Parental Depression and Child Psychopathology:
Mechanisms of Risk and Effect of Remission

by

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Abstract

Depressive disorders are among the most commonly diagnosed psychiatric disorders in adults. Parental major depressive disorder (MDD) is the strongest risk factor for MDD and other psychiatric disorders in children: including depressive, anxiety, and behavioral disorders. Possible mechanisms involved in the transmission of risk include genetic heritability, neuroregulatory mechanisms during development, early-life stress, and psychosocial correlates. The current dissertation examined psychopathology in children of depressed parents with a focus on the psychosocial correlates most commonly examined in this group. The study used a sample of 168 children aged 7-17 with either a mother (N= 82) or father (N= 11) enrolled in a double-blind treatment study combining antidepressants to hasten remission of MDD. Children (including siblings), parents, and co-parents received diagnostic assessments and questionnaires in 6 assessments over 9 months. The first aim was to examine baseline data to determine current and lifetime prevalence rates of psychiatric disorders in children of depressed mothers compared to depressed fathers and to examine previously identified general and specific risk factors in this population. The second aim of this work was to replicate previous research showing that parental remission from depression is associated with improved child outcome. Children of depressed parents had elevated rates of psychopathology, consistent with previous work. Children of depressed mothers had significantly more psychiatric symptoms than children of depressed fathers, although both groups had similar rates of anxiety symptoms. However, the findings with children of depressed fathers were limited by a small sample size. Rates of psychopathology in children of depressed mothers were similar across study sites, despite significant demographic differences. Results also

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replicated the finding that parental remission from depression is associated with improved child outcome. This study was the first to examine children of remitting parents, compared to non-remitters and relapsers. The key finding among these groups was that children of parents who relapse do not do any better than children of non-remitters. Thus, sustained remission is crucial to outcome. Improvements in parental functioning and the parent-child relationship among remitting parents was found to partially explain children's improvements.

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CHAPTER 1: INTRODUCTION

1.1 PARENTAL MAJOR DEPRESSION

Approximately 1 in 5 women and 1 in 10 men will experience a depressive disorder in their lifetime (Hasin et al., 2005; Kessler et al., 2003a). Parental depressive disorders are one of the greatest risk factors for psychopathology in children (Hammen & Brennan, 2003; Lieb, Isensee, Höfler, Pfister, & Wittchen, 2002; Weissman et al., 2005, 2006). Clinical symptoms of depressive disorders may negatively impact parenting behaviors and increase children's risk of illness. There are a number of general and specific risk factors that may also be involved directly or indirectly to effect child outcome. The focus of the present study is to investigate factors associated with increased risk of psychopathology among children of depressed mothers and fathers and to determine how parental response to depression treatment affects child outcome.

The following will discuss the clinical features of depressive disorders in adults, psychiatric disorders implicated in children of depressed parents, and a discussion of general and specific risk factors involved in outcome.

1.1.1 Unipolar Depressive Disorders

Prevalence, Features, Clinical Course, and Treatment. Unipolar depressive disorders are mood disorders without episodes of mania or hypomania. Depressive disorders cause significant family, social, work, or school impairments and vary in their presentation based on age, severity, and diagnostic features (American Psychiatric Association, 2000).

Prevalence. The time point prevalence of MDD in the general population is approximately 5% and the lifetime prevalence is around 17% (Kessler et al. 2007; WHO

2008). Currently, the highest rates of depressive disorders occur in women in their reproductive years. In fact, the WHO (2008) ranked unipolar depressive disorders as causing the greatest degree of Disability Adjusted Life Years (DALYs) in women ages 15 to 44 worldwide, and ranked first for DALYs in middle to high income countries, ranking higher than ischemic heart disease. MDD can have significant detrimental health effects and is associated with poorer outcomes when present with other medical disorders (Lespérance, Frasure-Smith, Talajic, et al., 2002; Thapar, Kerr, Harold, 2009). Due to the high prevalence, accompanying dysfunction, and high economic burden, depression is currently a major public health problem that continues to grow.

Features. MDD is characterized by a depressed mood or a loss of interest or pleasure in nearly all activities for a period of at least 2 weeks. The affected individual must also present at least 4 to 5 of the following symptoms in addition to a depressed mood and/or anhedonia: changes in appetite or weight, sleep, and psychomotor activity, fatigue or decreased energy, feeling of worthlessness or guilt, decreased ability to think, concentrate, or make decisions, and recurrent thoughts of death or suicide. Depressive disorders may also have seasonal components (seasonal affective disorder), occur in reaction to a life stressor (Adjustment Disorder with Depressed Mood), or be characterized by clinical symptoms that are significant but less severe (e.g. Dysthymic Disorder) (American Psychiatric Association, 2000).

Depression is a heterogeneous disorder that may vary significantly in its presentation. MDD episodes may be characterized by features such as psychosis (i.e. delusions, hallucinations), atypical features (i.e. significant weight gain, hypersomnia, leaden paralysis, extreme rejection-sensitivity), melancholy (loss of pleasure in nearly all

activities, low reactivity, excessive guilt, excessive weight loss), and catatonia (motor and behaviour disturbances such as immobility). One particular type of unipolar depressive disorder which has garnered significant attention is postpartum depression (PPD). PPD occurs within one month of delivery and is usually characterized by intense depressive symptomatology (American Psychiatric Association, 2000). PPD is of particular interest to many because it occurs at a critical period of parent-offspring bonding.

Clinical Course. The course of depressive disorders can vary significantly depending on factors such as age, life stressors, genetics, previous episodes, and comorbidities. When depressive episodes go untreated, it is estimated that most episodes last 6 to 8 months, and up to 20% of individuals will get well within the first 3 months (Posternak et al 2006; Posternak & Miller, 2001). Unipolar depressive disorders have high recurrence rates, and studies have indicated that approximately 50-70% of individuals will suffer at least one more MDD episode after their first. After the second episode there is a 70% chance of having a third and this recurrence risk is estimated to be 90% after a third episode (Fava, Park, & Sonino, 2006; Holma, Holma, Melartin, Rytsälä, & Isometsä, 2008). Suicidal ideation is a common symptom associated with depressive disorders. Approximately 15% to 20% of individuals with MDD will attempt suicide in their lifetime (Angst, Stassen, Clayton, & Angst, 2002). There are about 3,700 suicides per year in Canada and it is estimated that approximately half of individuals who commit suicide have MDD (Statistics Canada, 2009).

Treatment. There are an array of available treatment options for depressive disorders, such as pharmacological intervention and therapies. When patients adhere to treatments utilizing pharmacological and/or cognitive behavioural therapy, approximately

25-45% of them will fully recover (Butler, Chapman, Forman, & Beck, 2006; Thase, 2003). Treatment with antidepressants results in significant reduction in symptoms in approximately half of individuals (Rush, 2003). Even mild depressive symptoms are associated with impaired functioning, so full remission, rather than just symptom reduction, is critical to improve well-being (Geddes et al., 2003) and to reduce risk of relapse (McIntyre & O'Donovan, 2004). Adherence to medication is a common problem in treatment of depression, but continuation of antidepressant medications after recovery can reduce the chance of relapse significantly.

Given the pervasiveness of symptoms associated with MDD, it is not surprising that many problems associated with the illness also impact parenting, relationships, and family functioning. Thus, considerable attention has been focused on parents with Major Depressive Disorder.

1.1.2 Depression in Parents

Depressed Mothers. Numerous studies have shown that children of depressed mothers have increased rates of depressive, anxiety and behavioral disorders (Pilowsky et al., 2008; Weissman, Wickramaratne, et al., 2006) and are approximately three times more likely to experience a lifetime episode of MDD than children of nondepressed parents (Lieb et al., 2002; Weissman, Warner, Wickramaratne, Moreau, & Olfson, 1997). Furthermore, they are also at greater risk of educational problems (Fletcher, 2008, 2010; Keenan-Miller, Hammen, & Brennan, 2007) and social, cognitive and medical difficulties which continue into adolescents and adulthood, extending risks to the next generation (Brennan, Hammen, Katz, & Le Brocque, 2002; Hay et al., 2001; Kramer et al., 1998; Lieb et al., 2002; Rohrer, Cicchetti, Rogosch, Toth, & Maughan, 2011; Sohr-Preston &

Scaramella, 2006; Talge, Neal, & Glover, 2007; Weissman et al., 2005; Weissman, Wickramaratne, et al., 2006). The onset of disorders is highly dependent on the child's developmental stage (Pilowsky et al., 2008). Research shows that younger children of depressed mothers are more likely to develop anxiety and behavioral disorders (Hammen & Brennan, 2003) and adolescent offspring of depressed mothers are at increased risk of MDD during adolescence and into adulthood (Weissman, Wickramaratne, et al., 2006). Studies have also indicated an increased risk for substance abuse disorders in these children, with onset beginning in early to late teens and into adulthood (Weissman et al., 1997).

Work done examining the intergenerational transfer of depressive disorders has demonstrated a risk of transmission that gets passed down. Genetic and environmental contributions have been implicated in the development of these disorders in childhood and their continuity into adulthood (Kendler, Gardner, & Lichtenstein, 2008; Kendler & Gardner, 2010; Levinson, 2006; Levinson et al., 2007). Children of depressed mothers are at higher risk for maltreatment, including physical abuse, psychological abuse, and neglect (Kotch et al., 1997) increasing their risks of psychopathology and dysfunction in life (Gilbert et al., 2009). Other environmental factors such as child-parent bonding, attachment, or socioeconomic status may significantly influence the impact of parental depression on child outcome (Goodman, 2007; Feder et al., 2009).

Depressed Fathers. The majority of the research on parental depression and child outcomes has been conducted primarily with depressed mothers. Yet fathers have been increasingly recognized for their integral role in child development (Flouri, 2003; Flouri, 2008; Sarkadi, Kristiansson, Oberklaid, & Bremberg, 2008). Transactional models of

developmental psychopathology underscore the importance of each caregiver's influence on child outcome (Cicchetti & Toth, 2007). Analogous to this approach, there is an increasing body of research examining the effects of father's depression, but the literature is scarce compared to the data available on maternal depression. Much of the available work has focused on the effect of paternal depression during the postpartum period. While there is some indication that paternal depression may have deleterious effects similar to maternal depression whether it occurs during the postpartum period (Ramchandani, Stein, Evans, & O'Connor, 2005) or later in childhood (Kane & Garber, 2004a), the majority of this work has relied on self-report measures and includes primarily community samples, rather than currently depressed clinical samples (Wilson & Durbin, 2010). Thus, there is limited capacity to make comparisons regarding diagnostic characteristics between depressed fathers and mothers. The studies available suggest that children of depressed fathers may have increased rates of parent-child conflict and elevated rates of externalizing disorders similar to children of depressed mothers (Connell & Goodman, 2002). However, maternal depression has been associated with a significantly greater risk of developing internalizing disorders, (Beardslee, Gladstone, Wright, & Cooper, 2003; Kane & Garber, 2004b; Klein, Lewinsohn, Rohde, Seeley, & Olino, 2005) carrying on into adulthood (Currier, Mann, Oquendo, Galfalvy, & Mann, 2006).

A study by Weitzman et al. (2011) examined a national sample 21,993 children ages 5 to 17 and their mothers and fathers. They found that living with a father who has depressive symptoms was associated with increased rates of emotional and behavioral problems in offspring, but this risk was three to five times greater if the mother was the

one with mental health problems. Children who had two parents with mental health issues had the highest risk of behavioral and emotional problems. Further work needs to be done to examine the specific risks associated with depression in fathers in clinical samples and with currently depressed dads to further investigate the impact. Such data has been notoriously difficult to obtain due to lower rates of depression in men, the limited number of fathers seeking treatment, and an unwillingness of fathers to include their children in research.

Dual Parent Morbidity. Assortative mating refers to a tendency for an individual to select a partner who is similar to them. Also referred to as non-random mating, there is ample evidence that individuals with psychiatric disorders including alcohol abuse, anxiety and depression, have a tendency to have children with other psychologically troubled individuals (Dubuis-Stadelmann, Fenton, Ferrero, & Preisig, 2001; Maes et al., 1998). Depressed woman often marry men with significant psychiatric symptoms that preceded the marriage (Maes et al., 1998; Mathews & Reus, 2001; Merikangas, 1984). In a study of 43 families where youth were referred for clinical intervention of a depressive disorder, Hammen et al. (1999) found that over half of the women with a depressive disorder had mated with a man with a psychiatric diagnosis, mostly substance abuse, depressive disorders, or antisocial personality disorders. Moreover, in the mothers who were coupled with new partners, 64% of those men had significant problems including drug or substance abuse, arrests or incarceration, and antisocial conduct.

Development of psychopathology in spouses and partners may also occur due to prolonged marital interactions and stressors incurred with having a depressed partner (Fadden, Bebbington, & Kuipers, 1987; Merikangas, 1984), or due to mating among

individuals with similar social backgrounds, and thus similar environmental risk factors (Maes et al., 1998). Regardless, dual-parent morbidity has an additive effect on children, placing them at higher risk for psychopathology (Fendrich et al., 1990; Keller, Cummings, Peterson, & Davies, 2009). A study by Nomura, Warner, and Wickramaratne (2001) found that compared to children with one depressed parent, children with two depressed parents were more likely to develop psychopathology and approximately twice as likely to develop MDD. Parents concordant for depressive disorders tend to have higher marital conflict (Keller et al., 2009) with poor ability to resolve their problems (Cummings, Keller, & Davies, 2005) and higher rates of divorce (Merikangas, 1984). Significant clinical symptoms in both parents may preclude spouse's abilities to support one another or give adequate support to their children. The increased risk of poor outcomes in children with dual-parent morbidity is likely due to a number of variables that increase exposure to stress and conflict and impede children's support systems.

1.2 Psychopathology in Children of Depressed Parents

The most common symptoms and disorders described among children of depressed parents include affective (depressive), anxiety, and behavioral disorders (Weissman et al., 2006). The problems associated with affective and anxiety disorders are often referred to as internalizing disorders, whereas significant behavioral problems are referred to as externalizing disorders. These disorders occur in the general population but their incidence is significantly higher among children with a depressed parent (Hirshfeld-Becker et al., 2008; Lieb et al., 2002; Pilowsky, Wickramaratne, Rush, et al., 2006; Weissman et al., 2005). While examination of clinical symptoms associated with these disorders can be informative, research that includes clinical diagnostic assessments of

psychopathology in children of depressed parents provides data on severity and specificity of the illness.

1.2.1 Depressive Disorders

At any given time point, the prevalence of clinical depressive disorders in children in the general population is approximately 3% for those under the age of 13, and 4-7% for adolescents aged 13-17 (Costello, Erkanli, & Angold, 2006). In data from the Oregon Adolescent Depression Project, Lewinsohn et al. (1994) found a mean onset of age 14.7 for girls and 15.4 for boys. Comparatively, children and adolescents of depressed parents have considerably higher prevalence rates, are about 2 to 4 times more likely to experience a depressive disorder than children of non-depressed parents (Hammen & Brennan, 2003; Pilowsky et al., 2006; Weissman, Wickramaratne, et al., 2006), and are more likely to have earlier onset (before age 12), longer duration, and higher likelihood of recurrence (Warner et al., 1992, Weissman, Wickramaratne, et al., 2006). The presenting symptoms and risk factors associated with depressive disorders in childhood and adolescence may vary as a function of age (Hammen & Brennan, 2003). Aspects of the child's environment such as family conflict, poor parenting, socioeconomic status, and peer rejection may contribute to depressive symptomatology. The diagnostic criteria defining clinical depression in children is comparable to adulthood, but irritability may replace the criteria of depressed mood in children and teens. The presentation of depressive symptoms in pre-pubescent children may differ significantly from those seen in later adolescence and adulthood. In general, children with depressive disorders are more likely to present with primary symptoms including

irritability, somatic complaints, poor self-esteem, and withdrawal (American Psychiatric Association, 2000a).

Childhood onset of depressive disorders has been associated with poorer outcome overall, with over 50% experiencing a recurrent episode within 2 to 5 years (Birmaher, Ryan, Williamson, Brent, & Kaufman, 1996; Goodyer, 2001). In general, the risk of depressive disorders is equal for both genders until adolescence, when girls become about twice as likely to develop a depressive disorder (Cyranowski, Frank, Young, & Shear, 2000; Dunn & Goodyer, 2006; Nolen-Hoeksema & Girgus, 1994). This gender difference may be even larger in adolescents of depressed parents. In a sample of offspring of depressed parents followed longitudinally by Wickramaratne and Weissman (1998), they found that 43% of the adolescent daughters of depressed mothers became clinically depressed by age 19, compared to 16% of sons. This suggests that adolescent daughters of depressed mothers may be particularly at risk of developing a major depressive episode into late adolescence and early adulthood. Possible explanations for this sex difference include an increased sensitivity to interpersonal stress in adolescent females (Shahar, Gallagher, Blatt, Kuperminc, & Leadbeater, 2004), hormonal changes in puberty, genetic influences, and coping styles (Lewinsohn, Clarke, Seeley, & Rohde, 1994). Angold and colleagues (1998) reported that pubertal development, specifically reaching mid-puberty where menstruation has begun and there is notable breast development, was the best predictor of depression in females. Commensurate with this theory is the finding that early-maturing girls are at an increased risk for depression (Ellis & Garber, 2000; Ge, Conger, & Elder, 2001). History of maternal depression has been associated with earlier pubertal timing in daughters, particularly when there is family

discordance (Ellis & Garber, 2000). In contrast to girls, pubertal development in boys has been associated with a decrease in depressive symptoms, particularly around mid-puberty (Angold, Costello, & Worthman, 1998; Marceau, Ram, Houts, Grimm, & Susman, 2011).

After puberty, clinical symptoms of depression become more similar to those experienced in adulthood, with depressed mood, sleep difficulties, poor concentration, and weight and appetite disturbances being the most common primary symptoms (Lewinsohn et al., 1994). Like adults, depressive disorders in youth are associated with increased risk of suicide (Brent et al., 1993; Brent et al., 2004; Hallfors et al., 2004) with more than half of adolescent suicide victims reported to have a depressive disorder at the time of death (Hawton & van Heeringen, 2009). Having a parent with depression puts youth at an even greater risk of suicide (Brent et al., 1993) and suicidal behavior has a familial transmission component, with parental suicide attempts increasing the risk of suicide attempts in their offspring (Brent, 2010; Brodsky et al., 2008). In Canada, suicide is the second leading cause of death for individuals aged 10-19, and rates of female suicide in adolescence has increased in recent years (Skinner & McFaull, 2012).

It is very common for children and adolescents with depressive disorders to have one or more comorbid psychiatric disorders (American Psychiatric Association, 2000a; Thapar, 2012), particularly anxiety disorders (Moffitt et al., 2010). Parental depression is the single greatest risk for the development of depressive disorders in children and adolescence (Hammen, Burge, Burney, & Adrian, 1990; Lieb et al., 2002; Weissman et al., 2005), thus rendering it an extremely valuable tool for early identification of depression in children.

1.2.2 Anxiety Disorders

Anxiety disorders are the most common disorder in childhood (Beesdo, Knappe, & Pine, 2009; Costello, Egger, & Angold, 2005; Rapee, Schniering, & Hudson, 2009). At any given time the prevalence of anxiety disorders among children in the general population of children is approximately 2.5% to 5%, with this rate remaining fairly stable into adolescence (Costello et al., 2005; Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Ford, Goodman, & Meltzer, 2003). The various anxiety disorders are characterized by overlapping symptoms such as chronic worry, physiological arousal, behavioral symptoms such as avoidance, and cognitive symptoms such as negative appraisal and rejection sensitivity (American Psychiatric Association, 2000a). As children develop they express a range of fears and anxieties, however these become pathological when they significantly impair the child's functioning and well-being (Peter Muris, Merckelbach, Mayer, & Meesters, 1998). Children experiencing anxiety disorders are more likely to have difficulties with family, peers, and school functioning (Beesdo et al., 2009; Espejo et al., 2007).

The development of specific types of anxiety disorders can vary as a function of age. Prior to 12, children are more likely to experience onset of separation anxiety disorder and specific phobias (Becker et al., 2007; Kessler et al., 2005). The onset of social phobia is more common in later childhood and throughout adolescence (Kessler et al., 2005). Anxiety disorders such as Generalized Anxiety Disorder, Panic Disorder, and Agoraphobia are more commonly experienced in later adolescence and into adulthood (de Graaf, Bijl, Spijker, Beekman, & Vollebergh, 2003; Kessler et al., 2005). In general, all anxiety disorders are more common in females, with girls becoming about twice as

likely to develop an anxiety disorder by adolescents (Pine, Cohen, Gurley, Brook, & Ma, 1998; Wittchen, Nelson, & Lachner, 1998). Early incidence of anxiety disorders is associated with higher rates of anxiety and depression, substance dependence, and suicidal behavior later in life (Biederman et al., 2007; Kendler et al., 2008; Pine et al., 1998).

Parental depression and anxiety disorders have both been identified as risk factors for anxiety in offspring (Lieb et al., 2002; Weissman, Wickramaratne, et al., 2006). Conversely, higher rates of depression are found among children of parents with anxiety disorders (Johnson, Cohen, Kasen, & Brook, 2008). Although there is some evidence of familial transmission of specific anxiety disorders independent of depression (Fyer, Mannuzza, Chapman, Martin, & Klein, 1995), parental depression with or without comorbid anxiety remains a major risk factor for the development of anxiety disorders in offspring (Lieb et al., 2002; Weissman, Wickramaratne, et al., 2006). The risk for anxiety disorders in children of depressed parents is especially high when the parent has a comorbid anxiety disorder (Biederman et al., 2007; Pilowsky et al., 2006). Multiple studies have found that children of depressed parents who experience anxiety disorders in childhood have an elevated risk for later developing depressive disorders (Warner, Weissman, Mufson, & Wickramaratne, 1999; Weissman et al., 2005). Espejo (2007) examined the connection between depression, anxiety disorders, and adverse life events in adolescents of depressed parents. He found that youth of depressed parents who had an early anxiety disorder and were exposed to adversity in childhood had a heightened stress response and exhibited more depressive symptoms after low levels of episodic stress. Thus, it is possible that early anxiety disorders in children of depressed parents may be

indicative of a dysfunctional stress response that puts them at risk for depression, particularly in the presence of early life adversity. Research investigating hypothalamus-pituitary-adrenal (HPA) axis activity as an indicator of stress response has found that dysfunction of the HPA is highly heritable (Kumsta et al., 2007; Witt et al., 2011), is influenced by early life adversity (McCrory, De Brito, & Viding, 2010; Witt et al., 2011) and maternal depression (Murray, Halligan, Goodyer, & Herbert, 2010; Oberlander et al., 2008). Similarly, there is also indication that differences in autonomic responses, such as vagal tone and heart rate, may differ in response to emotional stimuli as a result of heritability (Porges, 2009).

Poor parental attachment during infancy (Sroufe, Carlson, Levy, & Egeland, 1999) has been associated with increased risk of anxiety disorders for children. Parental rejection and negative parenting styles, such as overprotection and critical parenting, are also associated with increased rates of anxiety disorders in children (Knappe, Beesdo, et al., 2009; Knappe, Lieb, et al., 2009). Children may also model their parents' anxious behaviors and fears (Dubi, Rapee, Emerton, & Schniering, 2008; Gerull & Rapee, 2002; Muris, Steerneman, Merckelbach, & Meesters, 1996). Characteristics of the child's personality and temperament may be another factor that makes them vulnerable. For instance, anxiety disorders may be more common in children who were fussy babies (Rapee & Szollos, 2002). Children who are fearful in unfamiliar situations, distressed by novel experiences or people, and demonstrate restricted social behavior are at risk for developing anxiety disorders (Biederman et al., 2001; Hirshfeld-Becker et al., 2007). Recently, Schwartz et al., (2011) suggested a highly reactive (HR) phenotype that can be identified in children as early as 4 months and can predict specific patterns of reactivity

later in life. For instance, males who were HR as infants showed high levels of reactivity to novel stimuli as adults. Thus, underlying neurobiological mechanisms involved in basic reactivity may predispose certain individuals to being hyper-reactive and more prone to anxiety disorders.

Comorbid conditions occur very commonly with anxiety disorders. Most commonly, children will experience other anxiety disorders or a comorbid depressive disorder (Beesdo et al., 2009; Costello et al., 2003). Parental depression is a potent risk factor for anxiety disorders (Biederman et al., 2007; Pilowsky et al., 2006) and early anxiety is strongly associated with the development of depression in adulthood (Beesdo et al., 2009; Costello et al., 2003; Pine et al., 1998). Thus, early identification of these disorders is essential to improving children's outcome.

1.2.3 Behavioral Disorders

Behavioural disorders in childhood and adolescence include Attention Deficit Hyperactivity Disorder (ADHD) and disruptive behaviour disorders, such as Conduct Disorder (CD) and Oppositional Defiant Disorder (ODD). Although these disorders are characterized by distinct clinical criterion, they often co-occur, with an estimated 25% to 60% of individuals with a diagnosed disruptive behaviour disorder also having a comorbid diagnosis of ADHD (Brown et al., 2001; Szatmari, Offord, & Boyle, 1989; Waschbusch, 2002). Maternal depression has been identified as a significant risk factor for the development of behavioural disorders in children (e.g., Brennan et al., 2002; Burt, Hay, Pawlby, Harold, & Sharp, 2004; Hay, Pawlby, Waters, & Sharp, 2008a; Wickramaratne et al., 2011). Specifically, children of parents who have highly irritable

depressive symptoms are especially vulnerable to developing an externalizing disorder (Pilowsky, Wickramaratne, Rush, et al., 2006).

ADHD is one of the most commonly diagnosed psychiatric disorders in childhood, with prevalence rates ranging from 4% to 12% in the general population (American Psychiatric Association, 2000; Brown et al., 2001). It is characterized by symptoms such as attentional difficulties, hyperactivity, and impulsivity that seriously impair functioning, and lead to difficulties in school and at home (American Psychiatric Association, 2000). Studies of children of depressed parents have found rates of ADHD to be between 15% to 30% (Mars et al., 2012; Pilowsky et al., 2006; Wickramaratne & Weissman, 1998).

ODD is characterized by a pattern of difficult, hostile, and defiant behaviour such as frequently arguing with adults, vindictive acts, refusal to follow rules, and temper outbursts. It is generally diagnosed before the age of 8 and prevalence rates are between 2% to 16% in the general population. Prior to puberty it is more common in males, but becomes more evenly distributed in adolescence (American Psychiatric Association, 2000; Kessler et al., 2005). ODD is often considered a precursor for the development of CD, but there is considerable variation found in the progression rates (Rolf Loeber, Hipwell, Battista, Sembower, & Stouthamer-Loeber, 2009; Barbara Maughan, Rowe, Messer, Goodman, & Meltzer, 2004). While only a small portion of children with ODD go on to develop CD, the majority of youth diagnosed with CD had a previous diagnosis of ODD (Rey, 1993). CD is characterized by more severe behavioural problems that include breaking the law, vandalizing, theft, violent crimes, and general violations against societal norms. Prevalence rates for CD in the general population have been estimated to

be between 1% and 10% (American Psychiatric Association, 2000). The rates of ODD and CD in children of depressed parents are elevated and generally range from 7% to 32% (Beardselee et al., 1998; Hammen et al., 1990; Pilowsky et al., 2006; P. J. Wickramaratne & Weissman, 1998).

Disruptive behaviour disorders and ADHD in childhood have been associated with adverse outcomes longitudinally, including risky sexual behaviour, substance abuse disorders, psychosocial impairments, and legal troubles (Barkley, Guevremont, Anastopoulos, DuPaul, & Shelton, 1993; Burke, Loeber, & Birmaher, 2002; Barbara Maughan et al., 2004; Rey, 1993). These risk are heightened when children have comorbid ADHD with a disruptive behaviour disorder (Biederman et al., 2008; Loeber, Burke, Lahey, Winters, & Zera, 2000).

A great deal of work has been done investigating possible parenting, genetic, and developmental factors that contribute to the development of behavioural disorders in children. Frequently this research has focused on externalizing disorders as a group rather than examining the distinct disorders within this group. There is evidence that antisocial traits in parents may put children at risk for development of ADHD and disruptive behaviour disorders (Drabick, Beauchaine, Gadow, Carlson, & Bromet, 2006), especially when combined with parental depression (Hirshfeld-Becker et al., 2008; Marmorstein, Malone, & Iacono, 2004). There is also evidence that parenting may account for some variance. For instance, Chronis et al. (2007) found that positive parenting practices acted as a protective factor for children at risk for conduct problems, and children of depressed parents who experienced positive parent-child interactions had fewer conduct problems longitudinally. However, parental depression has consistently been found to be an

independent predictor of externalizing disorders in offspring, particularly for conduct disorders (Hirshfeld-Becker et al., 2008; Kim-Cohen, Moffitt, Taylor, Pawlby, & Caspi, 2005). Depressed mothers' expressed affective attitudes and traits such as emotional lability, poor communication, high criticism, and irritability (Chronis et al., 2007; Frye & Garber, 2005; Pilowsky, Wickramaratne, Rush, et al., 2006), and marital discord (McCarty & McMahon, 2003) are associated with increased externalizing problems in these offspring. In general, the mechanism of risk for behavioural disorders in children of depressed parents remains nonspecific, and work to parse out the various genetic and environmental influences remains inconclusive (see review by; Burke et al., 2002).

Behaviour disorders are associated with high rates of comorbid depressive, anxiety, sleep problems, and substance abuse disorders (Barkley et al., 1993; Kessler et al., 2005). A well known study by Biederman et al. (1996) found that 70% of the children referred to clinics for depression had a comorbid diagnosis of ADHD. Other studies have found comparably high rates of ADHD amongst depressed children and adolescents (Butler, Arredondo, & McCloskey, 1995; Kessler et al., 2005). Longitudinal outcome studies have shown that children with comorbid depression and behavioural disorders have poorer prognosis than those with a behavioural disorder alone and are at high risk for a wide range of adverse psychiatric outcomes (Biederman et al., 2008; Biederman et al., 2006). The high morbidity associated with behavioural disorders demonstrates the importance of early identification and intervention with these children. Further research will help to delineate the specific risk and protective mechanisms effecting outcome in children of depressed parents.

1.2.4 Treatment of Children

Our understanding of mental illness in childhood has certainly expanded in recent years, yet the dearth of knowledge available regarding effective treatment and intervention strategies with this group remains problematic (Costello et al., 2005; Gericke, Riesberg, & Busse, 2005). In contrast to adulthood, treatments for these childhood psychiatric disorders remains limited and controversial (Neal, 2005). First of all, psychopharmacological interventions in children are rarely based on evidence of efficacy in clinical trials with children or adolescence. In fact, an estimated 70% of current medication therapies used with children have only been tested on adult samples (Roberts, Rodriguez, Murphy, & Crescenzi, 2003). Less than half of depressed young people receive treatment for mental illnesses before the age of 18 (Kessler, Avenevoli, & Ries Merikangas, 2001; Kessler & Walters, 1998). Furthermore, even when children receive treatment, their outcome may be mediated by the status of the parental depression (van Loon, Granic, & Engels, 2011). Thus, considerable attention has focused on characteristics of the parent's illness affecting child outcome as a target for intervention strategies.

In the Sequential Treatment Alternatives to Relieve Depression-Child Study (STAR*D-Child), Pilowsky et al. identified high rates of psychopathology in children of depressed parents (Pilowsky, Wickramaratne, Rush, et al., 2006). The same group also found that remission of maternal depression was associated with significant reductions in child diagnoses and symptoms longitudinally (Weissman, Pilowsky, et al., 2006). Thus, one of the most promising and reliable means to effectively treat these children of depressed parents may be through intervention of the parent's illness. In continuing to

examine the complex relationship between parental depression and child outcome, we can further identify specific risk factors and mediating variables that can improve outcome.

1.3 Risks Factors Associated with Development of Psychopathology

1.3.1 General Risks

Parental depression is a specific risk factor for psychopathology in offspring. However, the development of psychiatric disorders, such as depression, can occur in children who have not been exposed to parental depression (Puig-Antich et al., 1985). Also, some children exposed to parental depression do not go on to develop any psychopathology (Beardslee, Gladstone, & O'Connor, 2011b; Brennan, Le Brocque, & Hammen, 2003; Pargas, Brennan, Hammen, & Le Brocque, 2010). Therefore, when examining transmission of risk due to parental depression, it is important to consider general risk factors associated with psychopathology that may account for the variance in child outcomes. There are a number of nonspecific risk factors that increases children's risk for psychiatric disorders (National Research Council, 2009) including exposure to early life adversity, qualities of the parent-child relationship, and demographic characteristics (England & Sim, 2009). Such risks factors may work directly, indirectly, or in aggregation to effect children's outcomes (Atzaba-Poria, Pike, & Deater-Deckard, 2004). This section will discuss early life adversity and demographics characteristics as general risk factors. Specific risk factors will include characteristics of parental depression associated with child outcome.

Early Life Adversity- Stress. Chronic and acute stressful life events have been associated with a number of adverse health outcomes for both children and adults (Clark,

Caldwell, Power, & Stansfeld, 2010; Taylor, Way, & Seeman, 2011). Robust correlates of psychopathology include stressors that are long lasting, severe, and negatively impact important relationships (Tiet et al., 1998). There is extensive evidence to support the increased risk for psychopathology from exposure to stressors such as childhood abuse (Kendler et al., 2004; Mullen, Martin, Anderson, Romans, & Herbison, 1996; Weiss, Longhurst, & Mazure, 1999), parental illness, family discord (Chase-Lansdale, Cherlin, & Kiernan, 1995; Fendrich et al., 1990; Knappe, Beesdo, et al., 2009), bullying (Hawker & Boulton, 2000), and neglect (Espejo et al., 2007; Kendler & Gardner, 2010; Kendler et al., 2004). Stressful life events may be more strongly associated with first onset of disorders rather than recurrence (Lewinsohn, Allen, Seeley, & Gotlib, 1999), can double risk of depressive and anxiety disorders (Maughan & McCarthy, 1997), and multiple negative life effects can have a cumulative effect (Benjet, Borges, & Medina-Mora, 2010; Sánchez, Ladd, & Plotsky, 2001).

Children living with depressed parents are exposed to high levels of stress (Hammen & Brennan, 2003). Compared to non-depressed families, families with a depressed parent have higher rates of marital discord and divorce (Knappe, Beesdo, et al., 2009; Merikangas, 1984), family conflict (Kane & Garber, 2004a; Keller et al., 2009), financial difficulties (Fadden et al., 1987), and parenting difficulties (Mars et al., 2012; Wilson & Durbin, 2010). Exposure to stressful life events may be substantially influenced by genetics that are also correlated with major depressive disorder (Kendler et al., 1995; Kendler & Karkowski-Shuman, 1997; Levinson, 2006). Evidence has shown that children of depressed parents tend to be more likely to experience dependent stressful life events by selecting risky situations (Kendler & Karkowski-Shuman, 1997),

thus genetically-influenced traits in children of depressed parents may further increase their vulnerability. Children of depressed parents have also been shown to have poorer coping skills (Garber, 2006; McMakin et al., 2011) which can significantly impede their ability to deal with encountered stressors, leading to prolonged exposure.

As previously discussed, stress-related hormonal responses are mediated by the HPA axis, which responds to stress by secreting cortisol. There has been extensive research conducted on animals that indicate that early adversity can result in altered HPA function and a resulting dysfunction in the stress response, such as elevated glucocorticoid levels when exposed to stress (Hayley, Poulter, Merali, & Anisman, 2005; Plotsky, Owens, & Nemeroff, 1998). Such a response is particularly intriguing when examining PPD and children of parents with chronic depression. Children of depressed parents may inherit a dysfunctional stress response (Kumsta et al., 2007; Witt et al., 2011) and/or children may develop an abnormal stress response due to early life adversity (McCrory et al., 2010; Witt et al., 2011) in the form of a depressed parent (Murray et al., 2010; Oberlander et al., 2008). Abnormal autonomic functions including high heart rate, lower vagal tone, and higher cortisol levels has been found in children of depressed parents (Ashman, Dawson, Panagiotides, Yamada, & Wilkinson, 2002; Davis et al., 2007; Vreeburg et al., 2010), but there is some variability in the data (Adam, Sutton, Doane, & Mineka, 2008). There is also some evidence of asymmetries in the right prefrontal cortex in children of depressed parents (Bruder, Tenke, Warner, & Weissman, 2007; Dawson et al., 1999; Rao, Hammen, & Poland, 2009) indicative of underlying neurobiological mechanisms that may be involved in the high risk of psychopathology in children of depressed parents.

Demographic Correlates of Risk. Demographics characteristics of the child and family have been associated with increased risk of psychopathology (Bradley & Corwyn, 2002) and the transfer of risk in parental depression (Ackerman & Brown, 2006; Eirini Flouri, Tzavidis, & Kallis, 2010). Children in families who are ethnic minorities, low income, and single-parent homes may experience additional stressors that increase the risk of psychopathology and limit interventions(Ackerman & Brown, 2006).

Children in ethnic minority families are often exposed to a wide range of psychosocial difficulties including poverty, limited access to health care, discrimination, and poor resources (Flaskerud & Hu, 1992; S Sue, Fujino, Hu, Takeuchi, & Zane, 1991; Stanley Sue, 2009). Although depression is common across all demographics, there is some evidence that socioeconomic inequalities may exist in the prevalence and course of depression (Lorant et al., 2003). Studies have found that approximately half of mothers living in poverty score high on measures of depression (Brown & Moran, 1997). Socioeconomic status (SES) has been associated with an array of outcomes in children's cognitive and psychosocial functioning, including internalizing and externalizing disorders, social difficulties, and poor academic performance (Ackerman & Brown, 2006, 2006; Bradley & Corwyn, 2002). Thus, it is not surprising that children of depressed parents in low SES households have greater risks for psychopathology than those in middle or high SES households (Brown & Moran, 1997; Eirini Flouri et al., 2010).

In households where children have a depressed parent, poverty may act as a moderator between the maternal depression and child's cognitive and motor development (Petterson & Albers, 2001). Family composition may also be a significant correlate of child outcome. There are high rates of single-mother households in lower SES categories

and children of depressed single mothers have an increased risk for psychopathology over children living with both parents (Talati et al., 2007). The combined effect of demographics risks and maternal depression on child outcome may be mediated by parenting behaviors (Conger & Donnellan, 2007). Parents who are supportive, warm, and offer guidance to their children may improve their child's outcome in spite of SES and parental depression risk factors (Klebanov, Brooks-Gunn, & McCormick, 2001). Overall, demographic correlates may increase the risk of psychopathology in children of depressed parents. Furthermore, depressed parents living in lower socioeconomic status households may have fewer resources to receive help for themselves or for their children, which may result in worse outcome longitudinally.

1.3.2 Specific Risks

Parental depression as a Specific Risk Factor. There is ample evidence of parental depression as a pervasive risk factor for the development of psychopathology in their offspring. Researchers have isolated proposed specific mechanisms of risk involved with having a depressed parent, including; genetic heritability, exposure to negative parental affect and behaviors, modeling maladaptive cognitions, neuroregulatory mechanisms, sociodemographic variables, and dysfunctional stress response due to early childhood adversity (Goodman & Gotlib, 1999; Goodman, 2007). Children of depressed parents may have a cognitive vulnerability to depressive symptoms (Hammen & Brennan, 2001). Transactional models are increasingly used to examine the particular risk factors, accounting for complex interacting mechanisms such as genetics, environmental factors, child characteristics, parent-child interactions, and stressful life events to explain the risk associated with parental depression (Goodman, 2007). Twin studies have

generally estimated the heritability of depression to be around 50% (Bierut, 1999; Kendler, Gardner, Neale, & Prescott, 2001; McGuffin, Katz, Watkins, & Rutherford, 1996; Reich et al., 1987). Children of clinically depressed mothers show cognitive vulnerabilities to depression at a very young age, such as self-blame, negative self-talk and attributional style, and poorer academic performance (Hammen & Brennan, 2001) which may be inherited attributes. While there is modest evidence of an inherited genetic component to the transmission of psychopathology in children of depressed parents, non-inherited factors are particularly important given the pervasive risks associated with parental depression (Harold et al., 2010; Lynskey et al., 2004; Tully, Iacono, & McGue, 2010).

Clinical Features of Depression Confer Risk. One particularly understudied mechanism of risk is the specific clinical features of the parent's depression. Examining such variables is complicated by the heterogeneity of depressive disorders themselves, with significant variation in presentation, severity of symptoms, duration, number of episodes, and age of onset (Kessler et al., 2003; Maj, 2012). Furthermore, many of the research studies conducted in this population use parents' reporting on prior depressive episodes, diverse treatment regimens, non-clinical or community samples, and significant time lapses between interviews. The work frequently groups together depressed parents of varying severity, chronicity, and with diverse clinical presentation. Therefore, it becomes difficult to isolate specific clinical features that may confer risk. Despite these limitations, work has been done to identify specific characteristics of the parental illness associated with child outcome.

Research done in the STAR*D-Child (2006) study showed that severe maternal depression and atypical depressive features were associated with increased risk of child psychopathology. Furthermore, maternal comorbid anxiety disorders were associated with markedly increased prevalence of depressive disorders in offspring (Pilowsky, Wickramaratne, Rush, et al., 2006). In general, the clinical features common to depression such as irritability and anhedonia may preclude quality parenting (Besser & Priel, 2005; Brennan et al., 2002; Feder et al., 2009; Goodman, 2007). Atypical features, including rejection sensitivity and excessive lethargy, could also have deleterious effects on the quality of relationships and level of care that parents give to children while they are ill. However, the deficiencies displayed by some depressed parents (Lovejoy, Graczyk, O'Hare, & Neuman, 2000) only account for a portion of the variance in childhood psychopathology (McLeod, Weisz, & Wood, 2007).

Characterizing the subtypes of depression according to clinical identifiers and severity may be useful in the analysis of offspring outcome. For instance, some research has suggested a familial subtype of depression identified by early onset (Sullivan, Neale, & Kendler, 2000; Weissman et al., 1997). It may also be necessary to differentiate between clinical depressive disorders and subclinical depressive symptoms in parents. Although subclinical depression has been found to be a predictor of poor outcome in children, the mode of transmission to children may differ significantly, and may be more dependent on environmental risk factors more so than hereditary mechanisms (Harrington, Rutter, & Fombonne, 1996).

Timing. Children of parents who experience recurrent, chronic, and severe depressive episodes have a higher likelihood of developing a psychological disorder

(Foster et al., 2008; Hammen & Brennan, 2003; Klein, Lewinsohn, Rohde, Seeley, & Olino, 2005). Children exposed to chronic and recurrent parental depression have elevated levels of behavioral problems, internalizing and externalizing symptoms, and poorer overall outcome (Hammen & Brennan, 2003; Klein et al., 2005). Child's functioning may also be affected by how recent the depressive episode occurred, meaning that children of current or recently depressed parents would fare worse than children who had a longer period of time without exposure to depression (Gunlicks & Weissman, 2008). A recent study by Mars et al. (2012) examining offspring of 337 recurrently depressed parents over 16 months found that children of parents who had a recent depressive episode had more self-reported psychiatric symptoms and were twice as likely to have a psychiatric disorder than children who had not recently been exposed to a parental depressive episode.

Timing of parental depression relative to the child's developmental stage may have implications for how vulnerable a child is to particular disorders. As discussed previously, the development of specific psychiatric disorders in children of depressed parents varies as a function of age and developmental stage. With increasing cognitive maturity, children may be better able to understand parent depressive symptoms at older ages (Pilowsky et al., 2008). Younger children of depressed parents are more likely to develop anxiety and behavioral disorders (Hammen & Brennan, 2003) and adolescent offspring more likely to develop depressive disorders (Weissman, Wickramaratne, et al., 2006). Such findings may be indicative of "critical periods" of development.

In recent years a great deal of work has been done assessing the impact of depression during pregnancy and in the post-natal period on child outcome. There is

evidence that children may be especially vulnerable to deleterious effects of maternal depression during pregnancy (Alder, Fink, Bitzer, Hösli, & Holzgreve, 2007; Talge et al., 2007) and infancy, especially in the post-natal period (Brand & Brennan, 2009; Murray et al., 2011; O'Hara, 2009). The prevalence of MDD can be as high as 13% during pregnancy and up to 15% in the postpartum period (Marcus, 2009; O'Hara, 2009; Pearlstein, 2008). MDD may results in suboptimal conditions for the developing foetus due to problems with sleep (Nutt, Wilson, & Paterson, 2008) and inflammatory responses to stress (Hayley et al., 2005; Plotsky et al., 1998). Babies born to mothers with MDD may have lower birth weight and APGAR scores, and may be at risk for neurodevelopmental insults (Alder et al., 2007). Following birth, the growth curves may be negatively impacted and research has shown that these stress-induced alterations in neuronal development that occur during fetal development are associated with deficits in executive functions such as working memory, attention and cognitive flexibility, as well as emotional dysregulation (Talge et al., 2007). MDD in pregnancy is the greatest risk factor for parental depression in the post-natal period (Milgrom et al., 2008; Robertson, Grace, Wallington, & Stewart, 2004).

Post-Partum Depression (PPD) is clinical depression occurring within 4 weeks of pregnancy (American Psychiatric Association, 2000) but the symptoms of PPD may occur at any time in the post-natal period (first year after giving birth) (O'Hara, 2009). These depressive symptoms are often severe and occur at a time when the infant is maximally dependent on parental care and is highly sensitive to the quality of the interaction (Murray et al., 2011). While growth retardation may be attributable to a suboptimal in utero environment, the quality of the parent-child relationship during the

first year of life is a consistent predictor of child outcome (Swain, Lorberbaum, Kose, & Strathearn, 2007). Depression during the post-natal period has been shown to negatively impact parenting behaviors, resulting in significant stress for children (Goodman & Gotlib, 2001; Hay et al., 2008a; Murray et al., 2011). Research shows that infant children of depressed mothers are more temperamental, receive lower scores on measures of cognitive and motor development, have less secure attachments to their mothers and increased negative reactivity to stress, and show delayed development of self-regulatory strategies (Luoma et al., 2001). These children may also exhibit poorer long term outcomes in regards to academic performance, self-esteem, and internalizing and externalizing problems (Field, 2010; Dale F Hay, Pawlby, Waters, & Sharp, 2008b).

Long-term follow ups have shown that problems related to exposure to maternal MDD in these early years may persist long after maternal recovery (Lyons-Ruth, Alpern, & Repacholi, 1993). However, others have found that mothers with a history of postpartum depression who sustained long-term remission were no different from mothers who were never depressed in their interactions with their children (Murray, Halligan, Adams, Patterson, & Goodyer, 2006). Little data exists that examines the temporal impact of MDD or the long-term cognitive outcome of children born to depressed parents (Goodman & Gotlib, 2001). Investigation of the mechanisms of risk and correlates of antenatal MDD and PPD that persist beyond the depressive episode itself, as well as longitudinal follow-up of early exposed children, is needed to further our understanding of child outcomes and to delineate the impact of maternal remission.

Overall, evidence from this research suggests that exposure to parental depression may be subject to critical periods and early exposure may have long term negative

effects. However, such findings are often complicated by repeated exposure of parental depression over development due to the high recurrence rate inherent to depressive disorders (Hay et al., 2008a). It may be that the deleterious effects of parental depression spans across development.

Child Characteristics. Childrens' temperament can significantly affect their response to the world and interactions with parents. Parent-child conflicts common to parental depression are widely recognized as bidirectional in nature (Callender, Olson, Choe, & Sameroff, 2012; Goodman & Gotlib, 2001; Gross, Shaw, & Moilanen, 2008). Researchers have found that children of depressed parents may have difficult temperaments (Bruder-Costello et al., 2007; Melchior et al., 2012), thus leading to especially tumultuous parent-child interactions. In a 20-year intergenerational study of depressive disorders, Bruder-Costello et al. (2007) found that among children of depressed parents, those who had a difficult temperament early in life were twice as likely to develop MDD, compared to children with an easy temperament. It is not clear whether children's difficult temperaments occur in response to parental depression, or acts independently as an additional interactive risk factor. Regardless, both factors contribute to poor parent-child relationships associated with increased risk of psychopathology in children.

Gender. As discussed previously, there are gender differences in the prevalence of different developmental psychopathologies. When looking at the gender effect in children of depressed parents, the research available is inconsistent. There has been some evidence that the effect of parental depression may be different as a function of gender. For instance, Essex et al. (2003) found that in children of depressed mothers who

experienced high family conflict, females were more likely to experience internalizing problems and males were more likely to experience externalizing problems. Others have found that daughters of depressed mothers may be more susceptible to modeling behaviors that increase their risk of depression, such as negative thinking and helplessness (Rolf Loeber et al., 2009; Mundt & Freeman, 1996). Girls may also be more vulnerable to the effects of maternal depression on the mother-daughter relationship and have relationships with their mothers characterized by higher conflict and a sense of responsibility for caring for the family (Goodman & Gotlib, 2001).

The current work examined child psychopathology in offspring of depressed mothers and fathers enrolled in a double blind treatment trial for Major Depressive Disorder. Child outcome was compared according to these general and specific risk factors implicated in risk of psychopathology. The work herein examined demographic correlates, such as socioeconomic status and family composition, characteristics of the parent's depression, such as comorbidities and severity, and characteristics of the children, such as gender, that have been previously indicated to elevate risk of psychopathology in offspring of depressed parents. The study also examined qualities of the parent-child relationship that may influence outcome.

1.4 Family Processes of Risk and Resilience

Introduction

Depression in parents often occurs at a time when children are highly dependent on their families. Therefore, it is essential to examine the effects of parental depression in the context of the family environment. The transmission of risk of psychopathology to offspring of depressed parents may be mediated by quality of parent-child relationship,

parent's marital satisfaction, parenting behaviors, and family cohesion (Nomura, Wickramaratne, Warner, Mufson, & Weissman, 2002). There are limited data available examining family stressors in the context of parents with clinical depression. The following will review the literature examining the role of parent-child relationship, family environment, and child characteristics on outcome in children of depressed parents.

1.4.1 Parent-Child Relationship

The relationship between parents and their children has been widely studied in the investigation of child psychopathology. Children's interaction with their parents are important in learning how to express and regulate their emotional responses (Denham, Wyatt, Bassett, Echeverria, & Knox, 2009). Within this construct, researchers have examined parenting behaviors, parent-child interactions, and parent-child bonding for their role in child outcome. Maladaptive parental behaviors such as negative affect, hostility, criticism, harsh discipline, and low warmth or responsiveness have been identified as risk factors for internalizing and externalizing disorders in offspring (Harold et al., 2010; Radke-Yarrow, Nottelmann, Belmont, & Welsh, 1993). The quality of parenting can be influenced by various determinants, including situational and circumstantial factors, genetic correlates, marital problems, and psychosocial difficulties (Kendler, Sham, & MacLean, 1997). Specifically, teen parents, low socioeconomic status, ethnic minorities, parental psychopathology, and parental history of abuse during childhood have all been associated with harsh parenting and resulting strained parent-child relationships (Abidin, 1992; Barkin, Scheindlin, Ip, Richardson, & Finch, 2007). Children who experience negative parenting practices are at risk even if it occurred infrequently (Taylor, Manganello, Lee, & Rice, 2010; Teicher, Samson, Polcari, &

McGreenery, 2006). Research examining the influence of depression on mother's and father's parenting has demonstrated that parental depression is a consistent predictor of negative parenting behaviors and conflict-related interactions with children, even more so than socioeconomic status (Lyons-Ruth, Wolfe, & Lyubchik, 2000). Clinical symptoms of depression may be associated with a broad array of suboptimal parenting behaviors, accounting for a nonspecific transmission of risk to offspring. Most commonly researchers have focused on parental warmth and expressed emotion.

High expressed emotion, characterized by hostility, emotional over-involvement, and critical comments has been implicated in transmission of risk to offspring (Asarnow et al., 2001; McCleary & Sanford, 2002). Schwartz et al. (1990) found that high expressed emotion in depressed parents was a significant predictor of poor outcome in offspring above and beyond chronicity and severity of the parental depression. Affectionless control, characterized by low parental warmth and high levels of control or discipline, has also been identified as a cluster of behaviors that puts children of depressed parents at increased risk for psychopathology (Fendrich et al., 1990; Sato et al., 1998; Weissman, Wickramaratne, et al., 2006). Furthermore, compared to non-depressed parents, depressed parents have been found to express low self-efficacy (D. Gross, Conrad, Fogg, Willis, & Garvey, 1995), induce feelings of guilt in children (Zahn-Waxler & Kochanska, 1988), and to be more disengaged (Chronis et al., 2007).

While it is well known that parental behaviors have an impact on children's outcome, it is also widely accepted that this process is bidirectional and that the child's behavior effects the parents' responses (Callender, Olson, Choe, & Sameroff, 2012; Goodman & Gotlib, 2001; Gross, Shaw, & Moilanen, 2008). Parent-child relationships

characterized by poor communication, high conflict, and poor bonding have been implicated as risk factors for psychopathology (Goodman & Gotlib, 2001). It is not surprising that the clinical characteristics of depression may preclude effective parenting leading to reciprocal negative interactions between parents and children (Hammen et al., 1990).

1.4.2 Family Environment

The psychosocial difficulties encountered in MDD have strong implications for family functioning. Characteristics and composition of families have effect on children's lives immensely and may also moderate the effect of parental depression on child outcome (Goodman & Gotlib, 2001). Research examining the family environment in children of depressed parents has examined the role of the co-parent, level of household conflict, and the quality of interactions within the household.

The majority of this research has examined family context with respect to depressed mothers. In this line of work, researchers have found that absent fathers are associated with greater risk of psychopathology in children (Flouri, 2008; Goodman & Gotlib, 1999; Hammen, 1991). However, fathers who are present in the household may significantly contribute to the well-being of both the mother and child. Presence of a supportive co-parents can help facilitate the spouse's recovery from depression (McLeod, Kessler, & Landis, 1992) and improve outcome for the children (Cairney et al., 2003). Whereas, presence of a co-parent with significant psychological problems may result in poorer outcomes for spouse and child (Coyne, Thompson, & Palmer, 2002; Keller et al., 2009; Spence, Najman, Bor, O'Callaghan, & Williams, 2002). As previously discussed, partners with a depressed spouse are at an increased risk of psychopathology (Fadden et

al., 1987; Merikangas, 1984) and depressed persons are more likely to seek out psychologically distressed partners (Maes et al., 1998; Mathews & Reus, 2001) which increases the likelihood of problems within the family.

Families with a depressed parent are less cohesive and have more conflict than families with healthy parents (Cummings et al., 2005; Fendrich et al., 1990; Knappe, Lieb, et al., 2009). Cummings, Keller, and Davies (2005) found that in a community sample of 235 children, depressive symptoms in parents were associated with high levels of marital conflict and insecure attachment with spouses. Similar findings have been found with other samples (e.g. Keller et al., 2009). The increase in marital conflict found in families with a depressed parent is not surprising given the pervasive effects of depression on psychosocial functioning. While many interventions focus on improving parenting skills, evidence suggests that problems in child outcome are mediated more by marital relations than parenting practices (Cummings et al., 2005; Keller et al., 2009).

1.5 Parental Remission from Depression and Child Health

Remission of depression refers to a clinically significant reduction in symptoms to the point where the individual is considered well. Parents who remit from their depressive episode are likely to experience improved functioning overall, which would likely be reflected in their interactions with children and family. Commensurate with this assumption, researchers have found that reduction in parental depression is associated with improved outcome in offspring (Talati et al., 2007; Timko et al., 2002; Weissman, Pilowsky, et al., 2006). The STAR*D trials, an ancillary study to a multi-site treatment trial of adult MDD, were designed to assess this effect. In their analysis, Weissman et al. (2006) found that after 3 months of treatment of parent's depression there was a

significant decrease in children's symptoms and psychiatric diagnoses compared to children whose parents did not remit. These results were confirmed longitudinally (Wickramaratne et al., 2011b) and also present among single mothers with higher demographic risk factors (Talati et al., 2007). A further analysis of this sample by Foster et al., (2008) examined parenting practices and family functioning at three months into mother's treatment. They found that reduction in maternal depressive symptoms was associated with improved parenting practices, such as warmth and acceptance, and reduction in children's psychiatric symptoms. Studies examining mother-infant interactions have also found a correlation between reduction of depressive symptoms and improved mother-child interactions (e.g. Kaplan et al., 2001), providing further evidence that alleviation of parental depression may positively effect parent-child interactions. However, others have not found that remission of maternal depression improves parenting (e.g. Forman et al., 2007; Murray, Cooper, Wilson, & Romaniuk, 2003), but these have focused on mother-infant relationships, were not longitudinal, and the treatment provided to the mothers relied on psychotherapy (Timko et al., 2002).

Although the findings are variable, researchers have found in some samples that remission of maternal depression is also associated with improved academic performance, social functioning, and global functioning, but alleviation of parent symptoms does not improve attachment, temperament, or emotional regulation (see Gunlicks & Weissman, 2008 for review). Some researchers contend that treatment of parental remission is essential but interventions also need to target other variables effecting the child such as parenting, poverty, and psychosocial stressors (Beardslee et al., 2011a; Riley et al., 2008). However, the resources are rarely available to provide

comprehensive interventions with these groups. Thus, one of the most promising and reliable means to effectively treat these children may be through intervention of the parent's illness.

1.6 Present Study

The results from the currently available work in this field contains several gaps in the literature that need to be addressed to better improve our understanding of how parental depression confers risk for psychopathology to offspring. More information is needed that utilizes a controlled treatment setting, includes depressed fathers, studies parental relapse, examines family processes by inclusion of co-parents and multiple siblings, and examines time sensitive information with respect to parental illness and response to treatment, and current child symptomatology. The current work used a sample of parents taken from a double-blind clinical treatment trial, included depressed mothers and father as well as any co-parents, and multiple siblings per family. Outcomes were examined in children of depressed mothers compared to depressed fathers, then according to study site, and then in children of depressed mothers according to maternal response to depression treatment. Child outcomes were compared between groups with respect to general and specific risk factors, such as socioeconomic status and parental clinical characteristics, which had previously been indicated as increasing risk for psychopathology. In order to investigate how parental response to treatment affected child outcome, children of depressed fathers were compared to children of depressed mothers who responded to treatment. Treatment response was defined as a 50% reduction in parent's depression symptoms on the Hamilton Depression Rating Scale (HAMD₁₇), a screening tool for depression administered by psychiatrists in the Adult Study. Next

children of depressed mothers were compared according to mothers' remission status. Groups were categorized as; children of mothers who did not remit from depression (nonremitters), children of mothers who remitted then became depressed again during the study period (relapsers), and children of mothers who had a sustained remission from depression (remitters). Remission was defined as achieving a score of 7 or less on the HAMD₁₇. Data was gathered through multiple study visits where all families came into the clinic for interviews at baseline and then five follow-up visits over a period of nine months. Visits occurred at Baseline, weeks 4, 8, 12, 24, and 36. Baseline visits were used to get current and lifetime history of psychopathology in children, and all demographic information for families. At each subsequent visit, assessments were done with children for psychiatric diagnoses, symptoms of depression, anxiety, behavioral problems, overall functioning, and bonding with parent. Parents were assessed at each visit for depression symptomatology, overall functioning, and bonding with child. Parents were also interviewed on status of childrens' psychopathology and functioning. Therefore, child outcome measures included clinician interviews, child self-report, and parental reports on functioning.

The present thesis had two aims. The first aim was to assess the role of MDD in mothers and fathers as a risk factor for child psychopathology. The second aim was to investigate the relationship between parental response to treatment and child outcome over 9 months.

Aim 1: Examination of Major Depressive Disorder in Mothers and Fathers as a Risk Factor for Child Psychopathology: General and Specific Risk Factors Effecting Outcome

In order to explore the first aim, data from the baseline visit was used to examine rates of psychopathology in offspring, to compare child outcomes in children of depressed fathers to depressed mothers, and to explore general and specific risk factors associated with child psychopathology. Currently, there is a paucity of research examining the outcome in offspring of fathers with MDD. There is some indication that paternal depression may negatively impact offspring (Ramchandani, Stein, Evans, & O'Connor, 2008; Weitzman, Rosenthal, & Liu, 2011), but the majority of available literature examines fathers in the post-natal period and/or relies on community samples using self-report measures rather than clinical populations (Wilson & Durbin, 2010). The current study addressed this issue by providing data on a sample of fathers with MDD in a controlled clinical setting and directly comparing the outcome to depressed mothers in the same study.

This work also analyzed incidence of child psychopathology in the context of general and specific risk factors previously implicated in developmental psychopathology in children of depressed parents. General risk factors included variables, such as poverty, that result in a common risk for poor outcome. Specific risk factors refer to characteristics of the parents' MDD such as severity and comorbidity. This study examined children's likelihood of developing a depressive, anxiety, or behavioural disorder with respect to general and specific risk factors, according to child gender, age, and family composition. The following three hypotheses were examined in Aim 1:

1. Parental MDD will be associated with elevated rates of depressive, anxiety and behavioral disorders in offspring of depressed parents.

2. Children of depressed mothers will have more psychiatric symptoms than children of depressed fathers.
3. The impact of parental depression on child outcome will be impacted by; a) Demographic factors- socioeconomic status; b) Family composition- single parent home; and c) Clinical features of parental depression- severity, and comorbidities.

Aim 2: Investigating the Relationship between Parental Response to Treatment and Remission from Depression and Child Outcome Over 9 Months.

The second aim of this thesis was to investigate the relationship between parental response to treatment, and remission from depression, with child outcome over 9 months. Building upon the results from the baseline analysis, I compared longitudinal outcomes for children according to parent remission status. Research examining parental remission from clinical depression has found that reduction in parental depressive symptoms is associated with significant improvement in offspring (Talati et al., 2007; Timko, Cronkite, Berg, & Moos, 2002; Weissman, Pilowsky, et al., 2006). However, there is very limited data available examining this construct in controlled clinical settings and no previous study has examined the impact of parental relapse after remission on child outcome. Parental depression has been associated with disturbances in parenting including hostility, emotional over-involvement, and being over-critical (Asarnow, Tompson, Woo, & Cantwell, 2001; McCleary & Sanford, 2002). Depressed parents may provide insufficient attention to children (England & Sim, 2009). Therefore, I also examined family processes involved in child outcome, including parenting behaviors, functioning, and bonding as a function of parental remission status.

In order to examine the impact of parental remission and the role of family processes in child outcome, I compared children of depressed fathers to children of depressed mothers on multiple measures of psychopathology over 9 months. I then examined, in greater depth, our larger sample of depressed mothers according to mothers' remission status. The following three hypotheses were examined in Aim 2:

1. Parental response to depression treatment will have benefits for all children but there will be a greater improvement among children of depressed mothers compared to children of depressed fathers.
2. Children of remitted parents will report better global functioning and fewer psychiatric symptoms at 9 months, compared to children of non-remitters and relapsers.
3. Changes in parenting, and parent functioning, will mediate the impact of parental remission from depression on children's psychopathology and social functioning.

1.6.3 Summary

The investigation herein offers valuable information by allowing a direct comparison of outcomes in offspring of depressed fathers versus mothers. Such work is essential in moving towards a better understanding of whether the deleterious effects of parental depression is specific to mothers or equal for both parents. Furthermore, it offers longitudinal outcomes examining the role of parental response to treatment on child outcome. This study was the first examination of the impact of parental remission from depression on child outcome in a double-blind treatment study that included siblings and co-parents, and utilized multiple assessment time points. It was also the first to follow a

clinical study and examine child outcome according to parents' remission status as remitters, relapsers, or non-remitters. The findings herein provide a comprehensive analysis of a sample of offspring of depressed parents and explore individual and family processes involved in child outcome. In addition to improving understanding of timing and mechanisms of risk, the data offers evidence that is clinically applicable in approaching treatment strategies of families with a depressed parent.

CHAPTER 2: METHOD

2.1 Sample

As shown in Figure 1, the study flow chart, the sample consisted of 93 parents (82 mothers and 11 fathers) who entered a double-blind clinical trial and their 168 children (145 children with depressed mother and 23 children with depressed father) ages 7-17 years. Parents were considered eligible if they were enrolled in a randomized double-blind clinical trial aimed to hasten remission from depression across three psychopharmacological treatments, hereafter referred to as “Adult Study”. All Adults entering the Adult Study who had at least one eligible child who lived with the parent at least half of the time, were approached by the child study coordinators at each site for participation. Eligible children included all children ages 7 to 17 that did not have a developmental disability that would preclude them from the interviews or any current psychosis. Children who were actively receiving treatment for any psychiatric disorders were not excluded from participation.

Study participants were recruited from sites in New York City, New York (Columbia University and New York Psychiatric Institute), Ottawa, Ontario (University of Ottawa Institute of Mental Health Research) and Gatineau, Quebec (Pierre Janet Hospital). Research personnel described the study to eligible parents entering the adult trials and all consenting parents along with co-parents and assenting children were enrolled in the child study. Interviews were conducted with children, the depressed parent (Index Parent) and, if available, the co-parent (Non-index Parent). The children and parents were interviewed by independent assessors, who were blind to the remission status of the Index Parent. All participating children and parents also completed a battery

of self-report assessments at baseline and each of the five follow-up interviews completed 1, 2, 3, 6 and 9 months after the baseline assessment. Measures of parental depression were given separately by the psychiatrists and research personnel of the Adult Study. Written informed consent from parents and children was obtained. Baseline assessments were conducted within 2 weeks of the parent's randomization into the drug trial.

Data analysis for Aim 1 utilized the entire baseline sample, while Aim 2 used the same sample and also subsamples within the group. Analyses in Aim 2 included assessments done at baseline, weeks 4, 8, 12, 24, and 36. The original sample included 93 parents with their 168 children. Of the 82 mothers and 145 children who received baseline assessment, 67 mothers (82%) and 121 children (83%) completed the full 9 months assessments. Among the fathers, 9 fathers (82%) and their 18 children (78%) completed each visit for the full 9 months. There were no significant differences in demographic or clinical characteristics between the 67 mothers who completed the study and the 9 who dropped out; neither were there any statistically significant differences in these characteristics between 121 children who completed the study and the 14 children of those who dropped out (see Table 18).

The protocol for the Child Study was reviewed and approved by the institutional review boards at each site.

2.2 Measures

Parent Psychopathology. Parents entering the Adult Study were assessed for present and lifetime history of psychiatric disorders using The Structured Clinical Interview for DSM-IV-TR Patient Version (SCID-IV-I/P) (First, Spitzer, Gibbon, & Williams, 2002a). This semi-structured interview was used to make DSM-IV diagnoses

including MDD and depressive subtypes, melancholia and atypical depression. Co-parents were assessed for past and current psychiatric disorders using The Structured Clinical Interview for DSM-IV-TR Non-Patient Version (SCID-IV-I/NP) (First, Spitzer, Gibbon, & Williams, 2002b). The SCID-IV is a broadly used research tool and inter-rater reliability of the SCID-IV has been found to be good, with coefficients ranging from 0.48 to 0.98 for symptoms and 90% accuracy on diagnosis (e.g. Lobbestael, Leurgans, & Arntz, 2010).

Parental Depressive Symptoms

Hamilton Rating Scale for Depression (HAM-D-17)

The HAM-D₁₇ is a clinician-rated scale used to assess severity and changes in depressive symptoms. It has been widely used in most US studies of depression and was included in every assessment in the Adult Study over the course of 9 months. The 17 item scale ranks symptoms from 0 (not present) to 4 (severe), with a total score ranging from 0-54. Participants in the Adult Study were classified as either moderately (HAM-D₁₇ score of 14-21) or severely (HAM-D₁₇ score of ≥ 22) depressed. Remission was defined as a score of 7 or less. The HAM-D₁₇ is highly correlated with other clinician-rated instruments, has good reliability of 0.70 or greater, and test-retest reliability scores from 0.81 to 0.98 (Endicott, Cohen, Nee, Fleiss, & Sarantakos, 1981; Hamilton, 1967; Hamilton, 1960; Kearns et al., 1982). This tool was used to determine severity of parent's depression and also response to treatment throughout the study. HAM-D₁₇ assessments were administered by clinicians in the Adult Study with child assessors blind to the scores.

Child Psychopathology*The Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS-PL)*

The KSADS-PL is a widely used, valid and reliable diagnostic instrument used to assess most major Axis I DSM-IV disorders in children and adolescents. It has good inter-rater reliability with scores ranging from .55 to 1.00 and good test-retest reliability with scores ranging from 0.63 to 0.90 (Kaufman et al., 1997). Parents and children are interviewed separately, thus generating child and parent reported symptom scores. These scores are combined to generate a summary score for each symptom. These summary scores are used to generate DSM-IV diagnoses (Kaufman et al., 1997). Diagnoses and symptom counts, from the screening section of the K-SADS-PL, were examined. In order to relieve participant burden, sections of the KSADS-PL were selected targeting disorders known to be highly prevalent among children of depressed parents: affective, anxiety, disruptive behavioral disorders, and substance use disorders.

Clinicians using the K-SADS-PL were blind to parental remission status. They underwent rigorous training in K-SADS interviewing. As part of their training trainees viewed and scored videotaped K-SADS interviews and discussed them with an experienced child psychiatrist. After the initial training, each interviewer observed three live interviews before conducting a supervised interview. Following the completion of training they completed at least one directly observed interview.

Child Global Assessment Scale (C-GAS)

The C-GAS is a clinician-rated measure of global functioning, and it provides a good estimate of overall severity of disturbance. It was completed using all available information about the child, including KSADS-PL symptoms. The C-GAS is a valid

measure that has been shown to be reliable between raters and across time. It provides a good estimate of overall severity of disturbance (range, 0-100) with scores above 90 indicating superior functioning, and scores below 70 indicating impaired global functioning (Shaffer et al., 1983).

The Child Behavior Checklist (CBCL)

The CBCL is a parent-rated checklist assessing behavioral and emotional problems as well as adaptive behaviors. It consists of 113 questions, scored on a three-point Likert scale (0=absent, 1= occurs sometimes, 2=occurs often). The current study used scores of internalizing, externalizing, and total scores as a measure of outcome in children. Internalizing scores reflect problems such as withdrawal, somatic complaints, anxiety, and depression. Externalizing scores reflect aggressive, oppositional, and delinquent behaviors. Lower psychopathology scores reflect less psychopathology, and scores above 70 are considered to be in the clinical range. It has good inter-rater and test-retest reliability, with scores of 0.75 and above. Studies have supported the construct validity and the criterion-related validity of this instrument. Also, demographic variables such as ethnicity and SES accounted for a relatively small proportion of variance in scores (Achenbach & Rescorla, 2001).

The Children's Depression Inventory (CDI)

The CDI was used to measure children's self-reported symptoms of depression. Each of the 27 items lists three statements in order of symptom severity. Children respond by selecting one statement from each set that best describes their feelings over the past two weeks (e.g. "I am sad once in a while", "I am sad many times", "I am sad all the time"). Total scores can range from 0 to 54, with higher scores indicating more

depressive symptoms. Psychometric properties of the CDI have been well researched. Many researchers have found good reliability with internal consistency reliability coefficients in the low to upper 0.80s (Crowly, Worchel, & Ash, 1992; Kovacs, 1985; Weiss et al., 1991) and test-retest reliability good, ranging from 0.48 to 0.87, (Edeisohn, Ialongo, Werthamer-Larsson, Crockett, & Kellam, 1992; Finch, Saylor, Edwards, & McIntosh, 1987; Weiss et al., 1991). Research findings have successfully employed the CDI in distinguishing between depressed and nondepressed children (e.g., Benfield, Palmer, Pfefferbaum, & Stowe, 1988; Wendel, Nelson, Politano, Mayhall, & Finch, 1988).

The Multidimensional Anxiety Scale for Children (MASC)

The MASC is a self report scale consisting of 39 items, distributed across four major factors measuring anxiety. The factors include physical symptoms of anxiety (tense/restless and somatic/autonomic), social anxiety (humiliation/rejection and public performance fears), harm avoidance (perfectionism and anxious coping), and separation anxiety. The MASC shows good internal consistency score ranging from .060 to 0.89, and good test-retest reliability with scores ranging from 0.70 to 0.93 across a three month period (March et al. 1997). It has good content validity and correlates well with other measures of anxiety (Reynolds & Richmond, 1985).

Quality of Parent-Child Relationship and Family Environment

Parental Bonding Instrument (PBI)

The PBI, developed by Parker et al. (1979), is a 25-item self-report which includes dimensions of "care" and "overprotection" in parenting behavior. Children completed the PBI on their index and non index parents, and both parents will complete a

PBI assessing their parenting of the child and with regard to the parenting received from each of their own parents, i.e., the offsprings' grandparents. Separate PBIs were completed for each child when there were multiple children enrolled. The PBI has been found to be an important predictor of onset of illness in the offspring of nondepressed parents (Fendrich et al, 1990). The PBI provides scores on scales of affectionate constraint (high care and high protection), affectionless control (high protection and low care), optimal parenting (high care and low protection), and neglectful parenting (low care and low protection). Thus presence of negative and positive parenting practice could be analyzed with respect to child outcome. The PBI has been shown to have good to excellent internal consistency, with scores of 0.88 for Care and 0.74 on Overprotection. It also has good stability with three week test-retest correlations of 0.76 for Care and 0.63 for Overprotection (Parker, 1979).

Social Adjustment Scale Self-Report (SAS-SR)

The SAS-SR is a 56-item self-report measure where participants complete sections reflecting their personal social roles in several important areas of functioning. Measures include instrumental and expressive role performance in: work as a worker, homemaker or student; social and leisure activities; relationships with extended family; and marital role as spouse (or partner), as a parent, and as a member of the family unit. Scores range from 1 to 5, with higher values representing poorer adjustment. Research has shown good internal consistency with scores ranging from 0.74- 0.90, and temporal stability of 0.80 across 2-week intervals (Edwards et al. 1978; Vittengl, Clark, & Jarrett, 2004). Validity evidence includes significant correlations with clinical ratings, and sensitivity to change in psychopathology (American Psychiatric Association, 2000,

Weissman et al., 2001; Weissman & Bothwell, 1976; Weissmann et al. 1978). It is a reliable and valid instrument, including for use in minority samples and across cultures (e.g. Suzuki, Y. et al, 2003). This will provide a measure of overall social functioning and role in family for parents and co-parents. This measure is indicative of social difficulties and family cohesion problems that may be present.

Family History and Demographic Data

Family History Screen (FHS)

The FHS was used to gather information about the co-parent of the child when they are unavailable to complete SCID-IV-I/NP, or when the current caregiver is not the biological parent I used the FHS to gather psychiatric history on the child's biological parent. The FHS collects information on 15 psychiatric disorders in informants and their first degree relatives. Since each question is posed only once about all identified family members the administration time is about 10 minutes depending on family size and number of illnesses. It has acceptable validity, as measured against diagnoses obtained blindly through direct interviewing of 305 first degree relatives, and reliability, as measured by test-retest (over 15 months) kappas above 0.50 for most psychiatric disorders (Weissman et al., 2000). The FHS offers an acceptable substitution to gathering clinical data where individuals are not available for interviews. The FHS has acceptable sensitivity and specificity against comparable interviews and other more lengthy instruments. The FHS has been tested in a mixed racial and ethnic group (Weissman, Pilowsky, et al., 2006). This tool will allow us to analyze and compare presence of psychiatric history in co-parents.

Demographic Data

Information on demographic variables such as income, ethnicity, and education level were gathered using a demographic questionnaire designed specifically for the study. It was completed by the clinical interviewers during baseline assessments with the parents. Medical history of children, treatment updates, and information about remedial education were also gathered.

2.3 Procedure

Children and family enrolled in the study came to the respective clinic for assessments at six time points. The initial baseline assessment was conducted within two weeks of the depressed parent (index parent) beginning their study medication for the Adult Study protocol. Assessments followed then at weeks 4, 8, 12, 24 and 36. Interviews took place at New York Psychiatric Institute, New York, Pierre Janet Hospital, Gatineau, Quebec, and the Mood Disorders Research Unit at the University of Ottawa Institute of Mental Health Research, Ottawa, Ontario. The baseline interview assessed current and lifetime prevalence of psychiatric disorders in children and co-parents. These assessments were also done for the index parents but were conducted by the adult team. At baseline, the non-index parent was interviewed using the Structured Clinical Interview for DSM-IV-TR (SCID). If the non-index parent was unavailable, the information was gathered using the Family History Screen.

All parent and child assessments were completed by clinical interviewers, with a master's degree in psychology, social work or counseling, and at least two years experience in clinical work with children. All child assessors and interviewers, who administered the K-SADS and the SCID-IV interviews, were trained by a Board

Qualified Child Psychiatrist at Columbia University. Inter-rater reliability checks were conducted both after initial training and at several points during the study. These tapes were blindly rated by Dr. Pilowsky, and his ratings were compared to those ratings completed by Dr. Martine Flament in Ottawa. The mean kappa for agreement on symptoms was 0.62; range: 0.54–0.81 and for diagnoses was 0.90 (range 0.60 to 1.00). Quality assurance activities included review of children's diagnostic assessments, monthly conference calls, and site visits to ascertain compliance and review of record to insure completion and check for logical inconsistencies. The clinical interviewers in the child study were blind to the index parents' response to assessments and response to treatment. Children and parents were interviewed by the same interviewer, in order to minimize inter-rater problems, so that discrepancies between parental and child reports could be identified and resolved. Children were always interviewed first so that the interviewer's scoring of the child was unbiased by the parental report. Children and parents were not interviewed in the presence of each other. All assessments were conducted outside of school hours whenever possible so that children would not need to be withdrawn from school in order to participate. I coordinated and conducted all of the interviews at the Ottawa site.

Parents were invited to include all eligible children for participation. Therefore, several families had more than one child enrolled. If one child in a family refused to assent to the study or wanted to cease participation at any point, the family was invited to remain in the study if there were any assenting siblings who remained enrolled. Parents who dropped out of the adult study were also invited to continue in the child study. When

parents dropped out, we continued to gather data and their depression status continued to be assessed.

Any issues that arose during the study were brought to the attention of the adjunct committee called the Child Committee, consisting in New York of Drs. Weissman and Dr. Pilowsky, and in Ottawa of Drs. Blier and Flament, who would deal with any issues accordingly.

CHAPTER 3: RESULTS

Aim 1. Examination of Major Depressive Disorder in Mothers and Fathers as a Risk Factor for Child Psychopathology: General and Specific Risk Factors Affecting Outcome

The present analysis examined current and lifetime prevalence rates of psychopathology in a sample of children of currently depressed mothers and fathers enrolled in a double-blind treatment study for MDD. The sample was analyzed as a group, separated by gender of depressed parents, and compared across sites and demographic variables in order to test the three hypotheses of Aim 1.

A summary of demographic characteristics for the entire sample is shown in Table 1. Preliminary data analysis examined current and lifetime prevalence rates and age of onset of psychiatric disorders among children of depressed parents, a comparison of demographic characteristics among participants, and analysis of child outcome according to parent gender, demographic variables, family composition, clinical features of parental depression, and child age and gender.

To compare demographic variables, analyses of the mean values for continuous outcomes were tested using the t-test and categorical outcomes were compared by the chi-square test or Fisher's exact test, depending on the number of observations. To analyze child outcome, all of the logistic regression analyses were performed within the framework of the generalized estimating equations (GEE) approach (Liang & Zeger, 1986) by means of the GENMOD procedure within the SAS software package, in order to obtain estimates adjusted for potential non-independence of outcomes of offspring from the same family (SAS/STAT 2012). Continuous child outcomes such as C-GAS

scores were analyzed using mixed model analysis with SAS PROC MIXED, where the correlation between sibling outcomes was addressed by treating the effect of family as a random effect.

Hypothesis 1: Parental MDD will be associated with elevated rates of depressive, anxiety and behavioral disorders in offspring of depressed parents.

Current and lifetime DSM-IV psychiatric diagnoses of children obtained in the baseline visit are shown in Table 2. The age of onset for each disorder was also indicated for the entire sample. Generally, onset is considered to be early if the disorder is present before the age of 12.

The rates of current and lifetime psychiatric disorders were elevated in this sample of children compared to the general population. At baseline assessment, 43% of the children had a lifetime history of a psychiatric disorder, including affective (19%), anxiety (22%), and behavioral disorders (24%). Additionally, 38% of children had a current disorder at the time of assessment, including affective (13%), anxiety (18%), and behavioral disorders (21%). The mean C-GAS score for current functioning in all children was 72.7 ($SD = 13.8$), scores below 70 are considered clinically significant impairment. On the CBCL, the mean total score was 54.5 ($SD = 10.4$), and the scores on the internalizing and externalizing scales were 55 ($SD = 11.6$) and 54.7 ($SD = 10.1$), respectively. Thus the mean CBCL scores for the entire sample were below the clinically significant cut-off of 70.

While early onset of certain anxiety and behavioral disorders is more common in children, it is less common to have a depressive episode before the age of 12. In our sample, nearly half of the children (47%) with a history of affective disorders had early

onset, endorsing at least one clinically significant depressive disorder prior to the age of 12. Overall, the majority of the children (72%) had early onset of any disorder.

There was significant comorbidity between current depressive, anxiety and behavioral disorders in children. 41% of children with a current depressive disorder were also diagnosed with a concurrent behavioral disorder, as compared to only 20% of children without a current depressive disorder. Furthermore, 50% of children with a current anxiety disorder were diagnosed with a concurrent behavioral disorder as compared to 17 % of children without an anxiety disorder. There was a statistically significant threefold increase in the odds of having a current behavioral disorder among children with depressive disorders compared to those without depressive disorders ($OR = 3.1$; 95% $CI [1.1-8.3]$; $p = .02$). There was a statistically significant fivefold increased odds of having a behavioral disorder among children with current anxiety disorders compared to those without anxiety disorders ($OR = 5.1$; 95% $CI [2.0-12.8]$, $p = .001$). The association between concurrent depressive and anxiety disorders was not found to be significant. The patterns of lifetime comorbidity between depressive, anxiety and behavioral disorders in children were similar except for the fact that the association between depressive and anxiety disorders was now significant ($OR = 3.1$; 95% $CI [1.1-9.8]$, $p = .03$).

As shown in Table 3, there was no increased risk of having any current disorder by child gender. Boys and girls had similar rates and distribution of psychiatric disorders in our whole sample. There were also no significant differences in distribution of lifetime diagnoses (data not shown). Overall, the rates of psychiatric disorders in this sample of

children with a currently depressed parent were elevated and consistent with previous work in this population.

Hypothesis 2: Children of depressed mothers will have more psychiatric symptoms than children of depressed fathers.

As shown in Table 4, a comparison of demographic characteristics of mothers and fathers revealed some significant differences with respect to group characteristics. Compared to the depressed fathers in this sample, depressed mothers were more likely to be single (57% vs. 18%; $p = .04$), and to be a public assistance recipient (37% vs. none; $p = .02$). Mothers and fathers did not differ significantly by age, education level, number of children in household, or clinical characteristics of their depressive episode (i.e. severity, comorbid anxiety, melancholy). There were no significant differences in gender ($\chi^2 = 1.45$, $df=1$, ns) or age ($t = 0.25$, $df=76$, ns) in children of depressed fathers compared to children of depressed mothers. However, compared to children of depressed fathers, children of depressed mothers were more likely to participate in remedial classes (27% vs. 9%; $p < .00$) and less likely to be living with both biological parents (37% vs. 74%; $p < .00$).

A logistic regression analysis was performed to predict the effect of parent gender on child outcome, with child diagnoses as the dependent variable and parent gender as the predictor variable. Age and gender of child were considered a priori to be confounding variables and were included as independent variables in the analysis in order to adjust for their potential confounding effects. Adjusted odds ratios were calculated for child outcome, adjusted for child age, gender, and family correlation (siblings).

In this sample, children of depressed fathers had lower current and lifetime prevalence rates of all psychiatric disorders examined in this study (see Table 5). After adjusting for child age and gender, children of depressed mothers were about five times more likely to have any current or a lifetime psychiatric disorder (Current: $OR = 5.3$; $95\%CI [1.5, 18.3]$; Lifetime: $OR = 4.9$; $95\%CI [1.6, 15.0]$) than children of depressed fathers. Compared to the offspring of depressed mothers, those with a depressed father also had better overall functioning according to mean C-GAS scores ($p = .01$).

In order to rule out the possibility of a reporting bias contributing to elevated rates of diagnoses in children of depressed mothers, a comparison was conducted between parents and children's reports of symptoms on the K-SADS by parent gender. It was found that although children tended to report fewer symptoms than their depressed parent, on average, the mean number of K-SADS symptoms reported by children of depressed mothers was higher than the mean number of K-SADS symptoms reported by children of depressed fathers (2.4 vs. 0.7; $p = 0.10$), suggesting that the higher prevalence of psychiatric disorders among children of depressed mothers is not likely to result from maternal or paternal reporting bias.

Children of depressed fathers were more likely to live with both biological parents than children of depressed mothers. Thus, it was possible that children of depressed fathers did better because they lived in two-parent homes. Because there were only two index fathers who were single/divorced/separated, it was not possible compare children of single parent homes by the conventional method of adjusting for single vs. two parent households in the analysis. Therefore, rates of psychopathology in children of two-parent families, where the father was the index parent, were compared with that of children

where the mother was the index parent. As shown in Table 6, children of married mothers had a 6-7 fold increase in the probability of having any disorder, compared to children of married fathers ($OR = 6.4$, 95% CI [1.4-29.4] and $OR = 6.8$, 95% CI [1.5-31.0], for current and lifetime child psychiatric disorders, respectively). In general, the odds of having a psychiatric disorder were increased in children for all single parent homes compared to dual parent homes of various composition when the sample of children of depressed fathers was included. When analyzing children of depressed mothers only, it was found that in this particular sample, being a child of a single biological depressed mother did not significantly increase the risk of having a current psychiatric disorder compared to being a child of a depressed married mother ($AOR = 1.5$, $p = .29$) but the increased risk of having a lifetime disorder was marginally significant ($AOR = 2$; $p = .06$).

To further investigate the differences between samples, an analysis was conducted comparing children of depressed married fathers ($N=9$ fathers and 19 children) to children of depressed married mothers ($N=34$ mothers and 59 children). As shown in Table 7, this sub-sample had no significant demographic differences. Table 7 shows that with respect to clinical characteristics, depression severity was similar for the mothers and fathers in this subsample, although, while no fathers were mildly depressed, 11.8% of mothers had mild depression at baseline.

Current and lifetime DSM-IV psychiatric diagnoses of children obtained in the baseline visit were compared for children of married mothers versus married fathers (Table 8). Children of depressed married fathers were less likely to have a psychiatric disorder than children of depressed married mothers, (11% vs. 37%; $p = 0.005$) and less likely to have a behavioral disorder (5% vs. 22%; $p = 0.040$), including ADHD,

Oppositional-Defiant and Conduct Disorder. Similarly, the average number of K-SADS symptoms was lower in children of depressed fathers, compared to children of depressed mothers, by child report (0.2 vs. 1.2 symptoms; $p = 0.052$) and parental report (0.6 vs. 2.0 symptoms; $p = 0.055$). Children of depressed married fathers, compared to children of depressed married mothers, also scored as having less overall impairment on the Columbia Impairment Scale (CIS) (6.5 vs. 11.6; $p = 0.006$), which looks at items such as getting into trouble in school, and getting along with friends and family. No significant differences were found for children on anxiety symptoms on the MASC, depressive symptoms on the CDI, overall functioning on the CGAS, or externalizing and externalizing problems on the CBCL.

A comparison of parenting style, using scores from the PBI, found no significant differences in parenting style in this subgroup that could account for the differences in rates of psychopathology in children of depressed married fathers versus children of depressed married mothers. To ascertain whether differences in child psychopathology and functioning by parental gender were due (at least in part) to depressed fathers being married to non-depressed wives, scores of general mental health and depressive symptoms from the family history screen were compared for the wives of index fathers to index married mothers. Wives of index married fathers had significantly less general mental health ($p = .01$) and depressive symptoms ($p = .01$) than index married mothers. Wives of index married fathers also had significantly less general mental health ($p = .01$) and depressive symptoms than husbands of index married mothers ($p = .05$) (see Table 9). Thus, children in homes of depressed married mothers had higher incidence of dual

parent morbidity than children in homes of depressed married fathers which may have contributed to the variance in scores between the groups.

Overall, these findings are indicative of more psychiatric symptoms in children of depressed mothers, as compared to children depressed fathers. However, given the small sample size of children of depressed fathers ($N=25$) compared to children of depressed mothers ($N=143$), the interpretation of this data must be done with caution. While isolation of the married fathers versus married mothers reduced the demographic differences in the sample, it also reduced the size of the sample and any interpretations are limited.

Hypothesis 3: The impact of parental depression on child outcome will be impacted by; a) Demographic factors- socioeconomic status, b) Family composition- single parent home, and c) Clinical features of parental depression- severity, and comorbidities.

Certain demographic characteristics, family composition, features of parental illness, and characteristics of children have been identified as variables affecting the relationship between parental depression and child psychopathology. In order to better analyze the effect of these variables, children of depressed fathers were excluded from this analysis because of the small number of fathers participating in the study and the significant difference between rates of psychiatric disorders in children by parental gender. Separating the sample of children with depressed mothers also facilitated comparison to previous studies.

Due to the demographic differences in participants by site (see Table 10), an analysis of the sample was conducted according to study site (hereafter identified as

Ottawa and New York). The New York sample was reminiscent of populations often recruited in community samples; characterized as predominately ethnic minorities of lower socioeconomic status (SES). The Ottawa sample was similar to common clinical samples, and was mainly Caucasian with middle to upper-class SES.

Table 10 compares demographic characteristics of depressed mothers and their children in Ottawa and New York. The total sample includes 82 mothers and their 145 children. As shown in Table 10, the mother's mean age, number of children, severity of parental depression, and chronicity did not differ between the sites. There were, however, significant differences between site samples on the demographic variables of education, ethnicity, marital status, employment, income and some clinical characteristics of the parent's illness. Nearly half (44%) of the Ottawa mothers were college educated and above, whereas 37% of the New York sample had not finished high school. Depressed mothers in the New York sample were predominately Hispanic (93%), compared to the sample in Ottawa which was mostly White (90%). A majority of the moms in New York (71%) were single, divorced, or separated, compared to 44% in Ottawa. Most of the mothers in Ottawa (73%) were employed and working, compared to only 37% of mothers in New York. Furthermore, 12% of Ottawa mothers were receiving public assistance, compared to 61% of New York mothers. Consistent with these demographics, while 81% of the Ottawa sample had a household income over \$40,000 a year, 63% of the New York sample had a household income of under \$15,000 a year. Children in New York were significantly less likely to live with both biological parents, with 68% of New York children living in single parent homes compared to 28% of Ottawa children. With respect to clinical features of the parental illness, compared to New York, Ottawa parents were

more likely to be melancholic (29.3% vs 9.8%) and less likely to have a comorbid anxiety disorder (14.6% vs 56.1%). There were no statistically significant site differences by children's age, gender, or educational level.

Table 11 shows children's current and lifetime psychiatric diagnoses at baseline by site. Rates of disorders were comparable across sites with the children in the New York sample having a significantly increased risk of having any current ($p = .04$) or lifetime psychiatric disorder ($p = .01$). The slightly lower rates in Ottawa were expected given the higher income and fewer single parents. Impairment rates on the C-GAS were slightly higher in New York than Ottawa, but did not reach statistical significance. Overall, in spite of significant demographic and socio-economic differences between the two sites, the current and lifetime prevalence of psychiatric disorders had similar distribution among children of depressed mothers, but was higher in the New York Sample. The difference in life time psychiatric disorder between the two sites is likely due to the differences in demographics including higher rates of poverty and single parent households in the New York sample.

In order to generate models analyzing the effect of certain maternal characteristics on child outcome for lifetime psychiatric disorders, a multivariate analysis was conducted. Six models, shown in Table 12, were compared from a multivariate logistic regression with child lifetime psychiatric disorders as the binary dependent variable, one or more maternal characteristics (which had been found to be significant predictors in univariate analyses) were entered as simultaneous predictors, child age and gender entered as control variables, and an adjustment made for intra-family correlation. When these variables were entered as predictors of child psychiatric disorders it was found that

characteristics of the parent's illness were significant indicators of child's outcome. Specifically, mothers with melancholic features, characterized by extreme anhedonia and lack of reactivity, or mothers with a comorbid anxiety disorder, increased the odds of having a child with any lifetime anxiety disorder ($p < .01$). Mothers with severe depression were more likely to have children with lifetime behavioral disorders ($p < .05$) and children of mothers with a comorbid anxiety disorder were more likely to have any lifetime disorder ($p < .05$). In this model, income and presence of panic disorder with agoraphobia were not found to significantly increase the risk of a lifetime affective disorder in offspring.

In order to explore clinical and demographic characteristics associated with current disorders in children, adjusted odds ratios were calculated for the proportion of children with current psychiatric disorders by maternal depression characteristics and demographic features. As shown in Table 13, certain features of the parents' depressive illness were associated with elevated risk of current psychiatric disorders in offspring. Children of parents with melancholic depression were nearly three times more likely to have a current affective or anxiety disorder than children of parents without melancholic depression ($p < .05$). Children of mothers with severe depression were nearly three times more likely to have a behavioral disorder than children of parents with mild or moderate depression ($p < .05$). Chronic depression, defined as having a current depressive episode lasting two years or longer, was not found to be a significant predictor of elevated risk of current psychiatric disorders in offspring.

Certain comorbid conditions in parents were found to increase the risk of current psychopathology among offspring. First of all, children of parents with any comorbid

anxiety disorder were four times more likely to have an anxiety disorder ($p < .01$) and about three times more likely to have any disorder ($p < .01$) than children of parents without comorbid anxiety. Having a depressed parent with comorbid PTSD was associated with offspring being nearly six times more likely to have a current anxiety disorder ($p < .01$). In this sample, children of parents with comorbid panic disorder with agoraphobia were about four times more likely to have a current affective disorder than children of parents without this comorbidity. While this finding is significant, I did not replicate previous work showing parental comorbid panic disorder with agoraphobia to be a marked risk factor for any psychiatric disorder in offspring (Pilowsky, Wickramaratne, Rush et al., 2006). However, due to stringent entry criteria of the adult study, only 12 of the parents had panic disorder with agoraphobia and only 12 had social phobia, thus, exploration of these variables in the current sample was limited. As shown in Table 13, I also did not replicate the finding of atypical parental depressive features being associated with increased risk of psychopathology in offspring (Pilowsky, Wickramaratne, Rush et al., 2006).

With respect to household characteristics, I did not replicate an association of low income (under \$15,000 a year) with increased rates of any current disorder in offspring. However, children in households with incomes over \$40,000 a year were slightly less likely to have a current affective disorder, compared to children in household with annual incomes below this ($p < .05$). In the current model, which controlled for gender, age, and family correlation, being from a single mother home did not significantly increase risk of current psychiatric disorder compared to offspring of dual parent homes.

As shown in Table 14, a comparison of distribution of psychiatric disorders in children of depressed mothers according to child gender found no significant differences in rates of current disorders between boys (N=90) and girls (N=78) in this sample. There was a slightly significant increased odds of having a behavioral disorder, specifically ADHD, when comparing lifetime diagnoses between boys and girls (OR = 0.5; 95%CI [0.2,1.1]; $p < .05$).

Given the stringent selection criteria for the adult study and the controlled nature of the trial, these findings are interesting and demonstrate how parental depression itself is a risk factor that goes above and beyond previously identified demographic risk factors, including poverty, ethnicity, and characteristics such as child gender.

Aim 1 Summary

Overall, in this sample of children ages 7-17 years of currently depressed parents seeking treatment, I found elevated rates of psychopathology consistent with previous work. Over a third of the children were diagnosed with at least one current psychiatric illness. While limited by a small sample size, it was found that the children of depressed mothers in this sample had significantly higher rates of psychopathology than children of depressed fathers. However, significant differences in family composition and co-parent mental health may contribute to this variance. Finally, I found that certain characteristics were associated with increased risk of psychopathology in children of depressed parents. Children of single homes were at increased risk of a lifetime psychiatric disorder for our entire sample, but this risk was not as powerful when only comparing children of single mothers versus married mothers. Higher family income was associated with reduced risk

of affective disorders but children in low-income houses did not have a significantly elevated risk of psychopathology.

Characteristics of mother's illness were associated with increased risk of psychopathology for children. Maternal melancholic depression, severe depression, and comorbid anxiety disorders were associated with increased odds of psychiatric disorders in offspring. There were no major gender differences in distribution of psychiatric disorders among children.

Aim 2. Investigating the Relationship between Parental Response to Treatment and Remission from Depression on Child Outcome Over 9 Months.

This analyses examined how parental response to treatment of depression impacted child outcome and how these changes were mediated by qualities of parental functioning and the parent-child relationship. Analyses compared children of depressed fathers to children of depressed mothers and then a more in-depth analysis was conducted for children of depressed mothers only. Mothers were grouped according to depression status as a relapser, non-remitter, or remitter. This analyses tested the three hypotheses of Aim 2.

Baseline variables were examined in subgroups of the sample (i.e. married mothers versus fathers). Baseline differences between means of offspring outcomes on continuous variables (i.e. C-GAS) by parents' remission status were determined by using analysis of variance. Differences in the distribution of categorical variables (i.e. diagnoses) by parental remission status were analyzed using contingency table analysis and associated Chi-square tests or Fisher's Exact tests when counts were low. Comparison of child baseline characteristics by parental remission status was analyzed

using linear mixed models for continuous variables and logistic regression analyses in the context of Generalizing Estimating Equations (Liang & Zeger, 1986) to adjust for correlation between siblings. Baseline characteristics found to be significantly different were adjusted for in subsequent analyses.

Correlations between related measures over time and non-independence of observations in siblings were handled by including nested random effects in the model within subject nested within family (Betensky et al., 2000). When child outcomes were either binary variables (i.e. child diagnoses) or count variables (i.e. child symptom counts on KSADS) logistic regression (for binary outcomes) and Poisson regression (for outcomes that are counts) were used in the framework of generalized estimating equations to determine differential effects of parent gender on these outcomes. Repeated measures over time and non-independence of siblings were accounted for by using an independence correlation matrix, since the clusters were perfectly nested (repeated measures over time within siblings) (Singer, 1998). Potential confounding variables were handled as described for continuous outcomes.

Missing covariate data was imputed using the MI procedure in SAS 9.3 based on existing responses measures (i.e. SAS-SR items) in order to maximize available data to test for mediated moderation analysis of the significant remission effect on child outcomes.

Hypothesis 1: Parental response to depression treatment will have benefits for all children but there will be a greater improvement among children of depressed mothers compared to children of depressed fathers.

Alleviation of maternal depression symptoms has been associated with improvement in child outcome. Little is known about whether children of depressed fathers experience the same benefits when fathers get better. However, given that the impact of paternal depression may not be as significant as maternal depression on child outcome, children of depressed mothers may also have more pronounced benefits when mothers get better.

Differential effects by parental gender on changes in child outcomes over the 9 month study period were investigated using a linear mixed effects regression model for continuous variables, fitted with child outcome measure as the dependent variable, parental gender and time (study week) as independent variables as well as an interaction term representing parental gender x time. In addition, age and sex of child and site were included as covariates. In order to control for the demographic differences between mothers and fathers in the sample, this longitudinal analysis was conducted using the subsample of married depressed fathers (N=9) compared to married depressed mothers (N=34).

A comparison of child outcome scores over the nine month study period for children of married depressed fathers compared to children of married depressed mothers found that the prevalence of most child psychiatric symptoms decreased (significantly or at the trend level) among children of married depressed mothers (see Table 15 and Figure 2). These children had significant decreases in parental rated psychiatric symptoms on the K-SADS ($p < .001$), depression scores on the CDI ($p < .001$), overall impairment on the CIS ($p < .001$), and measures of anxiety on the MASC, including the Social Anxiety

subscale ($p < .001$), Separation/Panic subscale ($p = .01$), Physical Symptoms Subscale ($p = .03$), and Total MASC score ($p < .001$).

While the decrease in psychiatric diagnoses was not significant in children of married depressed mothers, there was a trend linear trend with a decrease in disorders from 37% at baseline to 19% by month 9 (see Figure 2). Children of depressed married fathers had no significant changes in symptoms except for a significant decrease in measures of anxiety on the MASC, including the Social Anxiety subscale ($p = .02$) and Total MASC score ($p = .01$). A between group analysis found that only scores of depression on the CDI were significantly different between groups over time ($p = 0.03$), with a decrease of depressive symptoms in children of depressed mothers and a moderate increase in children of depressed fathers. The increase in depressive scores for children of depressed married fathers occurred in the final visit. Given that only 11% of children of depressed married fathers had a psychiatric diagnosis compared to 37% of depressed married mothers, we explored whether there were any significant differences in measures of child-parent bonding according to parent gender. As shown in Table 16, there were no significant differences in parenting style, as measured on the baseline PBI, between the groups that could explain these differences. However, these analyses were limited by the small sample size of fathers.

In order to determine differences in child outcome according to parental response to treatment, we examined child outcome as a function of parent response. Parent response to treatment was measured on the HAMD₁₇, which was administered to participating depressed parents at each visit by the study physician. We first examined differences in rate of response to treatment on the HAMD₁₇ by parent gender. As shown

in Table 7, baseline mean scores on the HAMD₁₇ were similar for depressed married fathers ($M = 22.7$, $SD = 4.4$) compared to depressed married mothers ($M = 21.8$, $SD = 5.1$). However, 12% of mothers, compared to none of fathers, were mildly depressed at baseline. Differential effects of parent gender on changes on parent's HAMD₁₇ scores were analyzed using linear mixed effects regression model analyses to test linear and curvilinear (quadratic) trends over time, using gender of parent as the independent variable and the age of the parents was included as a covariate. As shown in Figure 3, a fitted line of mean HAMD₁₇ scores for depressed married fathers compared to depressed married mothers at each study visit demonstrated that the HAMD₁₇ scores of fathers and mothers decreased at a similar rate between baseline and week 24 and leveled off thereafter. There were no significant differences in changes of HAMD₁₇ scores over time between married mothers and married fathers ($F = 0.93$; $df = 1,434$; $p = 0.337$). For all participants, there was a negative linear component ($\beta = -1.09$, $t = -15.31$; $p < 0.001$) over the 36 week study period suggesting that the decrease in HAMD₁₇ scores in the 20 weeks following baseline was statistically significant, and a slightly positive quadratic component ($\beta = 0.02$, $t = 11.61$; $p < 0.001$), reflecting the leveling off seen after week 24. Thus, all participants improved and there were no major differences in rates of improvement between mothers and fathers.

I then examined whether there was a difference in outcome according to parental response to treatment among children of married depressed mothers compared to married depressed fathers. Since the sample of married fathers was too small to categorize the parents as remitters, non-remitters, and relapsers, analysis of married mothers versus fathers was separated according to responders versus non responders. Response to

treatment was defined as a reduction in parent's HAMD₁₇ scores by at least 50% from baseline. To compare child outcomes between these groups I used a linear mixed effects regression model analyses which determined differential effects of gender on parents' over 9 months and all models were controlled for child age, gender, site, and within family correlation. Child outcomes included psychiatric diagnoses, psychiatric symptoms count on the KSADS, overall functioning on the CGAS, overall impairment on the CIS, anxiety symptoms on the MASC, and depressive symptoms on the CDI. This statistical method accounts for the nesting of time within person to test linear and curvilinear (quadratic) trends over time and their interaction with parental response category (responder or non-responder).

In the current sample, 78% of the fathers and 77% of the mothers responded during the 9 month follow-up interval which included 45 children of 26 responding mothers and 12 children of 7 responding fathers. There was a trend or statistically significant decrease over time in most symptoms among children of responding mothers. As shown in Table 17, children of responding married mothers had significant, or borderline significant, decreases in psychiatric symptoms on the KSADS child report ($p = .06$) and parental report ($p < .001$), depression scores on the CDI ($p < .001$), overall impairment on the CIS ($p < .001$), and measures of anxiety on the MASC, including the Social Anxiety subscale ($p < .00$), Separation/Panic subscale ($p = .06$), Physical Symptoms Subscale ($p = .03$), and Total MASC score ($p < .001$). There was a non-significant but linear trend for decrease in psychiatric diagnoses among children of responding mothers, decreasing from 36% at baseline to 20% at month 9 (Figure 2). Children of responding married fathers had a significant decrease in psychiatric

symptoms on the KSADS child report ($p = .04$) and measures of anxiety on the MASC, including the Social Anxiety subscale ($p = .04$), Physical Symptoms Subscale ($p = .02$), and Total MASC score ($p < .01$). No children of responding fathers had a psychiatric diagnosis throughout the study. There were no significant between group differences on scales.

Since the sample of children of depressed fathers was small compared to children of depressed mothers, estimates are more stable for mothers than for fathers, and statistical power to indicate between-group differences over time was limited.

Hypothesis 2: Children of remitted parents will report better global functioning and fewer psychiatric symptoms at 9 months compared to children of non-remitters and relapsers.

As previously mentioned, remission was defined as obtaining a sustained $\text{HAM-D}_{17} \leq 7$, relapsers included parents who remitted then became depressed again during the study period, and non-remitters never achieved remission status. In the current sample, 55/76 mothers (72.4%) and 5/9 fathers (55.5%) met remission criteria at or before the 9-month follow-up assessment. The average time to remission was 51.2 (SD = 38.3) days. In the sample of mothers, approximately 22% (12/55) of the mothers that remitted met criterion for a relapse, during the 9 months.

Due to the small sample size and differences between groups, fathers and their children were excluded from analyses exploring child outcome as a function of parents' remission status over 9 months. While only 67 mothers completed every visit over the 9 month study period, 76 of the mothers were included in the 9 month analyses because 80% or more of the study data was collected or missing data was handled using

maximum likelihood methods which assume the missing data are random, a standard assumption in the mathematical models used in the analyses. As shown in Table 18, there were no significant demographic differences between the 67 mothers and 121 children who completed the study and the 9 mothers and 14 children who dropped out. Remission status of mothers who dropped out before study completion was based on the status at the time of drop out. All mothers who dropped out were invited back for a terminal visit with the Adult Study team for an assessment. As shown in Table 19, there were no significant differences on any of the maternal or child baseline demographic or clinical characteristics according to mothers' remission status.

In order to examine child outcome according to parental remission status, linear mixed effects regression model analyses was used which compared outcome by mothers' remission status (remitters, relapsers, or non-remitters) while adjusting for child age, gender, site, and sibling correlation. Mean scores for child outcome measures by parental remission status at each visit is shown in Table 20 and Figure 4. During the 9-month follow-up, only children of remitting parents showed statistically significant improvements. As shown in Table 20, children of remitting mother's had significant decreases in psychiatric symptoms on the KSADS child report ($p = .05$) and parental report ($p < .0001$), depression scores on the CDI ($p < .0001$), overall functioning on the CGAS ($p = .008$), overall impairment on the CIS ($p < .001$), and measures of anxiety on the MASC, including the Social Anxiety subscale ($p < .0001$), Separation/Panic subscale ($p = .0001$), Physical Symptoms Subscale ($p = .0001$), and Total MASC score ($p < .0001$).

Analysis of these significant outcomes revealed several significant group by time differences. Formal tests of interaction found that there were statistically significant differences in child outcome according to mothers' remission status. There was a significant group by time effect for scores on the CGAS ($p = .04$), with pairwise comparison showing a significant difference between remitters and relapsers ($p = .01$), a significant group by time differences on the CDI ($p = .03$), with pairwise comparison showing a significant difference between remitters and non-remitters ($p = .01$), and significant group by time differences on both MASC Social Anxiety ($p = .04$) and MASC Total ($p = .05$), with significant differences between remitters and non-remitters ($p = .03$) and borderline significant differences between remitters and relapsers ($p = .06$). It is noteworthy that there were no differences found in pairwise comparisons between relapsers and non-remitters, demonstrating that even though children of relapsers were exposed to mothers in remission for some period of time, their outcome did not converge with children of parents' who never remitted.

Visual inspection of Figure 4 shows that among children of relapsers and non-remitters there was a general trend of worsening of symptoms after week 24. Among children of remitting parents, there was a general linear trend of improvement that continued into the final study visit, with the exception of a slight increase of scores on the MASC and CIS at week 36. There was also a trend in reduction of diagnoses among children of remitting parents, but it was not significant ($p = .08$).

Hypothesis 3. Changes in parenting, and parent functioning, will mediate the impact of parental remission from depression on children's psychopathology and social functioning

To explore parenting and parent functioning as potential mediating variables, I examined parent functioning on the SAS-SR and parent-child bonding on the PBI. The total score for parent functioning on the SAS-SR measures instrumental and expressive role performance in parent's functioning at work, home, social and leisure activities, relationships with extended family, as well as satisfaction as a spouse (or partner), parent, and as a member of the family unit. Higher scores are indicative of social difficulties and family cohesion problems that may be present. Mothers' scores on the SAS-SR were examined over 9 months according to remission status. This was analyzed using linear mixed effects regression analyses, which account for the nesting of time within person to test linear and curvilinear (quadratic) trends over time and their interaction with remission status. Only remitting mothers showed significant improvements for each individual item and the total score on the SAS-R (See Table 21 and Figures 5-6). Mothers who remitted showed significant improvements in functioning on measures of Overall Functioning ($p < .0001$), Work ($p < .0001$), Family ($p < .0002$), Social and Leisure Time ($p < .0001$), Finances ($p < .0001$), and Parental Functioning ($p < .0001$). Within the Parental Functioning scale, remitting mothers demonstrated improvement in interest in child's activities ($p < .0001$), ability to listen and talk to child ($p < .0001$), getting along with child ($p < .0002$), and feeling affection toward child ($p < .0003$). Relapsing mothers had significant improvements on Overall Functioning ($p = .03$), Work ($p = .03$), Family ($p = .03$), and Social and Leisure Time ($p = .03$), but to a much lesser degree than remitting mothers. Non-remitters showed a significant improvement on Overall Functioning ($p = .04$). Formal tests of interaction showed a significant group by time effect for Total Score ($F = 12.13$, $df = 2, 266$, $p < .0001$), Work ($F = 6.43$, $df = 2, 107$, p

= .002), Family ($F = 6.33$, $df = 2, 235$, $p = .002$), Social and Leisure ($F = 8.1$, $df = 2, 266$, $p = .0004$), Finance ($F = 3.59$, $df = 2, 258$, $p = .03$), and Parent Functioning ($F = 8.09$, $df = 2, 218$, $p = .0004$). Within Parenting Functioning Scale, there were significant group by time effects for the items; Interest in child's activities ($p = .05$), ability to listen and talk to child ($p = .0006$), getting along with child ($p = .006$), and feeling affection toward child ($p < .02$). It is notable that only remitting mothers had improvements on all measures of parenting and individual parenting items. As seen in Figure 6, pairwise comparison found that the item "being able to talk and listen to my child" was significantly different between remitting and relapsing mothers ($p = .01$), borderline significant between remitting and non-remitting mothers ($p = .06$), and was not different between relapsing and non-remitting mothers.

I then investigated changes in ratings of parental bonding on the PBI over 9 months as a function of remissions status. The PBI provides scores of high and low protection as well as high and low care to form scales of affectionate constraint, affectionless control, optimal parenting, and neglectful parenting. I examined both parent and child ratings of care, overprotection, and percentage of Parent-Child ratings that met criteria for Affectionless control (characterized by overprotection and low care). These ratings were chosen as Affectionless Control has been previously associated with increased risk of psychopathology in children of depressed parents (Fendrich et al., 1990; Sato et al., 1998; Weissman, Wickramaratne, et al., 2006). As shown in Table 22, there was a significant improvement on scores of overprotection over 9 months on child ($p = .01$) and parental ratings ($p < .0001$) among remitters but not relapsers. Non-remitters also had a significant decrease in overprotection scores according to children's reports (p

= .002). There was also a significant group by time interaction effect of Mother's reported Overprotection scores between the three groups ($F = 3.39$, $df = 2, 1.3$, $p = 0.037$). This demonstrated that remitting mothers' interactions with their children became less characterized by acts of overprotection such as invading privacy, not letting children make their own decisions, being overprotective, and not giving child freedom. There was a borderline significant improvement on mothers' report of care among remitters ($p = .07$). Thus, remitting mothers had a trend of improved ability to show care, as characterized by items such as using a warm and friendly voice, being affectionate, understanding child, and smiling at child. Furthermore, although the change was not significant, it is also noteworthy that rates of affectionless control increased by both child (+8.3%) and parent reports (+21.7%) among relapsers, indicating increasing hostile and overprotective interactions.

In order to investigate potential mediators on the impact of parental remission on child outcome, I selected child outcomes that showed statistically significant differences in trend parameters over time by maternal remission status and I investigated whether differential effects of changes in maternal functioning over time could explain these differences by including maternal functioning variables as time varying covariates in models with relevant child outcomes as dependent variables. I then tested for main effects and/or interactions of maternal functioning over time by maternal remission status.

As seen in Table 23, change in SAS-SR total functioning appeared to partially explain the effects of maternal remission status for improved scores on the MASC. Since there were significant differences in linear changes slopes between children of remitters vs non-remitters, a pairwise comparison of these two groups was conducted. In the

unadjusted model, maternal remission status over time was associated with significant change in MASC Social ($\beta = -0.07, p = 0.03$) and MASC Total scores ($\beta = -0.017, p = 0.04$). In the adjusted model, the addition of the Parents' overall functioning on the SAS-SR Total Score as a time dependent covariate decreased the effect of maternal remission on MASC Social ($\beta = -0.05, p = 0.09$) and MASC Total scores ($\beta = -0.13, p = 0.11$). Furthermore, the SAS-SR Total score was found to be a predictor of differential change in MASC Social ($\beta = 0.73, p = 0.02$) and MASC total scores ($\beta = 1.94, p = 0.03$). Therefore, change in parents' overall functioning, as indicated by SAS-SR total score, accounted for some of the variance in improved MASC Social and MASC Total scores and partially explained the effects of maternal remission status on these anxiety measures. Parent Functioning Total acted similarly in the model (see Table 23), and thus, also partially explained the effects of maternal remission status on MASC Social and Total scores.

Changes in children's scores over time on the CDI, MASC Social, and MASC total among remitting mothers was partially explained by the differential effects of parental functioning item "able to listen to and talk to my child". Among these outcome measures, a pairwise comparison was conducted for CDI scores because they also had significant difference in linear change slopes between children of remitting mothers and children of non-remitting mothers. In the unadjusted model, the significant interaction between change in CDI over time and maternal remission status ($\beta = -0.08, p = .021$) was decreased with the addition of average parental functioning item "able to listen to and talk to my child" ($\beta = -0.06, p = 0.09$). While the item "able to listen to and talk to my child" did not partially explain any change in CDI scores over time, the interaction

between “able to listen to and talk to my child” and maternal remission status was statistically significant ($\beta = 0.96, p = 0.04$) meaning that the relationship between parent functioning item “able to listen to and talk to my child” and improvements on the CDI varied as a function of maternal remission. For MASC Social and MASC Total Scores, the significant differential change in these scores over time by maternal remission status was decreased by the inclusion of parental functioning item “able to listen to and talk to my child” as a time dependent covariate and became non-significant. Furthermore, parental functioning was found to be a predictor of MASC Social ($\beta = 0.65, p = 0.00$) and MASC total scores ($\beta = 1.40, p = 0.01$), thus changes in the ability to listen and talk to child partially explained the improvements on MASC Social and Total scores among children of remitters.

Mother’s report on overprotection on the PBI showed similar but non-significant results to the parental functioning “able to listen to and talk to my child” for the MASC Social scores. Changes in Overprotection may partially explain improvements on the MASC-Social among children of remitters ($\beta = 0.11, p = 0.06$). The difference between the PBI scores and SAS-SR may be because the PBI assessments were made at fewer time points than the SAS-SR. Also the PBI has been shown to be stable over time and not strongly affected by current symptoms (Murphy et al., 2010).

I looked at treatment received by the children over the 9 months to see if it might explain the differential effect of mother’s remission. There was no difference in the number of children receiving some mental health treatment at baseline by mother’s status, remission relapse, no remission (22.4%, 16.7%, 38.2%, respectively) and during

the course of the 9 months (19.7%, 16.7%, 26.5%). Two children were hospitalized over the 9 months, one of a remitter and one of a non-remitter.

Aim 2 Summary

Over the 9 month study period, psychiatric symptoms of children of depressed mothers decreased. Children of depressed fathers showed only a reduction in measures of anxiety. A comparison of married fathers to married mothers according to treatment response found that children of responding mothers showed significant improvements on multiple measures of psychopathology but children of responding fathers only had a reduction in anxiety. However, any conclusions are limited by our small sample size.

A comparison of children of mothers who remitted, compared to relapsers and non-remitters, found that only children of remitting mothers had significant improvements on various outcome measures over the course of 9 months. Therefore, exposure to remission was only beneficial to children in the present study, if the remission was sustained. Mothers who had sustained remission showed improvements in overall functioning, parental functioning, and a reduction in overprotection with their children. The improved outcome in children of remitting parents on measures of anxiety and depression was partially explained by the mother's improved overall functioning and improved parental functioning. There was a significant interaction over time between parenting item "able to listen to and talk to my child" and parental remission status where the relationship in parent's ability to listen and talk to their children and child scores of depression on the CDI varied as a function of parental remission status.

CHAPTER 4: DISCUSSION

Aim 1. Examination of Major Depressive Disorder in Mothers and Fathers as a Risk Factor for Child Psychopathology: General and Specific Risk Factors Effecting Outcome

The current study investigated the prevalence of psychiatric disorders among children of mothers and fathers enrolled in a double blind treatment study for Major Depressive Disorder. Nearly half (43%) of the sample of 168 children had a history of a psychiatric disorder and the majority of children (72%) had early onset. There was a high incidence of comorbidity between behavioral disorders and depressive disorders, and behavioral disorders and anxiety disorders. These findings are consistent with previous work done in this population (Hammen & Brennan, 2003; Lieb, Isensee, Höfler, Pfister, & Wittchen, 2002; Weissman et al., 2005, 2006). There was also a high incidence of early onset of disorders in the sample, with 72% of children having an early onset of disorder. This is consistent with previous work and indicates that this sample of children is at high risk of recurrence (Warner et al., 1992, Weissman, Wickramaratne, et al., 2006). There were no gender differences in distribution of psychiatric disorders in our sample. Previous research has been inconsistent regarding gender differences in this population. Furthermore, the increased vulnerability to depressive disorders in daughters of depressed mothers (Goodman & Gotlib, 2001) may be more evident in later adolescence and early adulthood (Wickermanarte & Weissman, 1998).

Prior to this study, there was limited data available investigating psychopathology in children of clinically depressed fathers and the majority of the literature relied on self-report measures in community samples (Wilson & Durbin, 2010). Therefore, while our

sample of fathers was small, it still contributes important information to the investigation of parental depression. In our sample, children of depressed mothers were about five times more likely to have any current or lifetime psychiatric disorder compared to children of depressed fathers, which is consistent with previous investigations of a national sample (Weitzman et al. 2011). Our sample did not replicate the finding of increased externalizing disorders in children of depressed fathers (Connell & Goodman, 2002). However, we did find that the rates of anxiety disorders in children of depressed fathers did not differ significantly compared to children of depressed mothers. Thus, it is worth investigating the possibility that anxiety disorders are elevated among children of depressed fathers, however our sample is not large enough to draw any conclusions.

Since the majority of the children of depressed fathers sample lived in a dual parent home, and children in dual parents households in our entire sample were less likely to have psychopathology than children in single parent households, we conducted analyses of children of married fathers (N=9 fathers and 19 children) compared to children of married mothers (N=34 mothers and 59 children) to control for this variable. We found that children of married mothers were about six to seven times more likely to have a psychiatric disorder, compared to children of married fathers. Once again, there were no significant differences between the groups on rates of anxiety disorders or scores of anxiety on the MASC. A lower rate of disorders in the children of depressed fathers, as compared to mothers, was found even when controlling for living arrangements and when comparing rates of illness among children of married mothers and fathers. While the rates of current and lifetime disorders were lower in children of depressed fathers

versus mothers, the rates of disorders in the children of depressed fathers may be higher than found in unaffected parents.

Some research has found that children of depressed fathers may have parent-child conflict issues similar to children of depressed mothers (Beardslee, Gladstone, Wright, & Cooper, 2003; Kane & Garber, 2004b; Klein, Lewinsohn, Rohde, Seeley, & Olino, 2005). Investigation of measures of parental bonding and parent functioning found no association of parenting styles that accounted for the differences in psychopathology in children of depressed fathers compared to children of depressed mothers. However, the measures used were limited and a study utilizing direct observation of relationships would be better able to parse whether there were major differences in parent-child interactions and relationships between children of depressed fathers compared to children of depressed mothers.

In our sample, wives of depressed fathers had significantly less general mental health issues than husbands of depressed mothers, so it is also possible that dual parent morbidity is associated with elevated risk of psychopathology in offspring of depressed mothers (Keller et al., 2009). This supports previous work showing that depressed women often marry men with significant psychiatric symptoms that preceded the marriage (Maes et al., 1998; Mathews & Reus, 2001; Merikangas, 1984; Hammen et al. 1999) and may offer further support that dual-parent morbidity is associated with an increased risk of psychopathology in offspring (Fendrich et al., 1990; Keller, Cummings, Peterson, & Davies, 2009; Nomura, Warner, and Wickramaratne 2001). Therefore, some of the differences between the two groups may be a result of dual-parent mental health issues. Research has suggested a gradient of risk, with higher rates of depressive

symptoms in children of families with two parents depressed, followed by mothers only depressed, fathers only depressed and neither parent depressed was found (Weitzman, Rosenthal, & Liu, 2011). The findings on children of depressed fathers in our sample are tentative based on the small sample size of children of depressed fathers ($N=25$) compared to children of depressed mothers ($N=143$), and the impact of dual-parent morbidity warrants exploration in future analyses with larger samples.

Numerous studies have shown a lower rate of depression among men in different cultures (Kessler et al 2003a.) and their lower treatment utilization (Wang, Lane, Olfson, Pincus, Wells, & Kessler, 2005; Xu & Borders, 2003). These factors likely contribute to lower participation rates of depressed fathers enrolled in the study, despite our recruitment efforts. Overall, our work demonstrates that while there may be a higher risk of psychopathology among children of depressed mothers, offspring of depressed fathers may still be at risk and further research is needed with this population.

In order to explore general and specific risk factors that impact outcome in children of depressed parents, I examined only children of depressed mothers in our sample and then compared the groups across the two sites. The analysis by site was conducted given the differences in demographics. The Ottawa site was predominantly Caucasian, high income, and 56% dual-parent homes, while the New York site was predominantly Hispanic, low socio-economic status, and 70% were single parent homes. Previous work has found that children in families who are ethnic minorities, low income, and single-parent homes may be at increased the risk of psychopathology (Ackerman & Brown, 2006; Flaskerud & Hu, 1992; Sue, Fujino, Hu, Takeuchi, & Zane, 1991; Stanley Sue, 2009). A comparison of rates of psychopathology in children by site found that

despite significant differences in demographic risk factors, rates of psychiatric disorders were comparable across sites. Children in the New York sample were at a slightly increased risk of having any lifetime psychiatric disorder than the Ottawa sample, which was likely due to the demographic differences. In this particular sample, being a child of a single depressed mother only marginally increased the risk of having a lifetime disorder among offspring. In general, it is striking that despite the presence of these previously identified risk factors, the rates of illness among children at both sites was basically the same. This finding may indicate that the risk of psychopathology conferred by depressed mothers may hold across demographics and culture. Furthermore, it is possible that the risk of psychopathology passed unto children of depressed parents may be partially independent of other identified risk factors, such as low socioeconomic status. The characteristics of depressive disorders affect all areas of functioning in parents and may be particularly deleterious to the parent-child relationship. It is also possible that prolonged exposure to stress due to having a depressed parent also contributes to the increased risk. Overall, this work replicates that parental depression is a unique and significant risk factor for psychopathology in children of depressed parents, and may confer risk independent of other known risk factors. A longer follow up study would be required to determine whether the demographic risk factors in this sample have a negative impact on children of depressed parents at later time points in life, or if their risk remains the same despite major demographic differences.

Previous work in the STAR*D trials found that clinical features of depressed parents such as comorbid anxiety, PTSD, substance use, or panic disorder were associated with increased risk in offspring. They also found that characteristics of the

parent's depressive disorder, such as severity, might elevate risk for children (Weissman et al, 2006). In the current sample, maternal comorbid anxiety disorder, PTSD, and Panic Disorder with Agoraphobia predicted higher rates of children's disorders. Features of the parent's depression were associated with elevated risk of disorders, where melancholia increased risk of affective and anxiety disorders in offspring, and children of parents with severe depression were more likely to have a behavioral disorder. Maternal substance abuse was not examined in this study due to exclusion of patients with substance abuse. Furthermore, panic disorder was also not found to be as strong a predictor as in previous work, but the current sample was very strict on entry criteria for comorbid anxiety disorders and only 12 participants had panic disorder.

Variability in other depression subtypes e.g. melancholic depression, predicting childhood anxiety disorders in the current study but not in other studies, may be due to maternal clinical variations and subtype definitions between studies. However, it would be worth investigating whether characteristics of illness, such as melancholic depression, increase risk for anxiety disorders in a larger sample. Future research should focus on severity of individual symptoms within parental illness that may explain increased child risk. For instance, it has been shown that irritability and anhedonia may preclude quality parenting (Besser & Priel, 2005; Brennan et al., 2002; Feder et al., 2009; Goodman, 2007). Focus on particular symptoms within the illness may also help explain why other parental illnesses, such as anxiety disorders, increase risk of depression in offspring.

I found no differences in child outcome according to parents classification as having a chronic depressive episode (two years or greater). However, this finding may not capture differences that exist in children with earlier or more chronic exposure to

parental depression. Given that exposure to parental depression may impact children differently at different developmental stages, particularly when the depression occurs earlier and is more prolonged (Klein et al. 2005), future work would benefit from analysis that includes the number of previous episodes as well as childrens' exposure to prenatal and post partum depression.

From these findings, I can conclude that comorbid disorders and characteristics of the parent's depression place offspring at higher risk for current and lifetime psychiatric disorders. Previous work has demonstrated that adults with severe depression and comorbid anxiety have more difficulties with compliance to treatment and poorer outcomes overall. (Brown, Schulberg, Madonia, Shear, & Houck, 1996; Feske, Frank, Kupfer, Shear, & Weaver, 1998). Thus, it is possible that parents' with comorbidities are not only presenting with more symptoms but are also less likely to stick to treatments, thus exposing their children to longer periods of illness and possibility of relapse due to noncompliance. These factors would certainly increase stress within the house and may lead to more familial discord, increasing risk of psychopathology in children.

Aim 2. Investigating the Relationship between Parental Response to Treatment and Remission from Depression and Child Outcome Over 9 Months.

Remission of depression refers to a clinically significant reduction in symptoms to the point where the individual is considered well. Parents who remit from their depressive episode are likely to experience improved functioning overall, which would likely be reflected in their interactions with children and family. Commensurate with this assumption, researchers have found that reduction in parental depression is associated with improved outcome in offspring (Talati et al., 2007; Timko et al., 2002; Weissman,

Pilowsky, et al., 2006). The present study replicated these findings and found an alleviation of symptoms among children of remitting parents.

To date, no previous study has shown whether clinically depressed fathers' response to treatment, will lead to beneficial effects for offspring. In this sample, I compared outcomes of children from responding married fathers (50% or greater reduction in depressive symptoms from baseline) to children of responding mothers. Children of responding mothers showed improvements in depression, anxiety, overall functioning and a reduction in psychiatric symptoms over 9 months. Children of responding fathers only showed a significant improvement on scores of anxiety. Thus, maternal response to treatment had a greater impact on outcome of offspring in this sample, but both groups had similar changes in anxiety symptoms. This finding further illustrates that anxiety in offspring may be an important area to focus on when researching paternal depression. Perhaps when fathers experience depressive episodes it increases anxiety in children because they are not sure how to handle the situation. Men are generally not as overtly emotional as women and may be more likely to feel shame about their depression. Observing interactions between depressed fathers and their children would be beneficial in identifying qualities of the interaction that may explain anxiety symptoms.

Demographic differences could explain outcome differences between the offspring of depressed fathers and mothers (Talati et al., 2007). However, the lower prevalence of psychopathology and of impaired functioning among children of depressed fathers, compared to children of depressed mothers, was evident even after restricting the sample to married parents, which resulted in demographically similar samples of fathers

and mothers. I also found that measures of parental functioning and bonding did not account for differences in children of depressed married fathers compared to depressed married mothers. It is possible that the differential impact of parental depression could be related to the amount of time spent with mothers in addition to the higher incidence of dual parent morbidity in married mother households. In general, given that the sample size was small and that there were fewer psychiatric disorders in children of depressed fathers, conclusions examining the impact of parental response to treatment on offspring outcome are very limited.

Previous work examining the impact of parental remission from depression on child health has found that the amount of time children are exposed to a remitted parent increases the rates of improvement of children's psychiatric symptoms (Weissman et al. 2006). Therefore, longer exposure to remission may improve outcome for children. A recent study by Beardslee et al (2013) found that adolescents with a history of depression found treatment less effective in preventing illness onset if the parent was currently depressed when the adolescent's treatment began. Thus, when treating children it is very important to consider the parents' depression status and explore possible treatment options for both parent and child. Previously, research in parental remission has only included investigation of early remitters and late remitters, no study has investigated outcome in children of parents who get well then become ill again (relapse). Given that length of exposure to remission has been associated with improvements in children, it is important to investigate whether these benefits remain when parents relapse. Relapse is an important consideration because with current treatment standards only about 50% of patients respond to initial treatment with antidepressants (Rush, Trivedi, and Fava, 2003),

only 25-45% go into remission (Thase, 2003). Among adults who are treated for depression and still have mild symptoms, there is significant impaired functioning and early relapse (Judd, 1996; McIntyre & O'Donovan, 2004; Paykel, 1995). Depression has a high recurrence rate, with approximately 50-70% of individuals suffering a second MDD episode, which is followed by a 70% chance of having a third, 90% chance of recurrence after a third episode (Fava, Park, & Sonino, 2006; Holma, Holma, Melartin, Rytsälä, & Isometsä, 2008). Therefore, a majority of children of depressed parents are exposed to multiple episodes and periods of remission and relapse within episodes.

Since the sample of fathers was small, I examined outcomes in children of relapsers, non-remitters, and remitters in children of depressed mothers only. It is noteworthy that in the current sample of adults, the remission rates were high and predominantly occurred early (within the first two months). This may reflect the nature of the Adult Study which included frequent visits and maximal medication dosing in order to optimize patient response. The early remission rates were similar to those found by Swartz (2008) which included psychotherapy for depressed mothers compared to mothers receiving treatment as usual. He also found that child outcomes were significantly improved at 9 months if mothers' received therapy and had a reduction in depressive symptoms, compared to treatment as usual. Therefore, it may be possible that intensive treatments that include multiple visits and encourage compliance may be important for benefitting both child and parent. Furthermore, in our results, all parents received intensive treatment so it is possible that all study participants benefitted to some extent, which would reduce some differences between groups. Future work should compare

outcomes in children of parent's receiving intensive treatment compared to parents receiving standard treatment.

While it is possible that all of our participants improved, there were significant differences found according to maternal remission status. The results add to the body of research showing that mothers' remission is associated with a significant improvement in child symptoms. In our sample, children of remitting mothers had a reduction in all areas of psychopathology measured. These findings are similar to the STAR*D findings at one year which used the same measures as the current work and found significant improvements in child outcomes among children of remitters only (Pilowsky et al., 2008). In STAR*D the benefit for children was greater when mothers remitted early, however, children of late remitting mothers also experienced a statistically significant decrease in symptoms. I was unable to compare early versus late remitters in the present study because, as mentioned, the majority of mothers in the current study remitted before 3 months. STAR*D also found that children of non-remitters actually got worse over time. We did not replicate this finding but it may be due to the much earlier remission rates, lower drop-outs, stricter Adult Study entry criteria resulting in less parent comorbidities, and overall trend of improvement for all parents enrolled in the study. These results of the current study are also consistent with other work examining longitudinal outcomes in children as a function of changes in parental depressive symptoms. A study by Garber et al. (2011) showed that a reduction in parent's depressive symptoms predicted changes in children's depressive symptoms over 2 years. Garber's study also used the CDI as a measure of depression but did not examine relapse in

parents. However, they did show that subsequent increases in parental depression were associated with increased symptoms in children.

Importantly, in addition to replicating the benefits of maternal remission on child outcome, I also found that if parents relapsed, the children did not show any improvements in functioning and were no better off than children of non-responders. Thus, it is essential that parent's remission is maintained for children to benefit longitudinally. It is possible that parental remission and subsequent relapse may create more chaos and stress within the home which may negate any benefits children would have had from the exposure to remission. Multiple depressive episodes and relapse within episodes may create multiple negative life effects which can have a cumulative negative effect on children (Benjet, Borges, & Medina-Mora, 2010; Sánchez, Ladd, & Plotsky, 2001).

Previous work examining child outcome as a function of parental depression status has shown that reduction of maternal depressive symptoms is associated with an improvement in parent-child interactions, such as warmth and acceptance (Foster et al. 2008). Research examining the influence of depression on mother's and father's parenting has demonstrated that parental depression is a consistent predictor of negative parenting behaviors and conflict-related interactions with children, even more so than socioeconomic status (Lyons-Ruth, Wolfe, & Lyubchik, 2000). In order to investigate the potential mediating role of parent functioning and behaviors on child outcome I examined mothers' self-reports on overall functioning and both children's and parent's reports on bonding. Clinical characteristics of depression negatively impacts functioning in several areas of life and may preclude effective parenting leading to reciprocal negative

interactions between parents and children (Hammen et al., 1990). In this sample, only remitting mothers showed an overall improvement on all scores of functioning. But, nonremitters and relapsers had a significant overall improvement on the total functioning score. However, the improvements in these groups were not as strong, and given that all participants were actively receiving treatment, it is not unexpected that there would be some improvement in all participants' functioning.

Among remitters, there were significant improvements in functioning on individual items including social and leisure time, family relationships, work, and parenting functioning. Furthermore, only remitting mothers had significant improvements in parental functioning, including; ability to listen and talk to child, interest in child's activities, getting along with child, and feeling affection toward child. Improved parental functioning partially explained the effects of maternal remission on the reduction of anxiety scores in offspring, specifically, overall anxiety and social anxiety. Thus, as remitting parent's ability to function more optimally in the world improves, children may experience less anxiety and increased positive interactions. Improvements in being able to talk to and listen to children partially explained the improvements on measures of anxiety and also partially explained changes in scores of depression as a function of remission status. Mothers who go into remission may demonstrate improvements in their ability to communicate, as well as in their interactions with offspring, and overall functioning that partially explain improvements in child outcome.

I then wanted to determine whether changes in measures of parental bonding were associated with improved outcomes for children, since poor bonding has been associated with increased risk of psychopathology (Goodman & Gotlib, 2001). I found that over the

9- month study period, parents that went into remission had improved scores on measures of overprotection by both parent and child report. Overprotection is characterized by hostility, emotional over-involvement, and critical comments and has been shown to increase risk of psychopathology in offspring (Asarnow et al., 2001; McCleary & Sanford, 2002). Alleviation of parental symptoms of depression, such as irritability, could certainly explain improvements in overprotection.

Mother's scores of overprotection also helped to partially explain the effects of maternal remission status on measures of anxiety. Therefore, when remitting mothers' became less overprotective, there was a decrease in anxiety among the children. It is possible that reduction in parental depressive symptoms such as rumination, irritability, or even a reduction in comorbid anxiety may contribute to the improvements in the parent-child bond that reduce anxiety. A larger sample would be needed to explore these facets and a focus on individual symptom severity.

Remitting mothers had a marginally significant increase in measures of care, indicating increasing amounts of affection with children. These improvements were not seen in non-remitters or relapsers. Furthermore, mothers who relapsed demonstrated non-significant but increasing levels of affectionless control. Affectionless control, characterized by low parental warmth and high levels of control or discipline, has also been identified as a cluster of behaviors that puts children of depressed parents at increased risk for psychopathology (Fendrich et al., 1990; Sato et al., 1998; Weissman, Wickramaratne, et al., 2006). Relapse may be particularly difficult for parents and stressful for children, resulting in increased discord leading to increased affectionless control. Children who are exposed to remission then relapse could possibly react

negatively to the change which may increase conflict with parents. Furthermore, parents who relapse will have an increase in depressive symptoms that may preclude effective parenting and conflict resolution.

The fact that the measures of bonding did not predict children's depressive symptoms to the extent of the SAS-SR measures of parental functioning, may be due to the fact that the PBI was given at fewer time points than the SAS-SR and has been shown to be stable over time and not strongly affected by current symptoms (Murphy et al., 2010). Nonetheless, these findings are consistent with previous work showing that the association between reduction in parent's depressive symptoms and child's improved outcomes may be partially mediated by improvements in parenting behavior such as warmth and communication (e.g. Garber et al 2011).

Overall, it may be that changes in parent's overall functioning and their ability to communicate with children over the course of their depression treatment may be important for understanding outcome in offspring. Previous work has identified that parenting practices in depressed parents only account for a portion of the variance in childhood psychopathology (McLeod, Weisz, & Wood, 2007), but very little work is available to investigate time-sensitive changes occurring during parent's treatment and remission from depression. Therefore, this study offers valuable information regarding the types of changes occurring while parents are getting better, mainly improved ability to talk and listen to children and less overprotection. While it is recognized that parent-child conflicts common to parental depression are bidirectional in nature (Callender, Olson, Choe, & Sameroff, 2012; Goodman & Gotlib, 2001; Gross, Shaw, & Moilanen, 2008) it is important to note that children receiving mental health treatment during the

study did not explain any differences in outcome. Also, parental relapse was not associated with any improvements in childrens' outcomes or parent functioning, meaning that some exposure to remission was not enough to pass any benefits onto the child. This further illustrates that the parents' depressive illness is a key target and risk factor for offspring and even if children receive an intervention, it may not be as great a predictor of improvements as sustained parental remission from depression.

Although the findings herein offer valuable information there are some shortcomings to interpretations. First of all, our findings of current prevalence apply to children of treatment-seeking parents with moderate to severe MDD, and may not apply to other groups such as parents with mild depression or non-treatment-seeking community samples. Furthermore, I did not examine the prevalence of all child psychiatric disorders, although the choice of disorders examined was guided by the literature on children of depressed mothers. Also, given the structure of the KSADS, children were only asked about multiple psychiatric symptoms if they met the initial screening criteria. Such a method may not capture various subclinical symptoms or alternate presentation of disorders. There has been recent debate and growing dissatisfaction with a categorical diagnostic system for children, stating it would be better characterized as a spectrum (Angst, 2007; Akiskal & Benazzi, 2006; Hudziak et al., 2007; Tsuang, 2001). Future work integrating a spectrum method of measurement of disorders may capture psychopathology in these children more accurately and offer improved insight and improve our understanding of this population and the changes occurring in children as parents' receive treatment.

Interpretations regarding children of depressed fathers must be viewed cautiously since the number of children of depressed fathers was small ($N=19$) resulting in unstable estimates of outcomes in these children and in limited statistical power to examine differences in outcomes among children of depressed fathers and mothers. Additionally, I know that children who have two depressed parents are at an increased risk of psychopathology (Beardslee et al., 1998; Nomura, Warner, and Wickramaratne 2001). While I explored symptom count on the family history screen for spouses of depressed mothers compared to spouses of depressed fathers, I did not gain much additional information on spouses in the study. Given the limited participation of spouses in the sample and high number of single mothers, I was limited in our exploration of dual-parent morbidity and presence of any marital discord within the house. Since parents concordant for depressive disorders tend to have higher marital conflict (Keller et al., 2009) with poor ability to resolve their problems (Cummings, Keller, & Davies, 2005), it is possible that some of the variance in child outcome in our sample could be accounted for by co-parent mental health and quality of marriage. I also did not investigate whether children were exposed to prenatal or postpartum depression or whether there were significant psychosocial stressors, such as bullying, that may increase risk of psychopathology.

Finally, given that multiple analyses were conducted on the same sample, there is a potential for experimental-wise errors. While, this effect is likely limited by conducting pre-planned tests and independence of outcome measures, it was also controlled for by using multiplicity adjustments in means in pairwise comparison procedures. However, confidence intervals were not adjusted for and should be interpreted accordingly.

Conclusions

Overall, this research has shown that parental depression is associated with an increased risk of psychopathology, characterized by early onset and similar distribution across genders. Children of depressed parents in this sample had an increased risk of psychiatric disorders above and beyond previously identified demographic risk factors. I also found that while children of depressed mothers may fare worse than children of depressed fathers, both groups may have elevated rates of anxiety. The most important clinical implication of this work is that improvement in child outcome is associated with sustained parental remission. This supports the increasing number of studies showing the close relationship between successful treatment of maternal depression and relief of child's symptoms, whether treatment is medication or psychotherapy (Gunlicks & Weissman, 2008; Pilowsky, Wickramaratne, Talati, et al. 2008; Weissman, Pilowsky, Wickramaratne, et al. 2006; Birmaher, 2011; Coiro, Riley, Broitman, & Miranda, 2012; Garber, Ciesla, McCauley, Diamond, & Schloedt, 2011; Siegenthaler, Munder, & Egger, 2012). Thus, clinicians treating parents should not only work to maintain remission status but offer psychoeducation to patients that may motivate better treatment compliance. The improvements in overall functioning and parent-child interactions that occur when parents go into remission may be important to children's outcome.

This research further illustrates the importance of asking ill parents about their children's health and vice versa. Identification of mental illness is essential for treatment and may result in earlier interventions with children at risk. Improvements in parenting should be an area of focus for clinical interventions as it seems to play an important role in child outcome. Specifically, interventions that target improved communication

between parents and children may be important. More work is needed to further explore the changes occurring in parental remission that benefit children, the role of spouse mental health and marital relationships, and also the impact of depressed fathers on child outcome.

Table 1

Demographic Characteristics of Participants

<u>Child Characteristics (n=168)</u>		
Age X(SD)		11.65(3.35)
Ethnicity, N (%)	White	78(46%)
	Black	6(4%)
	Hispanic	68(40%)
	Other ^a	16(10%)
Living Status	Both Biological Parents	70(42%)
	Biological Mother / Step Father	18(11%)
	Biological Mother Only	60(36%)
	Other ^b	20(12%)
Gender	Female	78(46%)
	Male	90(54%)
Education	Grade 1-6	75(46%)
	Above 7th Grade	88(52%)
Remedial Classes ^c		41(24%)
<u>Index Parent Characteristics (n=93)</u>		
Age X(SD)		42.05(5.05)
Education	Some High School or Less	17(18%)
	High School Graduate	24(26%)
	Some College	21(23%)
	College Graduate +	31(33%)
Ethnicity	White	42(45%)
	Black	3(3%)
	Hispanic	40(43%)
	Other ^a	6(9%)
Marital status	Married with Spouse	43(46%)
	Single/Divorced/Separated	49(53%)
Employment	Employed Full-time/Part-time	53(58%)
	Full-time Student/Unemployed	25(27%)
	Other ^d	14(16%)
<u>Household Characteristics (n=93)</u>		
Public Assistance		30(32%)
Income	Under \$15K	28(30%)
	\$ 15-39K	14(15%)
	Over 40K	45(48%)
Children Per Family X(SD)		2.05(0.95)

Note.: Percentages may not sum up to 100 due to rounding or missing data. ^a4 American Indian children (1 parent), 1 parent unknown ethnicity, and rest more than one race. ^bIncludes any combination of biological, adopted, or stepparents ^cChildren enrolled in at least one remedial class due to learning difficulties. ^dFull-time or part-time disability benefits or qualified sick leave

Table 2

Current and Lifetime Prevalence Rates and Age of Onset for Children's Psychiatric Disorders (N=168)

Psychiatric Disorders n(%)	Current Diagnosis	Lifetime Diagnosis	Age of Onset	
			<12 years	≥12 years
Any Disorder	64(38%)	72(43%)	52(72%)	20(28%)
Affective				
Any	22(13%)	32(19%)	15(47%)	17(53%)
Adjustment Disorder with Depressed Mood	1(1%)	3(2%)	2(67%)	1(33%)
Depressive Disorder NOS	6(4%)	6(4%)	4(67%)	2(33%)
Dysthymia	2(1%)	2(1%)	2(100%)	...
Major Depressive Disorder	13(8%)	21(13%)	7(33%)	14(67%)
Anxiety				
Any	30(18%)	37(22%)	33(89%)	4(11%)
Agoraphobia	1(1%)	1(1%)	1(100%)	...
GAD	6(4%)	8(5%)	7(88%)	1(13%)
OCD	3(2%)	3(2%)	2(67%)	1(33%)
PTSD	1(1%)	5(3%)	3(60%)	2(40%)
Separation Anxiety	15(9%)	16(10%)	15(94%)	1(6%)
Simple Phobia	7(4%)	7(4%)	7(100%)	...
Social Phobia	5(3%)	6(4%)	6(100%)	...
Behavioral				
Any	36(21%)	41(24%)	36(88%)	5(12%)
ADHD (All subtypes)	30(18%)	32(19%)	32(100%)	...
Conduct Disorder	3(2%)	7(4%)	5(71%)	2(29%)
Oppositional Defiant Disorder	12(7%)	16(10%)	9(56%)	7(44%)
Substance Use/Abuse				
Any	3(2%)	5(3%)	...	5(100%)
Alcohol Abuse	...	1(1%)	...	1(100%)
Cannabis Abuse	...	2(1%)	...	2(100%)
Drug Dependence	3(2%)	3(2%)	...	3(100%)

Note. Number of Distinct Families in the study = 93 parents. Percentages may not sum up to 100 due to rounding or missing data.

Abbreviations: OR = odds ratio; ADHD = attention-deficit/hyperactivity disorder; PTSD = Post Traumatic Stress Disorder; OCD= Obsessive Compulsive Disorder; GAD=Generalized Anxiety Disorder; NOS = not otherwise specified.

Table 3

Current Prevalence Rates and Odd Ratios According to Gender for Children's Psychiatric Disorders (N=168)

Psychiatric Disorders	Current Diagnosis		Girls vs Boys		
	Girls (N=78)	Boys (N=90)	OR	95% CI	p
Any	26(33%)	38(42%)	0.67	[0.34,1.31]	0.24
Affective					
Any	12(15%)	10(11%)	1.51	[0.6,3.76]	0.38
Adjustment Disorder with Depressed Mood	1(1%)	...	...	...	
Depressive Disorder NOS	2(3%)	4(4%)	0.57	[0.1,3.24]	0.53
Dysthymia	1(1%)	1(1%)	...	...	
Major Depressive Disorder	8(10%)	5(6%)	2.01	[0.62,6.48]	0.24
Anxiety					
Any	14(18%)	16(18%)	1.04	[0.46,2.33]	0.93
Agoraphobia	1(1%)	...	...	...	
GAD	3(4%)	3(3%)	1.18	[0.23-6.08]	0.84
OCD	...	3(3%)	...	...	
PTSD	...	1(1%)	...	...	
Separation Anxiety	7(9%)	8(9%)	1.03	[0.35,3.02]	0.96
Simple Phobia	5(6%)	2(2%)	3.1	[0.58,16.58]	0.17
Social Phobia	3(4%)	2(2%)	...		
Behavioral					
Any	13(17%)	23(26%)	0.58	[0.26,1.26]	0.17
ADHD (all subtypes)	10(13%)	20(22%)	0.51	[0.22,1.19]	0.12
Conduct Disorder	...	3(3%)	...		
Oppositional Defiant Disorder	6(8%)	6(7%)	1.19	[0.36,3.9]	0.77
Substance Use/Abuse					
Any	1(1%)	2(2%)	0.58	[0.05,6.56]	0.66
Alcohol Abuse	...	...	...		
Cannabis Abuse	...	...	...		
Drug Dependence	...	2(2%)	...		

Note. Number of Distinct Families in the study = 93 parents. Percentages may not sum up to 100 due to rounding or missing data.

Abbreviations: OR = odds ratio; ADHD = attention-deficit/hyperactivity disorder; PTSD = Post Traumatic Stress Disorder; OCD= Obsessive Compulsive Disorder; GAD=Generalized Anxiety Disorder; NOS = not otherwise specified.

Table 4

Demographic Characteristics of Mothers (N=82), Fathers(N=11), and Children (N=168)

		Father	Mother	t / χ^2 ^a	p
<u>Index Parent</u>					
	Age X(SD)	43.8(4.6)	40.9(6.4)	1.45	0.15
Education	Some High School or Less	0(0%)	17(21%)	6.13	0.21
	High School Graduate	6(55%)	19(23%)		
	Some College	2(18%)	19(23%)		
	College Graduate and beyond	3(27%)	26(32%)		
Ethnicity	White	6(55%)	38(46%)	13.19	0.00
	Black	1(9%)	2(2%)		
	Hispanic	1(9%)	39(48%)		
	Other ^b	3(27%)	3(4%)		
Marital status	Married with Spouse	9(82%)	34(41%)	6.37	0.04
	Single/Divorced/Separated	2(18%)	47(57%)		
Employment	Full-time/Part-time	7(64%)	45(55%)	4.79	0.30
	Homemaker	0(0%)	4(5%)		
	Fulltime Student/Unemployed	1(9%)	24(29%)		
	Other	3(27%)	8(10%)		
<u>Household</u>		<u>N=11</u>	<u>N=82</u>		
	Public Assistance	0(0%)	30(37%)	6.54	0.03
Income	Under \$15K	1(9%)	27(33%)	4.24	0.27
	\$15-39K	2(18%)	12(15%)		
	Over \$40K	8(73%)	37(45%)		
	Children Per Family X(SD)	2.1(0.8)	1.8(1)	1.06	0.29
<u>Children</u>		<u>N=23</u>	<u>N=145</u>		
	Age M(SD)	12.1(3.1)	11.9(3.3)	0.25	0.80
Living Status	Both Biological Parents	17(74%)	53(37%)	28.93	<.0001
	Biological Mother and Step				
	Father	2(9%)	16(11%)		
	Biological Mother Only	0(0%)	60(41%)		
	Biological Father and Step				
	Mother	0(0%)	3(2%)		
	Biological Father Only	2(9%)	0(0%)		
	Other ^d	2(9%)	9(6%)		
Gender	Female	8(35%)	70(48%)	1.45	0.22
	Male	15(65%)	75(52%)		
Education	Grade 1-6	11(48%)	67(46%)	0.02	0.89
	Above 7th Grade	12(52%)	78(54%)		
	Remedial Classes n(%) ^e	2(9%)	39(27%)		

Note. Percentages may not sum up to 100 due to rounding or missing data. ^aFisher's Exact method was used to test for significance when appropriate ^b Includes 4 American Indian children, 1 mother of unknown ethnicity, and remainder more than one race. ^cIncludes receiving Full-time/part-time disability benefits, and qualified sick leave ^dAny combination of adoptive parents or other caretaker. ^eChildren enrolled in at least one remedial class due to learning difficulties.

Table 5

Prevalence of Current and Lifetime Childrens' Psychiatric Disorders according to Parental Gender in Children of Depressed Mothers (N=145) and Children of Depressed Fathers (N=23)^a

Psychiatric Disorders	Children's Current Diagnosis				Children's Lifetime Diagnosis			
	Mothers	Fathers	AOR	95% CI	Mothers	Fathers	AOR	95% CI
	N(%)	N(%)			N(%)	N(%)		
Affective	22(15%)	0(0%)	---		31(22%)	1(4%)	6.5 [†]	[0.8, 55.1]
Anxiety	27(19%)	3(12%)	2.5	[0.6,11.1]	34(24%)	3(12%)	3.3	[0.7,14.7]
Behavioral	33(23%)	3(12%)	3.5 [†]	[0.8,15.4]	38(27%)	3(12%)	4.4*	[1,19.3]
Substance	3(2%)	0(0%)	---		5(3%)	0(0%)	---	
Any Disorder	60(42%)	4(16%)	5.3**	[1.5,18.3]	67(47%)	5(20%)	4.9**	[1.6,15]

Note. Percentages may not sum up to 100 due to rounding or missing data.

^a 168 children of 93 index parents (82 mothers and 11 fathers);

Abbreviations: AOR = Adjusted Odds Ratio (Logistic regression models adjusted for child age, gender, and family correlation); CI= Confidence Interval

[†]P<.10; *p < .05; **p < .01

Table 6

Odds of having a Psychiatric Disorder among Children of Depressed Parents according to Living Arrangement^a

Living arrangement	Any Current child disorder			Any Lifetime Child disorder		
	AOR	95% CI	χ^2	AOR	95% CI	χ^2
Biological mother only vs. both biological parents (OR=1.0)	2.1	[1.4.4]	3.9*	3	[1.4.6.3]	8.21***
Biological mother only vs. any two-parent household (OR=1.0)	1.9	[1.3.8]	3.65*	2.7	[1.4.5.4]	8.02***
Single parent vs. both biological parents	2	[1.4.1]	3.38 [†]	2.8	[1.3.5.8]	7.27***
Single parent vs. any two-parent household	1.8	[0.9.3.6]	3.04 [†]	2.5	[1.3.4.9]	6.89***
Married mothers vs. married Fathers	6.4	[1.4.29.4]	5.77**	6.8	[1.5.31]	6.05**
Biological mother only vs. married mothers	1.5	[0.7.3]	1.12	2	[1.4.1]	3.5 [†]

Note. ^a Biological mother only (N=60), Both biological parents (N=70), Single parent (N=62; includes single mothers and single fathers), Any Two-parent household (N=91), Married Mothers (N=72), Married Fathers (N=19)

Abbreviations: AOR = Adjusted Odds Ratio (Logistic regression models adjusted for child age, gender, and family correlation); CI= Confidence Interval

[†] $p < .10$; * $p < .05$; ** $p < .01$; *** $p < .001$

Table 7

Demographic and Clinical Characteristics of Married Depressed Parents and their Children

		<u>Total</u> N(%)	<u>Fathers</u> N(%)	<u>Mothers</u> N(%)	Statistic
<u>Index Parent</u>		<u>(N = 43)</u>	<u>(N = 9)</u>	<u>(N = 34)</u>	
Age X(SD)		41.7 (6.8)	43.6 (4.6)	41.2 (7.3)	0.86
Education	Some High School or Less	5 (12%)	0 (0%)	5 (15%)	1.5
	High School Graduate or Higher	38 (88%)	9 (100%)	29 (85%)	
Ethnicity	White	24 (56%)	4 (44%)	20 (59%)	0.6
	African American/Hispanic/Other	19 (44%)	5 (56%)	14 (41%)	
Employment	Full-time/Part-time	32 (74%)	6 (67%)	26 (77%)	0.36
	Homemaker/Student/Unemployed/ Other	11 (26%)	3 (33%)	8 (24%)	
Clinical Characteristics					
	HAMD ₁₇ X(SD)	22 (4.9)	22.7 (4.1)	21.8 (5.1)	0.65
Severity ^a	Mild	4 (9%)	0 (0%)	4 (12%)	2.27
	Moderate	12 (28%)	4 (45%)	8 (24%)	
	Severe	27 (63%)	5 (56%)	22 (65%)	
Comorbidities	Any Anxiety Disorder	13 (30%)	3 (33%)	10 (29%)	.05
<u>Household</u>		<u>(N=43)</u>	<u>(N=9)</u>	<u>(N=34)</u>	
Public Assistance		6 (14%)	0 (0%)	6 (18%)	1.85
Income	Under \$15K	5 (12%)	1 (11%)	4 (12%)	0.65
	\$15-39K	6 (14%)	2 (22%)	4 (11.8)	
	Over \$40K	32 (74%)	6 (67%)	26 (77%)	
Children Per Family, X(SD)		1.8 (0.9)	2.1 (0.9)	1.7 (0.9)	1.31
<u>Children</u>		<u>(N = 78)</u>	<u>(N = 19)</u>	<u>(N = 59)</u>	
Age X(SD)		11.3 (3.3)	11.9 (3.2)	11.1 (3.3)	0.89
Gender	Female	41 (53%)	7 (37%)	34 (58%)	2.49
Education	Grade 1-6	42 (54%)	10 (53%)	32 (54%)	0.01
	Above 6th Grade	36 (46%)	9 (47%)	27 (46%)	
Ever received treatment		9 (12%)	1 (5%)	8 (14%)	0.97

Note: Percentages may not sum up to 100 due to rounding or missing data.

Abbreviations: HAMD-17 = Hamilton Depression Scale, 17 items; MDD = Major Depressive Disorder

^aSeverity defined as mild, = HAMD17<14, moderate = 14≤HAMD17≤21, severe = HAMD17≥22† $p < .10$; * $p < .05$; ** $p < .01$; *** $p < .001$

Table 8

Baseline Psychopathology and Global Functioning among Children of Married Depressed Mothers and Fathers^{a,b}

	<u>Children of Fathers</u>	<u>Children of Mothers</u>	
	n(%)	n(%)	Statistic ^d
Child's Current Diagnoses ^c			
Affective Disorders ^e	0(0%)	7(12%)	2.48
Anxiety Disorders	1(5%)	11(19%)	2.22
Behavioral Disorders ^f	1(5%)	13(22%)	4.22*
Substance Use Disorders ^e	0(0%)	1(2%)	0.33
Any Disorder	2(11%)	22(37%)	7.89**
<u>Number of K-SADS symptoms</u>	<u>X(SD)</u>	<u>X(SD)</u>	
Child report	0.2(0.5)	1.2(1.8)	-2.02*
(range)	(0-2)	(0-8)	
Parent report	0.6(1.2)	2(3)	-1.99*
(range)	(0-4)	(0-14)	
<u>Outcome Measures</u>			
C-GAS score	81.1(8.8)	76.7(12.6)	1.27
CDI score	5.6(4.8)	8.3(6.1)	-1.38
CIS score	6.5(4.2)	11.6(7.7)	-2.83**
CBCL Total Score	50.2 (14.5)	55.4 (10.9)	0.88
MASC scores			
Social Anxiety	9.5(7.9)	11.7(5.2)	-1.02
Separation/Panic	7.2(5.2)	8.8(4.7)	-0.43
Physical Symptoms	8.2(6.4)	8.5(6.1)	0.18
Total	44.1(17)	46.7(13.8)	0.30

Note. ^a Nine fathers and their 19 children; 34 mothers and their 59 children

^b Unless otherwise noted models were adjusted for child age and gender, and within family correlation ^c Based on child and mother interview using the K-SADS-PL ^d Chi-square or Fisher's exact test for percent comparisons and t statistic for comparisons of means ^e Models did not converge due to low cell counts and they were not adjusted for covariates. ^f Includes ADHD, oppositional-defiant disorder, and conduct disorder

* $p < .10$; * $p < .05$; ** $p < .01$; *** $p < .001$ Note.

Table 9.

Baseline General Mental Health and Depressive Symptoms among Spouses of Index Parents

Symptoms by Group	N	M	T	<i>p</i>
General Mental health Symptoms ^a				
Wives of Index Fathers	9	1.0	-3.54	0.01
Index Mothers	34	2.5		
Wives of Index Fathers	9	1.0	-3.04	0.01
Husbands of Index Mothers	34	2.3		
Symptoms of Depression ^b				
Wives of Index Fathers	9	1.33	-3.08	0.013
Index Mothers	34	2.82		
Wives of Index Fathers	9	1.33	-2.68	0.05
Husbands of Index Mothers	34	1.84		

Note. Data obtained from the Family History Screen (FHS).^a General mental health: FHS items 1-4.^b Depressive symptoms: FHS item 5-7.

Table 10

Demographic Characteristics of Mothers and Children by Study Site.

		Ottawa N (%)	New York N (%)	Statistic ^a
Mothers		(n = 41)	(n = 41)	
	Age, M (SD)	40.8(5.7)	41(7.0)	-0.12
Education	Some High School or Less	2(4.9%)	15(36.6%)	15.15**
	High School Graduate	9(22.0%)	10(24.4%)	
	Some College	12(29.3%)	7(17.1%)	
	College Graduate +	18(43.9%)	8(19.5%)	
Ethnicity	White	37(90.2%)	1(2.4%)	69.54**
	Black	1(2.4%)	1(2.4%)	
	Hispanic	1(2.4%)	38(92.7%)	
	Other ^b	2(4.9%)	1(2.4%)	
Marital status	Married with Spouse	23(56.1%)	11(26.8%)	6.8**
	Single/Divorced/Separated	18(43.9%)	29(70.7%)	
Employment	Employed Full-time/Part-time	30(73.2%)	15(36.6%)	18.66**
	Homemaker	1(2.4%)	3(7.3%)	
	Fulltime Student/Unemployed	4(9.8%)	20(48.8%)	
	Other	6(14.6%)	2(4.9%)	
Clinical	HAMD ₁₇ , mean(SD)	21.9(4.3)	22(4.4)	-0.1
	Chronic MDE, n (%) ^c	19(46.3%)	18(43.9%)	0.01
Type of Depression	Atypical	10(24.4%)	7(17.1%)	0.67
	Melancholic	12(29.3%)	4(9.8%)	4.97*
Severity ^d	Mild	2(4.9%)	2(4.9%)	0.02
	Moderate	14(34.1%)	13(31.7%)	
	Severe	25(61%)	25(61%)	
Comorbidity	Any Anxiety Disorder, n (%)	6(14.6%)	23(56.1%)	15.42**
Household		(n = 41)	(n = 41)	
	Public Assistance	5(12.2%)	25(61.0%)	22.98**
Income	Under \$15K	3(7.3%)	26(63.4%)	42.28**
	\$15-39K	4(9.8%)	8(19.5%)	
	Over \$40K	33(80.5%)	4(9.8%)	
	Children Per Family. M (SD)	1.9(0.9)	1.7(1.1)	0.8
Children		N=76	N=69	
	Age, M (SD)	11.5(3.4)	12.4(3.3)	-1.55
Living Status	Two Parent Household ^e	55(72.4%)	23(33.3%)	22.17**
	Mother Only	21(27.6%)	46(66.7%)	
Gender	Female	36(47.4%)	34(49.3%)	0.05
Education	Grade 1-6	38(50.0%)	29(42.0%)	0.92
	Above 6th Grade	38(50.0%)	40(58.0%)	

Note. Numbers vary due to missing data. HAMD₁₇ = Hamilton Rating Score for Depression 17-item; MDD = Major Depressive Disorder; MDE = Major Depressive Episode ^at statistic for age comparisons, and chi-square statistic or Fisher's exact test for all other comparisons. ^bIncludes 1 American Indian, 1 than 1 race, and 1 unknown. ^cDuration of current major depressive episode ≥ 2 years. ^dSeverity defined as mild: HAMD₁₇ < 14, moderate: 14 ≤ HAMD₁₇ ≤ 21, severe: HAMD₁₇ ≥ 22. ^eIncludes any combination of biological, adopted, or step-mother and -father. †p < 0.1; *p < .05; **p < .01.

Table 11

Current and Lifetime Psychiatric Disorders in Children of Depressed Mothers According to Study Sites in New York (N=72) and Ottawa (N=96)

	New York	Ottawa		
Psychiatric Disorders	N(%)	N(%)	AOR ²	95% CI
Current Diagnosis				
Affective	13(18%)	9(9%)	1.9	[0.8,4.8]
Anxiety	17(24%)	13(14%)	2.1 [†]	[0.9,4.7]
Behavioral	19(26%)	17(18%)	1.7	[0.8,3.6]
Substance	1(1%)	2(2%)	0.5	[0,5.7]
Any	34(47%)	30(31%)	2*	[1.3,0.7]
Lifetime Diagnosis				
Affective	18(25%)	14(15%)	1.8	[0.8,3.9]
Anxiety	20(28%)	17(18%)	1.8	[0.9,3.8]
Behavioral	23(32%)	18(19%)	2.1*	[1,4.2]
Substance	1(1%)	4(4%)	0.2	[0,2.5]
Any	39(54%)	33(34%)	2.3**	[1.2,4.3]

Note. Numbers vary due to missing values

Abbreviations: NY=New York City site; OT=Ottawa-Gatineau site

¹ 168 children of 93 index parents

² Adjusted Odds Ratio (Logistic regression models adjusted for child age, gender, and family correlation)

†p < 0.1; *p < .05; **p < .01.

Table 12

Multivariate Analysis of Maternal Depression Characteristics Associated with Lifetime Child Psychiatric Disorders

Child Psychiatric Disorder	Maternal Predictors	AOR	95% CI	χ^2
Affective disorder	Income over \$40K vs. under \$15K	0.9	[0.8,1]	3.56
	Panic disorder with agoraphobia	1.1	[0.8,1.5]	0.50
Anxiety disorder	Melancholic depression	1.2	[1.1,1.5]	7.44**
	Any anxiety disorder (maternal)	1.3	[1.1,1.5]	12.46**
Behavioral disorder	Severe vs. mild/moderate MDD	1.2	[1,1.3]	5.30*
Any disorder	Any anxiety disorder (maternal)	1.2	[1,1.5]	5.04*

Note. Each of the six models shown is from a multivariate logistic regression with child psychiatric disorder category as the binary dependent variable, one or more maternal characteristics (which had been found to be significant predictors in univariate analyses) entered as simultaneous predictors, child age and gender entered as control variables, and an adjustment made for intrafamily correlation.

*p < .05; **p < .01.

Table 13

Adjusted Odds^a and Proportion of Children with Current Psychiatric Disorders, by Current Maternal Depression Characteristics and Selected Demographics^b

Maternal Characteristics	Affective			Anxiety			Behavioral			Any Disorder		
	n(%)	OR	95% CI	n(%)	OR	95% CI	n(%)	OR	95% CI	n(%)	OR	95% CI
Atypical Depression (n = 33)	6(18)	1.4	[0.5,4.2]	5(15)	0.8	[0.3,2.4]	6(18)	0.8	[0.3,2.1]	13(39)	1.1	[0.5,2.4]
None (n = 112)	16(14)			23(21)			28(25)			48(43)		
Melancholic Depression(n = 33)	8(24)	2.9*	[1,8.3]	11(33)	2.6 *	[1.1,6.3]	10(30)	1.5	[0.6,3.5]	18(55)	1.9	[0.8,4.4]
None (n = 112)	14(13)			17(15)			24(21)			43(38)		
Chronicity of Current MDE												
<2 Years (n = 80)	12(15)			17(21)			18(23)			33(41)		
≥2 Years (n = 64)	10(16)	0.9	[0.3,2.4]	10(16)	0.7	[0.3,1.7]	15(23)	1.1	[0.5,2.4]	27(42)	1	[0.5,2.1]
Mild/Moderate MDD (n= 55)	6(11)			10(18)			8(15)			20(36)		
Severe MDD (n = 86)	16(19)	2	[0.7,5.7]	18(21)	1.2	[0.5,2.8]	26(30)	2.6 *	[1.1,6.2]	41(48)	1.6	[0.8,3.3]
Comorbid Conditions ^d												
Anxiety Disorder (n = 49)	8(16)	1.3	[0.5,3.5]	16(33)	3.9 **	[1.6,9.4]	14(29)	1.7	[0.8,3.8]	27(55)	2.7**	[1.3,5.7]
No (n = 96)	14(15)			12(13)			20(21)			34(35)		
PTSD(n = 12)	2(17)	1.3	[0.2,7]	6(50)	5.7 **	[1.6,20.3]	5(42)	2.2	[0.6,7.6]	8(67)	2.7	[0.7,-9.6]
No (n = 133)	20(15)			22(17)			29(22)			53(40)		
Panic Disorder with Agoraphobia(n = 12)	5(42)	4.2*	[1.1,16.8]	4(33)	2.5	[0.7,9.1]	5(42)	2.5	[0.7,8.8]	8(67)	2.7	[0.8,9.3]
No (n = 133)	17(13)			24(18)			29(22)			53(40)		
Social Phobia (n = 12)	2(17)	1.2	[0.2,5.9]	5(42)	3.2	[0.9,11.5]	5(42)	2.4	[0.7,8.3]	6(50)	1.4	[0.4,4.4]
No (n = 133)	20(15)			23(17)			29(22)			55(41)		
Household Characteristics												
Income Under 15K	11(24)	1		9(20)	1		11(24)	1		23(51)	1	
\$15-39K	4(15)	0.8	[0.2,2.7]	8(30)	1.6	[0.5,4.8]	8(30)	1.1	[0.4,3.4]	13(48)	0.9	[0.3,2.4]
Over \$40K	5(8)	0.3*	[0.1,0.9]	9(14)	0.6	[0.2,1.7]	13(20)	0.7	[0.3,1.9]	21(32)	0.5	[0.2,1.1]
Single Mother (n = 67)	11(16)	1.1	[0.4,2.7]	11(16)	0.8	[0.3,2]	19(28)	1.8	[0.8,4.2]	30(45)	1.3	[0.7,2.6]
No (n = 78)	11(14)			17(22)			15(19)			31(40)		

Note. MDE = Major Depressive Episode. MDD = Major Depressive Disorder. PTSD = Post-traumatic Stress Disorder. ^aAdjusted for children's gender and age, as well as family correlation. The comparison group (OR=1.0) is all mothers without the specified characteristic/illness. ^bNs vary due to missing data. ^cSeverity defined as mild/moderate: HAM-D17≤21, severe: HAM-D17≥22. ^dAssessed using the SCID-IV **p* < .05; ***p* < .01.; *** *p* < .001

Table 14

Current Prevalence Rates and Odd Ratios According to Gender for Children's Psychiatric Disorders in Children of Depressed Mothers (N=145)

	Current Diagnosis, N(%)				Lifetime Diagnosis, N(%)			
	All	Girls (N=70)	Boys (N=75)	OR ^{b,d}	All	Girls (N=70)	Boys (N=75)	OR ^{b,d}
Any Affective Disorder ^c	22(15)	12(17)	10(13)	1.3(0.5,3.3)	31(21)	16(23)	15(20)	1.2(0.5,2.6)
Adjustment Disorder with Depressed Mood	1(1)	1(1)	0(0)	...	2(1)	2(3)	0(0)	...
Depressive Disorder NOS	6(4)	2(3)	4(5)	0.6(0.1,3.2)	6(4)	2(3)	4(5)	0.6(0.1,3.2)
Dysthymia	2(1)	1(1)	1(1)	1.2(0.1,19.2)	2(1)	1(1)	1(1)	1.2(0.1,19.2)
Major Depressive Disorder	13(9)	8(11)	5(7)	2(0.6,6.5)	21(14)	11(16)	10(13)	1.4(0.5,3.4)
Any Anxiety Disorder ^c	28(19)	14(20)	14(19)	1.1(0.5,2.5)	35(24)	18(26)	17(23)	1.2(0.6,2.5)
Agoraphobia	1(1)	1(1)	0(0)	...	1(1)	1(1)	0(0)	...
Generalized Anxiety Disorder	6(4)	3(4)	3(4)	1.2(0.2,6.1)	8(6)	4(6)	4(5)	1.2(0.3,5)
Obsessive Compulsive Disorder	2(1)	0(0)	2(3)	...	2(1)	0(0)	2(3)	...
Post Traumatic Stress Disorder	1(1)	0(0)	1(1)	...	5(3)	3(4)	2(3)	1.8(0.3,11.1)
Separation Anxiety	14(10)	7(10)	7(9)	1.2(0.4,3.6)	15(10)	7(10)	8(11)	1(0.4,3)
Simple Phobia	7(5)	5(7)	2(3)	3.1(0.6,16.6)	7(5)	5(7)	2(3)	3.1(0.6,16.6)
Social Phobia	5(3)	3(4)	2(3)	1.8(0.3,11.1)	6(4)	4(6)	2(3)	2.4(0.4,13.8)
Any Behavioral Disorder ^c	34(23)	13(19)	21(28)	0.6(0.3,1.3)	39(27)	14(20)	25(33)	0.5(0.2,1.1)*
ADHD (all subtypes)	29(20)	10(14)	19(25)	0.5(0.2,1.3)	31(21)	10(14)	21(28)	0.5(0.2,1.1)*
Conduct Disorder	3(2)	0(0)	3(4)	...	6(4)	1(1)	5(7)	0.2(0,2)
Oppositional Defiant Disorder	11(8)	6(9)	5(7)	1.5(0.4,5)	15(10)	6(9)	9(12)	0.8(0.3,2.3)
Any Substance Use Disorder ^c	3(2)	1(1)	2(3)	0.5(0,6)	5(3)	1(1)	4(5)	0.3(0,2.4)
Alcohol Abuse	0(0)	0(0)	0(0)	...	1(1)	0(0)	1(1)	...
Cannabis Abuse	0(0)	0(0)	0(0)	...	2(1)	0(0)	2(3)	...
Cannabis Dependence	2(1)	0(0)	2(3)	...	2(1)	0(0)	2(3)	...
Other Drug Dependence	1(1)	1(1)	0(0)	...	1(1)	1(1)	0(0)	...
Any Disorder ^c	61(42)	26(37)	35(47)	0.7(0.3,1.3)	68(47)	28(40)	40(53)	0.6(0.3,1.1)

Note: Number of Distinct Families in the table = 82 mothers

^a Ns may vary due to missing values.

^b Odds of receiving a specified diagnosis for male compared with female children (OR=1.0).

^c Model adjusted for family correlation

^d OR p-values: *p<0.1

Abbreviations: ADHD = attention-deficit/hyperactivity disorder, NOS = not otherwise specified, OR = odds ratio

Table 15

Change in Mean scores and Time Trend Changes on Child Outcome Measures over 9 months in Children of Married Depressed Mothers (N = 59) Compared to Children of Married Depressed Fathers (N=19)^{abc}

Measure	Fathers			Mothers			Group x Time
	Δ	β	p	Δ	β	p	p
KSADS							
Diagnosis	-2	--	--	-11	--	--	--
Symptoms- Child report	-0.06	0.013	0.74	-0.28	-0.012	0.08	0.57
Symptoms- Parent report	-0.4	-0.06	0.42	-0.91	-0.02	0	0.54
CGAS	4.44	0.077	0.38	1.48	0.002	0.96	0.45
CDI	2.48	0.032	0.42	-3.3	-0.065	0	0.03
CIS	-0.2	-0.017	0.68	-2.97	-0.066	0	0.31
MASC							
Social Anxiety	-3.44	-0.105	0.02	-4.44	-0.077	0	0.6
Separation/Panic	-3.43	-0.035	0.28	-1.99	-0.041	0.01	0.87
Physical Symptoms	-2.43	-0.074	0.08	-1.86	-0.045	0.03	0.52
Total	-13.96	-0.272	0.01	-8.58	-0.198	0	0.53

^a All models were controlled for child age, gender, site, and within family correlation

^b Difference between baseline score and final score.

^c Nine fathers and their 19 children; 34 mothers and their 59 children

^d Based on child and mother interview using the K-SADS-PL

^e Models did not converge. Thus, betas and group by time interactions could not be estimated

Table 16

Parental Bonding Scores among Children of Married Depressed Mothers and Fathers

	Child about Father	Child about Mother	statistic ^a
PBI scores			
Affectionless Control, n(%) ^b	2(11)	13(22)	1.27
Care X(SD)	27.2(5.1)	29(4.7)	-0.87
Overprotection X(SD)	12.1(6.3)	15.7(6.5)	-1.69

Nine fathers and their 19 children; 34 mothers and their 59 children

Models were adjusted for child age and gender, and within family correlation

^a Fisher's exact test for percent comparisons and t statistic for comparisons of means

^b Affectionless control defined as Low care score (below 27) and high score on overprotection (above 13.5)

* $p < .05$, ** $p < .001$.

Table 17

Change in Mean scores and Time Trend Changes on Child Outcome Measures over 9 months in Children of Responding Married Depressed Mothers (N = 45) Compared to Children of Responding Married Depressed Fathers (N=12)^{abc}

Measure	<u>Fathers</u>			<u>Mothers</u>			<u>Group x Time</u>
	Δ	β	p	Δ	β	p	p
KSADS							
Diagnosis	--	--	--	-5	--	--	--
Symptoms- Child report	0.35	0.076	0.04	-0.34	-0.013	0.06	0.16
Symptoms- Parent report	0.12	0.041	0.53	-0.91	-0.019	0	0.51
CGAS	2.14	0.068	0.56	1.31	0.006	0.91	0.63
CDI	0.94	0.003	0.94	-3.8	-0.083	<0.001	0.08
CIS	-0.58	-0.028	0.56	-3.49	-0.085	<0.001	0.29
MASC							
Social Anxiety	-5.49	-0.126	0.04	-3.78	-0.087	0	0.54
Separation/ Panic	-4.99	-0.061	0.12	-1.74	-0.034	0.06	0.53
Physical Symptoms	-4.89	-0.135	0.02	-2.14	-0.053	0.03	0.17
Total	-21.03	-0.422	0.01	-8.77	-0.208	<0.001	0.13

^a All models were controlled for child age, gender, site, and within family correlation

^b Difference between baseline score and final score.

^c 7 responding fathers and their 12 children; 26 responding mothers and their 45 children

^d Based on child and mother interview using the K-SADS-PL

^e Models did not converge. Thus, betas and group by time interactions could not be estimated

Table 18

Characteristics of Mothers and Children by Completion Status

		Completed study	Dropped out	Statistic ^a
		N(%)	N(%)	
<u>Mother Characteristic</u>		<u>(n = 76)</u>	<u>(n = 9)</u>	
Age, X (SD)		41 (6.4)	37.6 (5)	2.44
Education	Some High School or Less	15 (22.4)	0 (0)	5.2
	High School Graduate	14 (20.9)	4 (44.4)	
	Some College	18 (26.9)	1 (11.1)	
	College Graduate +	20 (29.9)	4 (44.4)	
Ethnicity	White	32 (47.8)	5 (55.6)	0.71
	Hispanic	31 (46.3)	3 (33.3)	
	Other ^b	4 (6)	1 (11.1)	
Marital status	Married with Spouse	28 (41.8)	5 (55.6)	0.61
	Single/Divorced/Separated	39 (58.2)	4 (44.4)	
Employment	Full-time/Part-time	35 (52.2)	7 (77.8)	5.76
	Homemaker	3 (4.5)	0 (0)	
	Fulltime Student/Unemployed	23 (34.3)	0 (0)	
	Other	6 (9)	2 (22.2)	
	HAMD ₁₇ , X (SD)	21.8 (4.5)	21.7 (3.9)	0.01
Clinical Characteristics	MDD Severity			
	Mild	3 (4.5)	1 (11.1)	0.71
	Moderate	23 (34.3)	3 (33.3)	
	Severe	41 (61.2)	5 (55.6)	
Comorbidity	Any Anxiety Disorder, n (%)	23 (34.3)	4 (44.4)	0.35
<u>Household</u>		<u>(n = 76)</u>	<u>(n = 9)</u>	
Public Assistance		27 (40.3)	1 (11.1)	3.01
Income	Under \$15K	24 (35.8)	2 (22.2)	3.13
	\$15-39K	12 (17.9)	0 (0)	
	Over \$40K	29 (43.3)	6 (66.7)	
Children Per Family, X (SD)		1.8 (0.9)	1.6 (1)	0.55
<u>Child</u>		<u>(n = 121)</u>	<u>(n = 14)</u>	
Age, X (SD)		11.9 (3.4)	11.6(2.9)	0.05
Living Status	Two Parent Household ^d	66 (54.5)	11 (78.6)	2.96
	Mother Only	55 (45.5)	3 (21.4)	
Gender	Female, n (%)	54 (44.6)	8 (57.1)	0.79
Education	Grade 1-6	57 (47.1)	7 (50)	0.04
	Above 6th Grade	64 (52.9)	7 (50)	
Ever received treatment		31 (25.6)	3 (21.4)	0.12

Note. Numbers vary due to missing data. HAMD17 = Hamilton Rating Score for Depression 17-item;

^at statistic for age comparisons, and chi-square statistic or Fisher's exact test for all other comparisons.

^bIncludes 2 African Americans, 1 American Indian, 1 identified as more than 1 race, and 1 unknown

^cSeverity defined as mild: HAMD17<14, moderate: 14≤HAMD17≤21, severe: HAMD17≥22

^dIncludes any combination of biological, adopted, or step mother and father* p<0.05, ** p<0.01

Table 19

Characteristics of Mothers and Children by Mother's 9 Month Remission Status

		9 Month Remission Status				Statistic ^a
Characteristic		Total N (%)	Remitter N (%)	Relapser N (%)	Non-remitter N (%)	
<u>Mother</u>		<u>(n = 76)</u>	<u>(n = 43)</u>	<u>(n = 12)</u>	<u>(n = 21)</u>	
Age, X(SD)		40.6 (6.4)	40.2 (7)	42.5 (5.6)	40.4 (5.5)	0.62
Education	Some High School or Less	15 (19.7)	7 (16.3)	5 (41.7)	3 (14.3)	8.26
	High School Graduate	18 (23.7)	14 (32.6)	1 (8.3)	3 (14.3)	
	Some College	19 (25)	10 (23.3)	3 (25)	6 (28.6)	
	College Graduate +	24 (31.6)	12 (27.9)	3 (25)	9 (42.9)	
Ethnicity ^b	White					0.38
	Other ^c	37 (48.7)	16 (37.2)	6 (50)	15 (71.4)	
Marital status	Married with Spouse	39 (51.3)	27 (62.8)	6 (50)	6 (28.6)	0.46
	Single/Divorced/Separated	33 (43.4)	19 (44.2)	6 (50)	8 (38.1)	
Employment	Employed Full/Part time	43 (56.6)	24 (55.8)	6 (50)	13 (61.9)	3.76
	Homemaker	42 (55.3)	23 (53.5)	6 (50)	13 (61.9)	
	Student/Unemployed	3 (3.9)	3 (7)	0 (0)	0 (0)	
	Other	23 (30.3)	13 (30.2)	5 (41.7)	5 (23.8)	
Clinical Characteristics	HAMD ₁₇ , X (SD)	8 (10.5)	4 (9.3)	1 (8.3)	3 (14.3)	0.74
	MDD Severity (current) ^d	21.8 (4.4)	21.8 (4.6)	23 (4.4)	21 (4.1)	
	Mild	4 (5.3)	3 (7)	0 (0)	1 (4.8)	
	Moderate	26 (34.2)	12 (27.9)	4 (33.3)	10 (47.6)	
Comorbidity	Severe	46 (60.5)	28 (65.1)	8 (66.7)	10 (47.6)	4.82
	Any Anxiety Disorder ^b	27 (35.5)	20 (46.5)	1 (8.3)	6 (28.6)	
<u>Household</u>		<u>(n = 76)</u>	<u>(n = 43)</u>	<u>(n = 12)</u>	<u>(n = 21)</u>	
Public Assistance		28 (36.8)	17 (39.5)	6 (50)	5 (23.8)	3.12
Income	Under \$15K	26 (34.2)	17 (39.5)	4 (33.3)	5 (23.8)	2.53
	\$15-39K	12 (15.8)	6 (14)	3 (25)	3 (14.3)	
	Over \$40K	35 (46.1)	18 (41.9)	5 (41.7)	12 (57.1)	
Children Per Family, X (SD)		1.8 (0.9)	1.8 (1)	2 (1)	1.6 (0.7)	0.62
<u>Child</u>		<u>(n = 135)</u>	<u>(n = 77)</u>	<u>(n = 24)</u>	<u>(n = 34)</u>	
Age, X(SD)		11.8 (3.3)	11.8(3.3)	11.7(3.6)	12(3.3)	0.09
Living Status	Two Parent Household ^e	77 (57)	44 (57.1)	12 (50)	21 (61.8)	0.8
	Mother Only	58 (43)	33 (42.9)	12 (50)	13 (38.2)	
Gender	Female	62 (45.9)	37 (48.1)	10 (41.7)	15 (44.1)	0.36
Education	Grade 1-6	64 (47.4)	38 (49.4)	10 (41.7)	16 (47.1)	0.44
	Above 6th Grade	71 (52.6)	39 (50.6)	14 (58.3)	18 (52.9)	
Ever received treatment		34 (25.2)	17 (22.1)	4 (16.7)	13 (38.2)	4.39

Note. Numbers vary due to missing data. HAMD₁₇ = Hamilton Rating Score for Depression 17-item; MDE = Major Depressive Episode; MDD = Major Depressive Disorder. ^at statistic for age comparisons, and chi-square statistic or Fisher's exact test for all other comparisons.

^bCochran-Mantel Haenszel test statistic reported after adjusting for site ^cIncludes 34 Hispanic, 2 African Americans, 1 American Indian, 1 parent who identified as more than 1 race, and 1 unknown ^dSeverity defined as mild: HAMD₁₇<14, moderate: 14≤HAMD₁₇≤21, severe: HAMD₁₇≥22

^eIncludes any combination of biological, adopted, or step mother and father * p<0.05, ** p<0.01

Table 20

Change in Mean scores and Time Trend Changes on Child Outcome Measures by Maternal Remission^a Status Over 9 Months Adjusted for Child Age, Gender, Site, and Within Family Correlation.

Measure	<u>Remitters</u>			<u>Relapsers</u>			<u>Nonremitters</u>			Group x <u>Time</u>
	Δ^b	β	p	Δ	β	p	Δ	β	p	p
KSADS										0.83
Diagnosis ^c	-20.8	-0.017	0.08	-4.1	-0.006	0.68	-12.2	-0.013	0.18	0.29
Symptoms- Child report	-0.57	-0.011	0.05	0.75	0.007	0.27	-0.01	-0.002	0.90	0.31
Symptoms- Parent report	-1.39	-0.02	<.00	-0.04	-0.006	0.40	-0.17	-0.007	0.50	0.04
CGAS	3.92	0.096	0.01	-3.66	-0.085	0.17	0.9	0.033	0.57	0.04
CDI	-4.71	-0.097	<.00	-0.97	-0.046	0.11	-0.66	-0.019	0.49	0.04
CIS	-3.86	-0.087	0.00	-0.07	-0.017	0.66	-0.78	-0.016	0.67	0.13
MASC										
Social Anxiety Separation/ Panic	-4.35	-0.102	<.00	-2.01	-0.039	0.17	-1.65	-0.034	0.19	0.04
Physical Symptoms	-2.42	-0.055	<.00	-0.53	-0.005	0.81	-0.74	-0.024	0.25	0.11
Total	-2.88	-0.059	0.00	0.1	-0.011	0.73	-0.52	-0.005	0.86	0.17
	-11.87	-0.262	<.00	-4.53	-0.11	0.12	-4.73	-0.097	0.15	0.05
Pairwise Comparison	<u>Remitters vs Nonremitters</u>			<u>Relapsers vs Non-remitters</u>			<u>Remitters vs Relapsers</u>			
	β	p		β	p		β	p		
CGAS	0.063	0.35		-0.118	0.16		0.181	0.01		
CDI	-0.079	0.01		-0.027	0.49		-0.052	0.12		
MASC										
Social Anxiety	-0.067	0.03		-0.005	0.91		-0.062	0.06		
Total	-0.164	0.03		-0.013	0.89		-0.151	0.06		

^a N = 77 children of 43 remitters, 24 children of 12 relapsers, 34 children of 21 non-remitters.

^b Difference between baseline score and final score.

^c Rates of diagnosis are displayed since diagnosis is a dichotomous outcome.

Relapsers are included as their own group in this scenario. Sig differences exist for CGAS, CDI, MASC-social, and MASC-total. 43 remitters, 12 relapsers, 21 non-remitters

Table 21

Measures of Functioning on the SAS-SR by Maternal Remission Status over 9 Months^{a,b}

Outcome ^c	N	Baseline	Time Trend		Change over time
			β	p	
SAS-SR Total					
Remitters	43	2.73	-0.029	<.0001	-1
Relapsers	12	2.86	-0.009	0.0278	-0.32
Non-remitters	20	2.75	-0.01	0.0367	-0.36
Group-by-time		F=12.13	df=2, 266	<.0001	
SAS-SR Work					
Remitters	19	2.32	-0.026	0.0002	-0.94
Relapsers	5	3.03	0.033	0.0298	1.19
Non-remitters	11	3.38	-0.011	0.535	-0.4
Group-by-time		F=6.43	df=2, 107	0.0023	
SAS-SR Family					
Remitters	41	2.98	-0.039	<.0001	-1.4
Relapsers	10	2.92	-0.017	0.0274	-0.61
Non-remitters	17	2.88	-0.014	0.0955	-0.5
Group-by-time		F=6.33	df=2, 235	0.0021	
SAS-SR Social and Leisure					
Remitters	43	3.22	-0.036	<.0001	-1.3
Relapsers	12	3.27	-0.014	0.0229	-0.5
Non-remitters	20	3.27	-0.012	0.0907	-0.43
Group-by-time		F=8.1	df=2, 266	0.0004	
SAS-SR Finance					
Remitters	42	2.71	-0.025	<.0001	-0.9
Relapsers	10	2.4	-0.006	0.5764	-0.22
Non-remitters	20	2.25	0.005	0.6521	0.18
Group-by-time		F=3.59	df=2, 258	0.0289	
SAS-SR Parental Functioning					
Remitters	35	2.3	-0.022	<.0001	-0.79
Relapsers	8	2	0.001	0.8379	0.04
Non-remitters	17	2.04	-0.002	0.8023	-0.07
Group-by-time		F=8.09	df=2, 218	0.0004	
SAS-SR Parental Functioning Item #1 Interest in child's activities					
Remitters	35	2.31	-0.024	<.0001	-0.86
Relapsers	8	2.38	-0.006	0.509	-0.22
Non-remitters	17	2.12	0	0.9714	0
Group-by-time		F=3.1	df=2, 215	0.0468	

Table 21 Continued

SAS-SR Parental Functioning Item #2 Able to talk to and listen to child					
Remitters	35	2.51	-0.034	<.0001	-1.22
Relapsers	8	2.25	-0.003	0.6769	-0.11
Non-remitters	17	1.94	-0.008	0.3927	-0.29
Group-by-time		F=7.63	df=2, 215	0.0006	
SAS-SR Parental Functioning Item #3 Getting along with child					
Remitters	34	2.56	-0.018	0.0002	-0.65
Relapsers	8	1.88	0.013	0.1248	0.47
Non-remitters	17	2.53	-0.006	0.5271	-0.22
Group-by-time		F=5.25	df=2, 215	0.006	
SAS-SR Parental Functioning Item #4 Feeling affection towards child					
Remitters	34	1.88	-0.014	0.0003	-0.5
Relapsers	8	1.5	0.002	0.7325	0.07
Non-remitters	17	1.59	0.005	0.5289	0.18
Group-by-time		F=3.9	df=2, 217	0.0217	

^aModels involving SAS-SR were adjusted for site. A negative beta over time suggests improvement. ^bN= 43 remitters, 12 relapsers, 21 non-remitters

^cThere was a trend or statistically significant decrease over time in all outcomes among remitting mothers.

Table 22

Child and Parental Reports of Parental Bonding on the PBI over 9 months According to Parental Remission Status over 9 Months^{a,b}

	N	Baseline	Child Report β	Δ^c	Baseline	Mother Report β	Δ
Care							
Remitters	68	28.12	0.003	0.11	28.29	0.038	1.37
Relapsers	24	28.2	0.014	0.5	28.3	-0.021	-0.76
Non-remitters	34	28.5	0.006	0.22	29.15	-0.018	-0.65
Group-by-time	F=0.04, df=2, 105, p = 0.96				Group-by-time F=1.68, df=2, 103, p = 0.19		
Overprotection							
Remitters	66	15.18	-0.055**	-1.98	15.89***	-0.092	-3.31
Relapsers	23	15.17	-0.017	-0.61	17.17	0.004	0.14
Non-remitters	34	15.56	-0.103**	-3.71	13.86	-0.05	-1.8
Group-by-time	F=1.8, df=2, 105, p = .17				Group-by-time F=3.39, df=2, 103, p = 0.03		
Affectionless Control- Overprotection and Low care							
Remitters	66	25%	-0.008	-7.4%	18.2%	-0.015	-7.6%
Relapsers	23	16.7%	0.014	8.3%	17.4%	0.039	+21.7%
Non-remitters	34	26.5%	-0.012	-11.8%	20.6%	-0.009	-8.8%
Group-by-time	X ² =1.19 df=2, 0.55				Group-by-time X ² =2.68 ,df=2, p = 0.26		

^aModels involving PBI were adjusted for child age, gender, site, and within family correlation.

A negative beta over time suggests improvement, except for PBI- Care

^bN= 77 children of 43 remitters, 24 children of 12 relapsers, 34 children of 21 non-remitters

^cChange in score over time

Table 23

Mother's Parental Functioning and Bonding and Child Outcomes in Remitting versus Non-Remitting Mothers

	Unadjusted Model		Adj Parental Functioning/Bonding Effect	
	β	p	β	p
SAS-SR Total Score				
MASC-Social				
Week x Remission status	-0.07	0.0316	-0.05	0.0921
Parental Functioning (SAS-SR Total)			0.73	0.0208
MASC-Total				
Week x Remission status	-0.17	0.0356	-0.13	0.1098
Parental Functioning (SAS-SR Total)			1.94	0.0292
Parental Functioning Total				
MASC-Social				
Week x Remission status	-0.07	0.0316	-0.05	0.0954
Parental Functioning			0.88	0.0011
MASC-Total				
Week x Remission status	-0.17	0.0356	-0.13	0.1071
Parental Functioning			2.17	0.0017
Parental Functioning item #2 (able to talk to and listen to child)				
CDI				
Week x Remission status	-0.08	0.0213	-0.06	0.0952
Parental Functioning item #2			-0.30	0.4616
Parental Functioning item #2 x Remission status			0.96	0.038
MASC-Social				
Week x Remission status	-0.07	0.0316	-0.05	0.128
Parental Functioning item #2			0.65	0.0028
MASC-Total				
Week x Remission status	-0.17	0.0356	-0.13	0.1199
Parental Functioning item #2			1.40	0.0115
PBI- Overprotection (Mother's report)				
MASC-Social				
Week x Remission status	-0.06	0.0998	-0.05	0.1268
PBI- Overprotection			0.11	0.0617

NOTE: All analyses were controlled for child centered age and gender, site, and within family correlation. All models were restricted to remitters and non-remitters.

Figure 1
Study Flow Chart

Figure 2

Percentage of Children with a Psychiatric Diagnoses in Children of Married Mothers Compared to Children of Married Fathers over 9 Months in Whole Subsample^a and in Responding Married Parents^b.

Note: Response defined as a 50% reduction in HAMD₁₇ scores from Baseline

^a 9 married fathers with their 19 children and 34 married mothers with their 59

^b 7 responding married fathers with their 12 children and 26 responding married mothers with their 45 children

Figure 3
Hamilton Depression scores (HAMD17) of Married Parents¹ Over 9 Months

Note: All models were controlled for site.

¹ Nine fathers and 34 mothers

Figure 4
Mean Scores on Child Outcome Measures Among Remitting, Relapsing, and Non-Remitting Mothers Over 9 Months

Note. Only children of remitters had a significant improvement on the CGAS ($p=.008$), and significant decreases in scores on the CDI ($p<.001$), CIS ($p<.001$), MASC ($p<.001$), and a significant reduction of symptoms on the KSADS ($p<.001$).

** $p < .01$, *** $p < .001$

Figure 5
Imputed Score for Overall Parental Functioning on the SAS-SR in Remitters, NonRemitters, and Relapsers

NOTE: Overall Parental Functioning on the SAS-SR includes measures of parent's perceived interest in children's activities, communication with child, arguments, and feelings of affection. Pairwise comparisons show significant differences between remitting and relapsing mothers ($\beta = -0.015$, $t = -2.30$, $p = 0.0217$), and no significant differences between remitting and non-remitting mothers ($\beta = -0.010$, $t = -1.62$, $p = 0.1114$), and relapsing and non-remitting mothers ($\beta = 0.005$, $t = 0.71$, $p = 0.4761$).

Figure 6
Imputed Score for SAS-SR Parenting item "Being Able to Talk to and Listen to My Child" Remitters, NonRemitters, and Relapsers

NOTE: SAS-SR Parenting item #2: "Being able to talk to and listen to my child" Pairwise comparisons show significant differences between remitting and relapsing mothers ($\beta = -0.023$, $t = -2.63$, $p = 0.0095$), borderline significance between remitting and non-remitting mothers ($\beta = -0.017$, $t = -1.97$, $p = 0.0625$), and no significant difference between relapsing and non-remitting mothers ($\beta = 0.006$, $t = 0.64$, $p = 0.5248$).

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