Inter-rater agreement for the number of positive comments was high (baseline $ICC = 0.91$; time 2 $ICC = 0.81$; time 3 $ICC = 0.87$). There was

substantial agreement for the number of negative comments (baseline $ICC = 0.75$; time 2 $ICC = 0.79$; time 3 $ICC = 0.62$) and moderate agreement for the number of neutral comments (baseline $ICC = 0.56$; time 2 $ICC = 0.65$; time 3 $ICC = 0.59$). Inter-rater reliability for warmth and hostility both showed substantial levels of agreement (warmth at baseline $ICC = 0.78$; time 2 $ICC = 0.69$; time 3 $ICC = 0.68$; hostility at baseline $ICC = 0.72$; time 2 $ICC = 0.79$; time 3 $ICC = 0.85$).

Appendix 3: Table 3.1. Complete and missing data at follow-up by baseline predictors

	complete data at follow-up (n = 209)	missing data at follow-up (n = 14)	p
Maternal age at baseline mean (SD) ^a	41.53 (5.56)	39.50 (5.45)	.219
Child female % (n)	58.9% (123)	64.3% (9)	.689
Child age at baseline mean (SD)	12.30 (1.97)	11.93 (2.09)	.495
Baseline maternal depression severity ^b mean (SD)	15.06 (10.54)	22.23 (10.32)	.018
Any maternal comorbid problems at baseline ^c % (n)	39.2% (82)	57.1% (8)	.186
Age of onset of maternal depression (years) mean (SD)	25.91 (7.83)	27.58 (5.9)	.468
Episode duration of maternal depression (months) mean (SD)	14.78 (17.19)	36.38 (51.23)	<.001
Past impairment ^d mean (SD)	47.19 (15.37)	45.57 (17.00)	.705

^a Standard Deviation; ^b Beck Depression Inventory; ^c Considers anxiety, antisocial behaviour, or alcohol misuse; ^d Global Assessment of Functioning scale

Appendix 4: Table 4.1. Association between clinical features of maternal depression and co-occurring psychopathology

	Number of co-occurring clinical problems in the parent at baseline	
	β , B (95% CI)	p
Age of onset	-0.19, -0.03, (-0.04, -0.01)	<.001
Adjusted for baseline maternal depression severity ^a	-0.09, -0.01 (-0.02, -0.00)	.019
Average episode duration	.10, .01 (.00, .01)	.020
Adjusted for baseline maternal depression severity ^a	-0.03, -0.00 (-0.01, .00)	.501
Mean GAF score ^b	-0.15, -0.01 (-0.02, -0.004)	.001
Adjusted for baseline maternal depression severity ^a	-0.03, -0.02 (-0.01, .003)	.400

^a baseline BDI score

^b Average GAF score for worst and second-worst episode

Appendix 5. Table 4.1. Correlations between maternal psychopathology and paternal psychopathology in mothers with recurrent depression

	Paternal depression severity ^a	Paternal anxiety ^b	Paternal alcohol use ^c	Paternal ASB ^d
Maternal depression severity ^a	.12	.13	-.13	-.02
Maternal anxiety ^b	.08	.11	-.01	-.03
Maternal alcohol use ^c	-.16*	-.17*	.15	-.11
Maternal ASB ^d	.07	.06	.00	.05

^a BDI questionnaire (Beck et al., 1979)

^b Anxiety subscale of HADs questionnaire (Zigmond & Snaith, 1983)

^c AUDIT questionnaire (Saunders et al., 1993)

^d ASR questionnaire (Achenbach & Rescorla, 2003)

Appendix 6. Maternal depression and co-occurring antisocial behaviour: testing maternal hostility and warmth as mediators of risk for new-onset offspring psychiatric disorder

As highlighted in chapter 3, when assessing ‘new-onset’ psychopathology it is possible to assess risk for psychopathology as it develops, and therefore identify risk markers for the onset of psychopathology. Therefore, as an extension of findings in chapter 5, disruptions in the mother-child relationship were examined as putative mediating mechanisms between maternal depression severity and co-occurring psychopathology, and child new-onset disorder.

The primary aim of these subsidiary analyses was to investigate whether maternal warmth or hostility mediated the effect of maternal depression severity on risk for offspring new-onset psychiatric disorder, after adjusting for maternal co-occurring antisocial behaviour (ASB). Given the findings in the present thesis, it was hypothesised that the effect of maternal depression severity on risk for new-onset psychiatric disorder would be mediated by disruptions in the mother-child relationship. However this relationship would be attenuated after adjusting for co-occurring maternal ASB.

Methods

Participants. Analyses utilised data from the three-wave ‘Early Prediction of Adolescent Depression’ (EPAD) study. The sample characteristics were identical to those in chapter 3. Multiple imputation with data augmentation was used to generate values for missing data across relevant theoretical variables within the proposed model using NORM 2.03 (Schafer, 1997, 1999). Subsequently generated datasets were then tested within Mplus 6.12 (Muthén & Muthén, 1998).

Measures

Maternal depression. Mothers completed the Beck Depression Inventory (BDI) (Beck et al., 1979) to assess the severity of depression symptoms at T1 ($\alpha = .91$).

Antisocial behaviour. Mothers reported on their own current ASB at T1 using the 34-item Adult Self Report (ASR) questionnaire (Achenbach & Rescorla, 2003) with items coded 0 (absent), 1 (somewhat or sometimes true) or 2 (very true). The item 'I have never been arrested' was excluded as it was the only item that referred to lifetime behaviour ($\alpha = 0.75$).

Child psychopathology at Follow-up. Details of the measure of the presence of new-onset psychiatric disorder in offspring are presented in chapter 3, and are described here briefly. Child psychiatric disorder was assessed using parent and child versions of the Child and Adolescent Psychiatric Assessment (CAPA) (Angold & Costello, 2000). A disorder was considered to be present if a diagnosis was made by either the mother or child interview (Angold & Costello, 1995). New-onset cases were defined where children received a DSM-IV psychiatric diagnosis at either of the two follow-ups, but not at baseline.

Maternal warmth and hostility. Maternal warmth and hostility were assessed at T2 by two different methods; a self-report questionnaire measure (Iowa Youth and Families project (IYFP) family interaction rating scales) (Melby et al., 1993) and an interviewer-rated five minute speech sample of expressed emotion (EE) (Caspi et al., 2004), as described in chapter five.

Analysis strategy

To test whether the mother-child relationship mediated the relation between maternal psychopathology and offspring new-onset psychiatric disorder, the direct effects between maternal depression severity or ASB at T1 and offspring new-onset psychiatric disorder (T2

or T3) were tested. Mediation analyses then tested whether maternal hostility/warmth at T2 mediated the association between maternal depression severity and offspring new-onset psychiatric disorder, after adjusting for maternal ASB. Analyses were conducted in Mplus 6.12 (Muthén & Muthén, 1998).

Results

Mediation analyses

Parent hostility and warmth as mediators of associations between parent psychopathology and child new-onset psychiatric disorder: A significant direct effect was observed between maternal depression severity (BDI) at T1 and new-onset psychiatric disorder in offspring ($OR = 1.03$, 95% CI 1.01, 1.06, $p = .044$). A significant direct effect was also observed between maternal ASB at T1 and child new-onset psychiatric disorder ($OR = 1.09$, 95% CI 1.01, 1.16, $p = .029$)

Maternal hostility (T2) was associated with the presence of new-onset offspring psychiatric disorder ($OR = 1.68$, 95% CI 1.31, 2.15, $p = <.001$). However, maternal warmth (T2) did not significantly predict offspring new-onset psychiatric disorder ($OR = 1.26$, 95% CI .98, 1.58, $p = .054$) and was therefore not included in analyses.

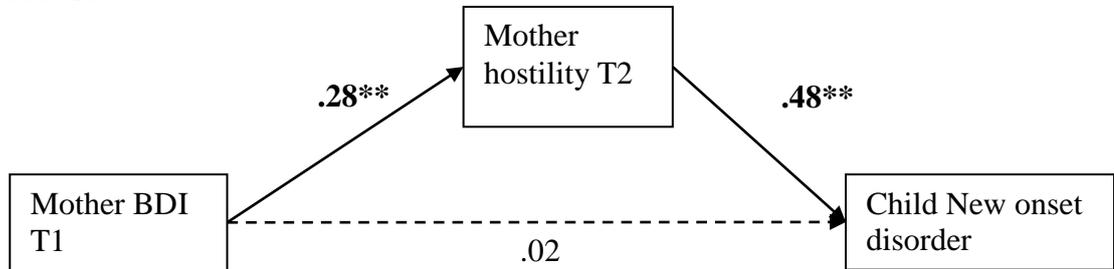
Tests of mediation revealed that the association between maternal depression severity and child new-onset psychiatric disorder was fully mediated by maternal hostility (Appendix Figure 5.1, panel a). However, after adjusting for maternal ASB, the association between maternal depression severity and maternal hostility was attenuated. Maternal ASB predicted maternal hostility which, in turn, predicted offspring new-onset psychiatric disorder (Appendix Figure 5.1, panel b).

Conclusion

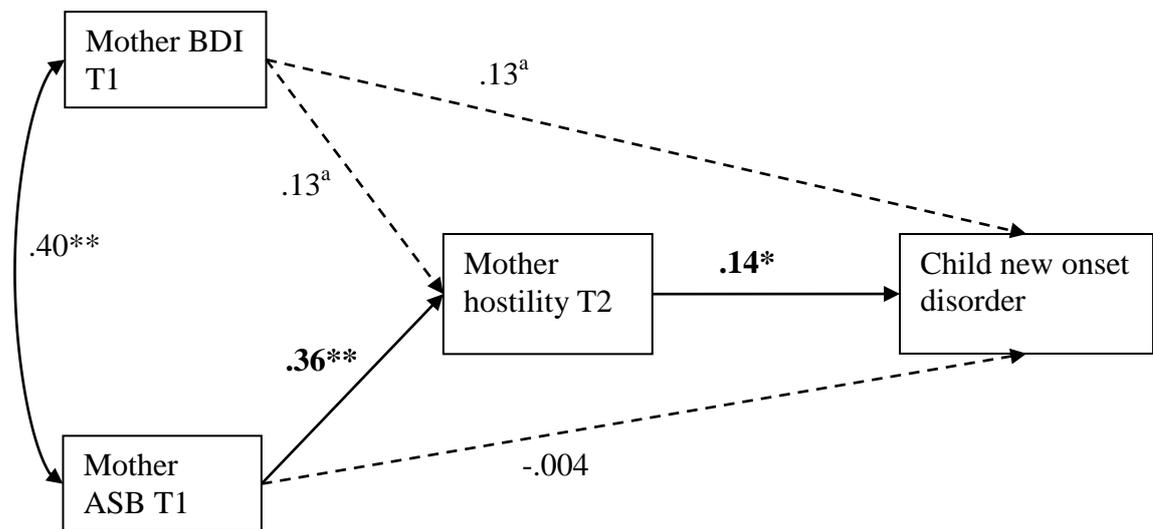
Variation in maternal depression severity was associated with the development of child psychopathology, consistent with previous research (Blatt-Eisengart et al., 2009; Foster, Webster, Weissman, Pilowsky, Wickramaratne, Talati, et al., 2008; McCarty & McMahon, 2003). However, findings here extend previous findings by demonstrating this effect for the *onset* of psychiatric disorder in offspring. However, when co-occurring antisocial behaviour was taken into account, maternal depression severity was no longer associated with maternal warmth or hostility. Co-occurring ASB symptoms in the mother predicted maternal hostility, which in turn predicted new-onset psychiatric disorder in the offspring. These findings are consistent with the findings in chapter 5 (focusing on symptoms of depression severity and ASB), and prior evidence that depressed mothers with co-occurring ASB symptoms may provide especially poor quality care-giving environments (Kim-Cohen et al., 2006). The effect of maternal ASB via parenting may be important for the *development* of psychiatric disorder in these high-risk offspring, particularly child disruptive behaviours, as identified in chapter five.

Appendix 6 Figures

Panel 1a



Panel 1b



Appendix Figure 6.1: Maternal hostility at time two mediated the relation between maternal depression severity at baseline and offspring new-onset disorder (panel a). After adjusting for maternal ASB, maternal ASB mediated the effect of maternal depression severity on maternal hostility. Maternal hostility mediated the effect of maternal ASB on new-onset psychiatric disorder in offspring (panel b).

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