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Intergenerational Transmission of Depression

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Abstract

The study of depression in mothers in relation to transmission of risk for the development of psychopathology in their children relies on solid foundations in the understanding of psychopathology, of development, and of developmental psychopathology per se. This article begins with a description of the scope of the problem, including a summary of knowledge of how mothers' depression is associated with outcomes in children and of moderators of those associations. The sense of scope then informs a theoretical and empirical perspective on knowledge of mechanisms in those associations, with a focus on what has been learned in the past 20 years. Throughout the article, and in conclusions at the end, are suggestions for next steps in research and practice.

Contents

1. INTRODUCTION

With depression being prevalent, particularly in women, and characterized by clinical characteristics and correlates that, even at face value, would suggest challenges to offsprings' well-being, researchers and practitioners have long had concerns about intergenerational transmission of depression. In this article, I provide an overview of several aspects of those concerns. First, I describe the scope of the problem, elaborating on bases for concern about intergenerational transmission of depression. I review the evidence for intergenerational transmission of depression and focus on the range of outcomes and strength of associations. This description of scope also includes knowledge of moderators of intergenerational transmission of depression, recognizing both exacerbating and mitigating conditions and taking into consideration that depression is unlikely to act alone in the intergenerational transmission of risk. Second, I review the predominant themes in our understanding of mechanisms in the intergenerational transmission of depression. Third and finally, I offer recommendations for research and practice.

2. SCOPE OF THE PROBLEM

In addressing the scope of the problem, I start with a description of depression in adults: what we mean when we say depression, how many are affected, and the variability within depression that might be relevant to intergenerational transmission. Then I address the scope of the problem in terms of how many different aspects of children's functioning have been found to be associated with depression in mothers and how strongly. Note that for this purpose, the literature treats depression in parents as the primary risk factor, thus eschewing a key tenet of a developmental psychopathology perspective: equifinality (I return to that issue in Section 2.3.1). I conclude Section 2 by delving into theories and empirical support for a role of moderators in this intergenerational transmission.

2.1. Depression in Adults: Definitions and Course

The term depression encompasses tremendous variability. First, depression may refer to a depressive episode or to elevated depression symptoms. With regard to episodes, one typically refers to

major depressive episodes (MDEs). (Although persistent depressive disorder—dysthymia—would be of interest, few research studies report on it in terms of intergenerational transmission.) To meet diagnostic criteria for MDEs, one must have at least five out of a specific set of symptoms, most of the day nearly every day for 2 weeks or more, and clinically significant distress or impairment in functioning. Although establishing that a group of participants has met criteria for MDEs sets a common standard for all participants, it still leaves a possibility of tremendous variability. For example, some participants may have met the minimum number of symptoms, and others may have reported all the possible symptoms. As another example, individuals vary in their particular combinations of symptoms, with hundreds of possible ways to meet the criteria (Zimmerman et al. 2015). Further, some may have met the symptom and impairment criteria for no more than the required minimum 2 weeks, and others may have had the symptoms for years, either intermittently or persistently. Also contributing to variability is the impairment, which may be limited to particular social roles or be widespread across a range of roles.

With regard to elevated depression symptom levels, these scores typically reflect both number and severity of symptoms, given that items on most of the well-established questionnaires require respondents to say how frequently or intensely they experience each symptom. Higher scores may reflect low severity of numerous items/symptoms or high severity of a smaller number of items/symptoms. Adding further variability is the fact that researchers may treat scores from depression rating scales either continuously or dichotomously, with the latter approach designating individuals as either exceeding or not exceeding an established cutoff score indicating clinically significant levels of depression.

Second, even putting aside the distinction between diagnosis and elevated symptom levels and the variability within each of those measurement approaches, samples of adults with depression are likely to vary on numerous other characteristics. These include comorbidities as well as a range of characteristics associated with course of depression: age of onset, duration/chronicity, severity, frequency and number of recurrences, and extent of recovery between episodes or carryovers from having been formerly depressed, such as in cognitive or interpersonal functioning (Klein & Allmann 2014, Scher et al. 2005). With each of these factors, there are reasons to be concerned about the variability they may introduce in studies of depressed parents and intergenerational transmission.

In terms of comorbidity, Kessler and colleagues (2003) found that nearly 75% of participants with lifetime major depressive disorder (MDD) had at least one additional lifetime disorder meeting *Diagnostic and Statistical Manual of Mental Disorders* (DSM) criteria. Depression was highly comorbid with several disorders: anxiety (59%), impulse control (32%) and substance use (24%). Thus, samples of mothers with depression will vary on the presence of comorbid conditions. Variability also arises from the temporal ordering of the onset of depression relative to the comorbid condition(s). Further, there are many reasons to believe that variability in comorbidity is relevant to understanding intergenerational transmission of depression. As just one example, the comorbidity of depression and anxiety may reflect both a common factor of distress or neuroticism and also some distinct contributions of each (Beuke et al. 2003), which is particularly relevant when thinking about (*a*) how to identify the early emergence of depression in offspring (e.g., whether anxiety may develop first) (Moffitt et al. 2007), (*b*) what children of depressed mothers may inherit that contributes to the intergenerational transmission of depression (e.g., neuroticism or high negative affectivity), and (*c*) implications of deficits in positive affectivity being specific to depression relative to anxiety (Mineka & Vrshek-Schallhorn 2014).

Turning now to variability related to course of depression, one example is that samples of parents with depression may include those with childhood onset, at one extreme, and others with recent onset. Childhood or adolescent onset of depression is associated with high rates of depressive

disorder in families (Kovacs et al. 1994) and is highly predictive of level of functioning in young adulthood, albeit at least partly explained by level of functioning during adolescence (Lewinsohn et al. 2003). Children of depressed mothers who become depressed do so at younger ages than other children who become depressed (Weissman et al. 1987), which could start a multigenerational negative cycle of increasing risk for later generations (Weissman et al. 2016). Earlier age of onset also increases the likelihood of multiple recurrent episodes, if only as a function of the opportunity of time, given that individuals with a history of depression have an average of five to nine subsequent depressive episodes (Kessler et al. 1997). Later onset of depression in parents would also be associated with the children having had more years of development with a depression-free parent (i.e., the opportunity for more years of healthy development). That is, although the concept of age of onset refers to the age at which the depressed parents have their first episode (i.e., one of the aspects of depression variability), the parallel concept relevant to this article is children's age at first exposure to depression in their parent(s). The earliest age at which children can be directly exposed is during fetal development with a prenatally depressed mother, although there is some suggestion that women's preconception depression matters too (Moss et al. 2020). Overall, the earlier the age of onset of the parents' depression, the more likely that they have had multiple episodes, earlier and more frequent exposures for the children, and more relatives with depression, suggesting greater heritability.

This notion has particular relevance for understanding intergenerational transmission of depression that occurs in mothers during the perinatal period. Mothers who are depressed at the time that infants are participating in a research study (i.e., postnatal depression) may or may not have also exposed their infants to depression during their infants' fetal development (i.e., prenatal depression). Given that depression during pregnancy is often found to be the strongest predictor of postnatal depression (Guintivano et al. 2018), it is not surprising that most women with postnatal depression have also been depressed during pregnancy (Heron et al. 2004). Thus, without prospective designs beginning in pregnancy, studies examining associations between postnatal depression and infant functioning may misinterpret the role of postnatal relative to prenatal depression.

Duration and chronicity are other ways that parents with depression might differ from each other—an issue that raises concerns similar to those described for age of onset. The longer the duration, the more exposure the child has to the experiences associated with their parent's depression. Moreover, longer duration increases the likelihood of the depression becoming chronic—that is, the likelihood that there is no recovery (for a review, see Richards 2011). Further, researchers find that longer and more persistent, more severe, or more frequent episodes for mothers are related to more problems in parenting and more adverse outcomes in their children (Netsi et al. 2018).

Parents with depression also vary in the extent and quality of their recovery. Formerly depressed adults are both similar to and different from currently depressed adults in some ways and also different from never-depressed adults, with much variability within a group of formerly depressed adults in terms of cognition, emotion, interpersonal functioning, and physiology (for a review of this literature, see part 1 of Segal et al. 2018). This aspect of variability has both methodological and conceptual implications. Most studies measure either current depression or history of depression and, thus, miss this aspect of variability in children's exposures. Conceptually, researchers often design their studies in ways that reflect an assumption that women who are not currently depressed are well, whereas research on recovery suggests that this is not a safe assumption. Moreover, what may matter for a child is not the chronicity patterns of their mother's depression or whether the mother is currently undergoing an episode but, rather, the personality factors that may underlie depression (e.g., neuroticism) (Jacobs et al. 2011). For example, in general population samples, higher levels of neuroticism are related to parenting with less warmth, less behavioral control, and less autonomy support (Prinzie et al. 2009).

One final aspect of variability that is relevant to intergenerational transmission of depression is treatment history of the depressed parent, although this factor is rarely taken into account in studies of intergenerational transmission. Rather, most studies of treatment examine effects of the treatment on the children. Some such studies have focused on prenatal depression, with concerns about fetal exposure to antidepressant medications (ADMs), and postpartum depression, with concerns about infant exposure to ADMs through breast milk. However, for obvious ethical reasons, these studies do not employ random assignment of women to ADMs relative to controls, thus constraining conclusions that can be drawn about the children (Goodman et al. 2018). It is also relevant to know the extent to which treatment or nontreatment of parents with depression differentially predicts functioning in the children, with treatment more broadly defined to include psychotherapy. In a review of randomized clinical trials of psychotherapy for depressed mothers, psychotherapy was significantly associated with children's better mental health, broadly defined, with a small to moderate effect, $g = 0.40$ (95% CI 0.22–0.59) (Cuijpers et al. 2015). However, there were only five eligible studies, and there was tremendous variability across studies; thus, this finding should be considered tentative. Further, as context for this consideration of mothers' receiving treatment for depression, fewer than 30% of adults who screen positive for depression receive any treatment, and 87% of those receive ADMs (Olfson et al. 2016).

2.2. Evidence for Intergenerational Transmission

Having described depression in adults with an emphasis on its variability, I turn now to the evidence for the intergenerational transmission of depression to further explicate the scope of the problem. From this point forward, I hone in on depression in mothers, given that prevalence of depression is twice as high in women as in men (Bromet et al. 2011) and is the focus of most of the research on intergenerational transmission of depression. Specifically, I describe the breadth of aspects of children's functioning that are associated with depression in mothers. I follow this discussion with the final section on the scope of the problem, which is a focus on moderators (Section 2.3). A full understanding of the scope of the problem requires an appreciation of which specific characteristics, both personal and situational, can lead to depression in mothers being more or less strongly associated with children's problems.

Consistent with the notion of multifinality (Cicchetti & Rogosch 1996), the risk factor of depression in mothers predicts a broad range of functioning in children relevant to transmission of depression. Taking a developmental perspective, I describe these aspects of functioning in terms of the ages at which they first appear. In this review, I heavily rely on two published reviews on associations between depression in mothers and children's functioning (Goodman et al. 2011, Stein et al. 2014) and other reviews of more targeted aspects of that literature, to which I add representative recent findings. It is important to note that this literature, with a few exceptions, gives insufficient consideration of the variability just described, given the limitations of typical study designs and measures.

One further consideration in the review that follows is that many studies of offspring of depressed mothers study children well before the age when depression per se is likely to emerge. Yet there are several reasons why such studies' findings are important to the understanding of intergenerational transmission of depression. First, they stand on their own in terms of revealing what it is about offsprings' development that is associated with depression in mothers. Second, the aspects of children's functioning found to be associated with depression in their mothers may reveal vulnerabilities to the later development of depression or other disorders, as discussed in Section 3.2.5). Third, even if such vulnerabilities do not lead to the later development of psychopathology, they may sufficiently pull a child off a normative developmental course to be concerning. Fourth,

these vulnerabilities may index particular challenges to a mother with depression, such as an infant with low positive affectivity, with implications for transactional mother–child processes unfolding in a negative direction over time. In each of the developmental period–specific sections that follow, I describe how the aspects of children's functioning found to be associated with depression in mothers might at least partly explain enhanced risk for the later development of psychopathology.

One final note before proceeding with the review of offspring functioning that has been found to be associated with depression in mothers is that effect sizes tend to be small. In a meta-analytic review, maternal depression and child functioning were associated with small, albeit meaningful effect sizes—that is, weighted means of 0.21 and 0.23 for internalizing and externalizing, respectively, and 0.15 and −0.10 for negative affect and behaviors and positive affect and behaviors, respectively (Goodman et al. 2011). Effect sizes like the one for internalizing problems can be interpreted to suggest that about 68% of children of depressed mothers (regardless of how depression was defined) scored higher than the average child of a nondepressed mother. I return to this point and its implications for research and policy in Section 4.2.

2.2.1. Fetal and newborn functioning. A few researchers have focused on fetal and newborn functioning, both behavior and physiology, to reveal the earliest evidence of risks to offspring associated with mothers' depression (for a review, see Kinsella & Monk 2009). In particular, depression in pregnant women is associated with fetal heart rate (FHR), including higher baseline heart rate, slower reactivity and recovery in reaction to stimuli, and lower heart rate variability. Of note, there is some variability in directions of these associations, which may be related to the particular stressor used in a given study but also could be related to variability within depression, such as comorbidity, as reviewed earlier in this article. A second fetal marker is fetal activity or movement or sleep patterns: Depression in mothers, particularly in the presence of comorbid anxiety, is associated with fetuses spending relatively more time being active (Dieter et al. 2008). A third set of fetal markers, derived from studies of newborns' brains via structural magnetic resonance imaging, reveals associations between mothers' depression and lower neonatal amygdala fractional anisotropy and axial diffusivity (but not volume) (Rifkin-Graboi et al. 2013). Studies of fetal brains are just emerging, with suggestive findings linking mothers' prenatal stress to fetal brain efficiency (Thomason et al. 2017).

Why does fetal functioning matter in the intergenerational transmission of depression? The fetal origins hypothesis (i.e., the Barker hypothesis) (Barker 1998) is that fetuses, relative to offspring at other ages, are particularly at risk of exposures, given the quantity and pace of neurodevelopment, with long-term effects. More specifically, FHR markers are understood to reflect individual differences in the development of autonomic and central nervous systems, and these differences are associated with emotion regulation and the later development of psychopathology (Sandman 2010). Fetal motor activity has been found to predict optimal newborn motor activity, and FHR variability and somatic–cardiac coupling predict brain stem auditory-evoked potential (DiPietro et al. 2010). Both slower FHR and less fetal movement were found to predict a specific aspect of child (aged 7–14 years) temperament, higher child behavioral inhibition temperament, whereas less FHR recovery after a maternal stimulation predicted more behavioral problems and lower prosocial behavior (Dipietro et al. 2018). The particular pattern of amygdala abnormalities found in newborns is associated with mood disorders in adults (Price & Drevets 2009).

In addition to this literature on fetal functioning, there are studies of neonates in which researchers typically have considered neonatal functioning to reflect fetal rather than postnatal exposures. Presence of elevated maternal prenatal depressive symptoms or MDD has been found to

predict newborns' right frontal electroencephalograph alpha asymmetry (Gustafsson et al. 2018), preterm birth and lower birth weight (Jarde et al. 2016), admission to neonatal intensive care units (Latendresse et al. 2015), adverse neurobehavioral outcomes (particularly lower attention scores, i.e., less alertness) (Salisbury et al. 2011), and altered microstructure of the right amygdala (Posner et al. 2016). As one example, prematurity is a concern because it has been found to predict attention regulation problems, emotional and behavioral problems, and poor social/interactive skills in the short term (i.e., infancy through childhood) (Mayes & Bornstein 1997) and adolescent depressive disorder in long-term follow-ups (Patton et al. 2004). Moreover, it is a stressor for mothers and a risk factor for postpartum depression (Vigod et al. 2010). Further reason for concern about mothers' depression being associated with babies' low birth weight comes from a finding that low birth weight was more strongly associated with risk for affective disorders among offspring of depressed parents (Nomura et al. 2007). On the other hand, findings from a large, population-based longitudinal study revealed that the association between high depressive symptom levels during pregnancy, even with elevated symptoms at two times in pregnancy, and newborns' low birth weight is better explained by confounders, particularly smoking, than by the mothers' high depression levels per se (Evans et al. 2007). I return to this point in my discussion of moderators and specificity in Section 2.3.

2.2.2. Infant and early childhood functioning. Studies of infants and older offspring of depressed mothers reflect fetal experiences and exposures as well as the accumulating postnatal and later exposures. Thus, I now bring into consideration notions of diathesis–stress, differential susceptibility, and other constructs central to a developmental psychopathology perspective. Important questions relate to how this combination of experiences, before and after birth, shapes ongoing brain development, development of stress response systems, emotion regulation skills, and so forth, including the later development of depression.

Beginning in infancy, depression in mothers is associated with offsprings' more observed negative or flat affect and less positive affect, higher-temperament negative affectivity and lower positive affectivity, poorer effective emotion regulation skills, more insecure and disorganized attachment, less social engagement, lower cognitive development (including language), greater functional connectivity between the amygdala and the left temporal cortex and insula (a pattern that is linked to major depressive disorders in adolescents and adults), problems with the hypothalamic–pituitary–adrenal (HPA) axis functioning (i.e., higher baseline cortisol levels), lower baseline respiratory sinus arrhythmia (which is linked to less sustained attention and self-regulation), more internalizing symptoms, and more externalizing symptoms (for reviews, see Aktar et al. 2019, Stein et al. 2014).

2.2.3. Middle childhood and adolescent functioning. In studies of older children and adolescents, researchers have reported maternal depression associations with two additional aspects of child functioning: lower school achievement (Letourneau et al. 2013) and onset of depression, whether the mother's depression is within the few years preceding the onset or even as early as during the pregnancy (Murray et al. 2011, Pearson et al. 2013). Lower school achievement is relevant to intergenerational transmission of depression in that it likely reflects the downstream effects of depression on adolescents' broader functioning. That is, the strong support for a negative association between adolescent depression and educational achievement has been explained by depression predicting subsequent academic achievement rather than vice versa (Hishinuma et al. 2012).

2.3. Moderation of Associations Between Depression in Mothers and Offspring Functioning

In the previous section, I have reviewed the literature on associations between depression in mothers and children's functioning. In this section, I hone in on the factors—within individuals or within contexts—that enhance or mitigate the strength of associations between depression in mothers and children's functioning. Knowledge of moderation helps us to understand some of the variability in those associations. Such knowledge also provides guidance in understanding how small effect sizes for those associations may be masking a range of larger-to-smaller effect sizes, which would be revealed if moderators were taken into consideration.

2.3.1. Multicausality. Depression in mothers, like any other single risk factor, is unlikely to function alone in the intergenerational transmission of depression (for a strong case against monocausal theories, see Kendler 2019). Rather, many factors are likely to add to or strengthen the risk, in a summative or interacting (moderated) manner, respectively. In studies of intergenerational transmission of depression, these factors are sometimes hypothesized to play such key roles and other times are treated as confounding or nuisance variables. Both such approaches to these factors are important relative to studies that fail to conceptualize and measure potential moderators or confounds. As one example of the value of considering confounds, consider the value added by information in a column on potential confounds in the tabled summaries in Stein and colleagues' (2014) review of literature on ante- or postnatal depression's associations with a range of offspring outcomes over development.

Studies that treat such factors as potential moderators provide information on what aspects of child functioning are only found, or found to be stronger, in relation to mothers' depression in the presence of those variables. Studies that treat such factors as confounds provide information on what aspects of child functioning have been found to be associated with depression in mothers regardless of the potential confounds that were measured. For example, in a publication with data from the Generation R study (Van Batenburg-Eddes et al. 2013), mothers' prenatal depression predicted their 3-year-old children's attention problems when the authors controlled for child sex, birth weight, birth order, ethnicity, mothers' smoking and alcohol use during pregnancy, and mothers' education and family income; however, when the authors controlled for mothers' symptoms after birth, mothers' prenatal depression was no longer associated with child attention problems.

Further, it is important to consider that associated risk or protective factors may matter more in certain circumstances (Reuben & Shaw 2015). For example, the more severe and persistent the mother's depression, the less it may matter whether she is also living in poverty, in terms of intergenerational transmission of depression. A specific finding supporting moderators potentially working together (moderated moderation) is that the typically protective effects of children's higher IQ were reversed among offspring whose mothers' depression was severe and chronic; perhaps the children's greater IQ enabled them to have a greater understanding of the situation and, thus, more distress (Horowitz & Garber 2003). Further, some researchers have found that it is only in the presence of multiple potential protective factors that offspring of depressed parents manage to stay well (Collishaw et al. 2016).

2.3.2. Evidence for specific moderators. The Developmental Model for Understanding Mechanisms of Transmission (Goodman & Gotlib 1999) identified several sets of variables that may exacerbate the association between mothers' depression and children's development of psychopathology. These variables were characteristics of the child, the father's mental health

and involvement, and the timing and course of the mother's depression. Despite 20 years having passed since that publication, these are essentially the same moderators under consideration today.

2.3.2.1. Child characteristics. Some researchers conceptualize child characteristics as potentially adding risk, along with exposure to the depressed mother. In this dual risk model, the child characteristic is expected to statistically add to or interact with mothers' depression to show exacerbation of the association. In one study that found support for both additive and interacting models, early adolescents' adaptive responses to peer stress lessened the associations between mothers' depression on youth depression and both the youths' initial depression symptom levels and their trajectories of depression symptoms over the subsequent 4 years of the study; youths' maladaptive responses to stress played an additive model in that youths' depression symptom levels were highest when they were exposed to mothers' depression and also exhibited maladaptive stress responses (Monti & Rudolph 2017). Additive effects also accounted for a role of children's greater effortful control in associations between mothers' depression and children's resilience (Yan 2016).

Regardless of the model, several child characteristics have been found to be associated with resilience or, conversely, greater risk. For example, resilience (i.e., staying well in the presence of a depressed mother) was associated with the following child characteristics: having good-quality social relationships, having higher self-efficacy beliefs, and engaging in more frequent exercise (Collishaw et al. 2016) and better self-understanding (Beardslee 1989). In contrast, as mentioned earlier, children's higher IQ was associated with worse outcomes for children, albeit specifically among offspring whose mothers' depression was severe and chronic (Horowitz & Garber 2003).

The most frequently studied aspects of children that are tested as moderators are their age and gender. Children's age was significantly negatively associated with the magnitude of the effect sizes for the relation between mothers' depression and children's internalizing problems and externalizing problems (Connell & Goodman 2002, Goodman et al. 2011) as well as with general psychopathology and negative affect/behavior (Goodman et al. 2011); that is, the younger the mean age of child samples, the stronger the effect. However, as interpreted by Goodman et al. (2011), despite many bases for supporting young child age as a sensitive period for exposure to their mother's depression, the meta-analytic finding is constrained by studies of older children not having specified the children's prior exposures to mothers' depression (i.e., prior to the time of the study). That is, samples of older children likely included children who had just recently been first exposed to depression in their mothers and others who had first been exposed early in development; moreover, the latter group would vary in terms of how much intermittent exposure they had experienced—that is, their mothers' course of depression, interepisodic levels of functioning, etc.

Another consideration with regard to children's age is that the relevant variable may be pubertal status rather than age in explaining some of the changes in the developmental pathway to disorder. For example, among never-disordered girls, some of whom had depressed mothers, the onset of depression by age 18 years was predicted by having demonstrated cortisol stress hyporeactivity at ages 9–15 years among those earlier in pubertal development and with cortisol hyperreactivity for those who were later in pubertal development (Colich et al. 2015). It may be that pubertal status would matter particularly for biological mechanisms of risk in the intergenerational transmission of depression.

In terms of child gender, in a meta-analytic review, the association was stronger for girls relative to boys for mothers' depression with children's internalizing problems, as predicted, and there were no child gender differences in the strength of association with child externalizing problems (Goodman et al. 2011). Similarly, associations between perinatal depression and offspring neurodevelopment (i.e., altered structural and functional brain connectivity) were stronger in female offspring (Duan et al. 2019). Girls, relative to boys, may carry greater heritability for depression

(Kendler et al. 2001), be more strongly socialized toward depression, experience more stressors or be more sensitive to stressors associated with depression in their mothers (Hammen 2002, Hankin et al. 2007), and be exposed to more deleterious aspects of parenting.

The latter point essentially proposes moderation (by child gender) of mediation (by parenting qualities). However, Lovejoy and colleagues' (2000) review of mothers' depression in relation to their parenting qualities did not examine child gender as a moderator. Gruhn and colleagues (2016) found that depression in parents (nearly all of whom were mothers) was associated with their withdrawn parenting of both sons and daughters; on the other hand, depression showed a small association with intrusive parenting of sons and no significant association with daughters. Thus, it is not clear whether exposure to particular qualities of parenting might explain why the association between mothers' depression and child internalizing problems is stronger for girls than for boys.

Finally, child gender may differently moderate the association between mothers' depression and child functioning at different child ages. This idea is particularly compelling given that rates of depression are similar in boys and girls until around puberty, when rates double in girls relative to boys (Nolen-Hoeksema & Girgus 1994). For example, in one prospective longitudinal study of adolescents, mothers' depressive symptoms showed only small associations with sons' depressive symptoms in early and mid-adolescence, but between ages 16 and 17, the relationship became significant and increased during that time period. In contrast, the strength of the relationship between mothers' and daughters' depressive symptoms increased steadily from early through late adolescence. Overall, as noted by Reuben & Shaw (2015) in their review of resilience, we have little understanding of the role of child gender in the intergenerational transmission of depression.

2.3.2.2. Context factors. Two primary ways of understanding contextual factors are that they add to the number of risk factors confronting a child (in addition to the mother's depression) and that they deplete or enhance the child's or family's resources for dealing with the potential effects of the mother's depression on the child. Another perspective is that depression in mothers typically occurs in a web of interrelated risks for their children's development of psychopathology, and depressed mothers generate more episodic and interpersonal stress relative to nondepressed mothers (Hammen 2002). In Section 3.2.4, I discuss how stressors may mediate rather than moderate associations between mothers' depression and children's functioning.

In a meta-analytic review of associations between depression in mothers and child problems, several findings emerged regarding contextual factors as moderators (Goodman et al. 2011). Family income (poverty relative to middle or higher income) was associated with a stronger effect size regardless of the aspect of child problems that was studied, with the exception of children's positive affect/behavior. It was expected that the association between mothers' depression and child functioning would be stronger among teenaged mothers; with the only two aspects of child functioning for which enough studies were found to test this prediction, either the finding was opposite the predicted outcome (i.e., the association with children's negative affect/behavior was weaker for teenage mothers) or no significant difference was found in relation to mothers' teenage status (i.e., for children's positive affect/behavior). In terms of mothers' marital status, samples with a higher percentage of married mothers had a weaker association between mothers' depression and children's externalizing problems and negative affect/behavior, but not between mothers' depression and children's internalizing problems or positive affect/behavior. For all child functioning variables except general psychopathology, the association with mothers' depression was stronger in samples with a higher percentage of ethnic minority families.

Information on contextual factors as moderators also comes from studies of specific stressors. For example, children whose mothers had prenatal depression and who also were exposed

to childhood maltreatment up to age 11 were significantly more likely to have depression or conduct disorder at age 11 or 16 (Pawlby et al. 2011). Mothers' depressive symptoms were more strongly associated with their 12- to 17-year-old sons' (not daughters') depressive symptoms in the presence of intimate partner violence (Augustyn et al. 2018). In another study, mothers' prenatal depression was more strongly associated with their 6-month-old infants' temperament (e.g., greater distress to limitations) among those infants whose mothers had been exposed to a natural disaster during pregnancy (Nomura et al. 2019). This finding supports an exacerbating effect of stressors on the association between mothers' depression and offspring vulnerabilities to the later development of depression.

2.3.2.3. Coparents. Fathers or others in a coparenting role are conceptualized to play a critical role in moderating the association between depression in mothers and their children's functioning. This may be indirect, as suggested by the finding that adolescent offspring of depressed mothers are more likely to sustain good mental health in the presence of support from the coparent (Collishaw et al. 2016). Alternatively, for children of depressed mothers, having a psychologically healthy second parent may provide direct benefits, such as the benefits of "healthy genes," exposure to a healthy role model, and the supports that the second parent may offer to the child; children may also benefit indirectly by having the depressed mother feel more supported in the presence of a coparent, especially a healthy coparent.

Findings from the empirical literature are mixed on the potential moderating role of depression in fathers. Goodman et al. (1993) found that fathers' psychiatric status, as well as parents' marital status, strengthened associations between mothers' depression and children's social and emotional competence. In the context of the child having a well father, depression in mothers was related to only one aspect of child functioning: being rated by teachers as less popular. Yet, findings from at least two other publications suggest that depression in fathers may not exacerbate the association between mothers' depression and children's functioning. One study failed to find that mothers' depressive symptoms were more strongly associated with child outcomes in relation to fathers' depressive symptom levels (Fredriksen et al. 2019). Another found no difference in adolescent or young adult offsprings' risk for depression based on whether the offspring had one or two parents with depression (Lieb et al. 2002). In a third study, which reported on findings from two large cohorts, fathers' depressive symptoms independently (i.e., additively) predicted adolescent depressive symptoms rather than in interaction with mothers' depression (Lewis et al. 2017, 2018).

2.3.2.4. Variability in mothers' depression. Among the numerous aspects of variability in depression, as described earlier, timing has received considerable attention as a potential moderator of associations between mothers' depression and child functioning. That is, does it matter when mothers' depression occurs, in terms of intergenerational transmission of depression? Is it only timing of first exposure that matters, or does timing of subsequent exposures matter too? As previously mentioned, answering these questions is complicated by the rarity of prospective longitudinal studies that have measured mothers' depression multiple times, along with measures of child functioning at the same or subsequent times. Thus, questions about timing often focus on the earliest years of exposure, which can be addressed with relatively shorter time frames than, for example, predicting the onset of depression in adolescent offspring.

Depression that occurs in mothers during the perinatal period allows for consideration of a role of timing of children's earliest exposure to their mothers' depression—that is, was the infant initially exposed during fetal development, or was the infant not exposed until after birth? This is important for many reasons, including that researchers have found that postpartum onset (within

6 weeks), relative to prepregnancy or prenatal onset of depression, is associated with mothers being older, more educated, more likely to be married or cohabitating, having one or no previous child, being Caucasian, and having private insurance (Fisher et al. 2016). Specifically, studies that prospectively examine both pregnancy and the postpartum period are able to address the extent to which postpartum depression moderates the association between prenatal depression and children's functioning. Most studies with these prospective data report their findings in terms of added variance or independent effects rather than moderation. Of those, some report that postnatal depression does not add to the effect of prenatal depression on child outcomes (Evans et al. 2012, Rouse & Goodman 2014), and others report the opposite: that after postnatal depression is controlled for, prenatal depression does not exert an independent effect on child outcomes (Bagner et al. 2010, Fredriksen et al. 2019). Another study that began data collection at delivery found that children who were first exposed to their mothers' depression between ages 2 and 3 years or between ages 4 and 5 years were twice as likely to have emotional disorders when 12–13 years old relative to children initially exposed at earlier or later ages (Naicker et al. 2012). A similar pattern emerges with studies of older children: There is no consensus as to whether mothers' later or concurrent depression adds significant variance in explaining children's functioning after accounting for earlier exposures. Thus, the notion of sensitive periods or of timing of mothers' depression, in general, even with regard to the earliest possible exposures, is not yet well understood.

Several researchers have considered roles of clinical characteristics of mothers' depression other than timing. These characteristics include severity, duration/chronicity (and the related concept of symptom trajectories over time), and comorbidity, all of which are expected to exacerbate associations between depression and children's functioning. From the older, longitudinal studies, findings consistently showed that mothers' more chronic depression was associated with children's worse outcomes, including higher rates of insecure attachment in infants (Campbell et al. 1995, Teti et al. 1995), lower school readiness and poorer verbal comprehension at 36 months (NICHD 1999), and severity of behavior problems and impaired cognitive functioning at 5 years of age (Brennan et al. 2000). In a study using data from the STAR*D study and controlling for child age (range 7–17 years), among children of depressed mothers, duration of the mothers' current episode (but not severity and number of episodes) was positively related to children's internalizing and externalizing scores (Foster et al. 2008). None of the clinical characteristics of mothers' depression were associated with children's psychosocial impairment or psychiatric diagnoses. In a prospective study of mothers' pre- and postnatal depression and infants' negative affectivity (temperament), chronic elevated prenatal depression symptoms were found to be associated with higher negative affectivity scores relative to infants whose mothers' depression levels remained low throughout pregnancy or were associated with an occasional spike in symptoms that was not sustained (Rouse & Goodman 2014). In a study of offspring in middle childhood, when current depression symptom levels were controlled for, mothers' past depression severity and chronicity were positively associated with youths' internalizing and externalizing symptoms, suggesting residual effects of past depression (O'Connor et al. 2017). Similarly, mothers' depressive symptom trajectories that reflected persistent depression were associated with children's IQ (Van der Waerden et al. 2015).

Researchers typically study comorbidity with mothers' depression in relation to intergenerational transmission, in terms of the two most commonly co-occurring disorders: anxiety and substance abuse. As with other potential moderators, researchers sometimes treat them as covariates/confounding variables and other times as moderators. As just one example with anxiety, from a large community-based twin sample, maternal depression comorbid with simple phobia was associated with a 0.44 increase in children's depression symptoms, in contrast to a 0.15 increase in mothers' depression not comorbid with anxiety (Foley et al. 2001). In an example with substance

use, mothers' depressive symptoms were more strongly associated with their daughters' (but not sons') depressive symptoms in the presence of the mothers' substance use (Augustyn et al. 2018). In a meta-analytic review of mothers' depression and five categories of children's functioning, Goodman et al. (2011) were unable to systematically review comorbidity as a moderator because of the small number of studies that had reported it.

One other aspect of variability in research on depression, mentioned in Section 2.1, is whether one defines depression as meeting diagnostic criteria or exceeding an established cut score on a symptom questionnaire. Findings from a meta-analytic review of associations between depression in mothers and a range of child outcomes revealed that the associations significantly differed in strength for only one of five children's functioning categories (Goodman et al. 2011). For children's internalizing, effect sizes were significantly stronger when mothers' depression was based on a diagnosis (weighted mean $r = 0.25$) than when depression was determined by a symptom questionnaire (weighted mean $r = 0.22$).

These findings suggest a need to continue working to understand how these two groups might differ from each other. For example, since impairment is a criterion for diagnosis, those with elevated symptom scores may be less impaired than those with a diagnosis. Studies need to include both measures and compare findings on those who meet criteria with findings on those who do not meet criteria yet have elevated symptom scales, and those with neither. In one such study design (albeit not including children), it was found that among women with history of depression prior to pregnancy, the correlates of depression during pregnancy were the same for the two depressed groups, both of which differed from women who did not become depressed during pregnancy (Goodman & Tully 2009). When the same approach was taken to predict infants' negative affectivity (temperament), no significant difference was found between those whose mothers met criteria for MDEs and those whose mothers exceeded the cutoff for clinically significant levels of depression but did not meet MDE criteria (Rouse & Goodman 2014). Descriptively, it was noted that in pregnancy, 32.5% of women met criteria for MDEs, whereas 49.4% exceeded the cutoff for clinically significant depression; in the first 3 months postpartum, those percentages were 12.7% and 32.5%.

2.3.2.5. Genetics. In this section, I focus on findings of genes as moderators of associations between mothers' depression and child functioning, albeit briefly. This topic is too large and its history too complicated to do it justice here. In Section 3.2.1, I discuss genetic mechanisms. Here, I mention a few select, recent studies on genetics as moderators.

Two recent studies support genetic moderation of associations between mothers' depression and offspring outcomes. In one, a genome profile risk score for major depression moderated the association between prenatal depression symptoms and neonatal neurodevelopment; although findings for specific brain structures differed between two samples, the finding for greater right amygdala volume was replicated across both samples (Qiu et al. 2017). Another study also found support for genetic moderation in two independent samples: Prenatal adversities, as measured by a cumulative risk score that included but was not specific to maternal depression, were more strongly associated with problematic emotional functioning and pervasive developmental problems in 48- and 60-month-olds with higher polygenic risk scores (Silveira et al. 2017). In further analyses of the latter findings, Belsky and colleagues (2019) found that the primary pattern of results supported the diathesis–stress model rather than a differential-susceptibility model, but only because the adversity score did not extend to supportive or positive prenatal exposures or experiences; an alternative approach, focusing on an index of affected cases, supported the differential-susceptibility model.

3. MECHANISMS IN THE INTERGENERATIONAL TRANSMISSION OF DEPRESSION

Perhaps the biggest problem facing the field of study and practice in the intergenerational transmission of depression is the need to understand how depression in mothers comes to be associated with depression onset or other adverse outcomes in their children, relative to resilience, including the multiple pathways to either outcome. The promise of understanding mechanisms in the developmental pathways of this transmission of risk is the potential to inform theory of the intergenerational transmission of depression and also to inform the design of more precise targets for preventive interventions than those that aim to reduce the risk (i.e., mothers' depression and its correlates) (Goodman & Garber 2017). Thus, a particular focus has been on modifiable mechanisms. What have we learned about mechanisms in the 20 years since the publication of the Developmental Model for Understanding Mechanisms of Transmission (Goodman & Gotlib 1999), which proposed four mechanisms—heritability; innate dysfunctional neuroregulatory mechanisms; exposure to negative maternal cognitions, behaviors, and affect; and the stressful context of children's lives?

3.1. Evidence for Mechanisms

Researchers now have a more nuanced understanding of statistical mediation in relation to mechanisms. That is, tests of mediation are now understood to be only a proxy for tests of mechanisms; statistical support from longitudinal mediation analyses is necessary, albeit insufficient evidence of causation (Tryon 2018). Thus, in this section, I rely not only on findings from tests of statistical mediation but also on results from interventions designed as tests of purported mechanisms. For example, although not specific to a particular mechanism, a review of randomized clinical trials to treat or prevent depression in pregnant women found that interventions designed to change maternal prenatal mood were associated with changes in offspring functioning; the effect size was very small, although higher for younger children (Goodman et al. 2018). It is likely that interventions informed by the fuller models proposed in this article—that is, not solely for depression in mothers—are required to show intergenerational benefits of interventions for mothers' depression.

3.2. Specific Purported Mechanisms

What follows is a brief update on what we have learned about mechanisms in the 20 years since the publication of the Developmental Model for Understanding Mechanisms of Transmission (Goodman & Gotlib 1999). This section separately considers the four mechanisms proposed by Goodman & Gotlib (1999): heritability; innate dysfunctional neuroregulatory mechanisms; exposure to negative maternal cognitions, behaviors, and affect; and the stressful context of children's lives.

3.2.1. Genetics. There have been rapid and major advances in the understanding of heritability, which have benefited the understanding of heritability as a mechanism in the intergenerational transmission of depression. These include findings from children-of-twins study designs (Natsuaki et al. 2014), studying in vitro fertilization as a human equivalent of prenatal cross-fostering designs that are common in animal studies (Rice et al. 2010), and findings regarding what may be unique about heritability of depression that occurs during the perinatal period relative to depression occurring at other times (Viktorin et al. 2016). Another interesting line of studies is examining the mechanistic role of epigenetic changes (e.g., DNA methylation) in offspring in response to fetal exposures or experiences during infancy or childhood that are related to depression in their

mothers (Conradt et al. 2018). These studies hold promise for revealing how early life experiences get embedded or "under the skin."

3.2.2. Prenatal exposures and experiences. Recent advances in the understanding of fetal development and prenatal exposures allow for a more nuanced understanding of how exposure to a prenatally depressed mother or genetic liability to depression may increase risk for the development of psychopathology (O'Donnell & Meaney 2017). In terms of fetal development contributing to intergenerational transmission of depression, we now understand the importance of developing neural systems (alteration of brain structure, e.g., reduced density of gray matter or reduced hippocampal volume; functional connectivity) and neuroendocrine systems (HPA axis functioning) and roles of endocrine pathways, the placenta (e.g., altered placental function or expression of particular genes), and fetal programming. As for fetal exposures, concerns about fetuses whose mothers are depressed center on ADMs, which are associated with increased risk of depression in offspring at early adolescence (Malm et al. 2016), but evidence for exposures as mechanisms also includes mothers' engagement in poorer health behaviors, such as less healthy nutrition (Barker et al. 2013). There also are a number of other biological mechanisms, although they vary in the extent of their empirical support as mechanisms (Sawyer et al. 2019). Glover and colleagues (2018) have added a global perspective on prenatal/fetal exposures that we often neglect to study—for instance, intimate partner violence, nutritional deficiencies, and environmental challenges, such as extreme cold or heat.

3.2.3. Parenting. Parenting, broadly defined, continues to garner strong support as a mechanism in the transmission of risk of depression. Research designs that allow for the isolation of environmental relative to genetic effects, such as children-of-twins studies, have revealed support for mothers' depression as an environmental risk factor for a range of children's functioning, including those aspects of children's functioning that are implicated in pathways to disorder among children at risk (Natsuaki et al. 2014). Parenting quality is a major feature of children's rearing environment. Large literatures consistently suggest that both warm, responsive, engaged parenting and harsh parenting can significantly influence children's mental health. Even stress exposures (discussed in Section 3.2.4), which we know to be important, at least partly manifest their effects on children through parenting qualities. The focus on parenting as a mechanism in the intergenerational transmission of depression is also supported by social, behavioral, cognitive, and biological theories. Further impetus to better understand parenting as a mechanism comes from support for parenting being modifiable, even among depressed mothers (Goodman & Garber 2017).

Among longitudinal studies that support parenting as a mechanism, mothers' directly observed parenting quality at child age 10–11 (i.e., autonomy-respective, supportive, nonhostile) partially mediated the association between mothers' persistent depressive symptoms in their children's first 2 years of life and their children's social skills at age 15 (DeRose et al. 2014). Another feature of DeRose and colleagues' (2014) study is their approach to analyses, which involves propensity score matching—using sociodemographic variables to match children with depressed mothers to children with nondepressed mothers and using weighting—to enable a more direct test of the contribution to children's functioning that is specific to mothers' depression rather than the common correlates of that depression. In another longitudinal study, mothers' more negative parenting at child age 7 years mediated the association between their higher postnatal depressive symptoms and their children's academic attainment at 16 years of age, with their children's mental health (total problems score) at 10–11 years of age being intermediate in the pathway (Psychogiou et al. 2020). In Section 3.2.5, I return to the idea of children's vulnerabilities as mechanisms in the intergenerational transmission of depression.

Other studies have revealed the expected complexity of predictive models. For example, empirical support for mothers' hostility and warmth as mediators of association between their severity of depression and offsprings' risk for psychopathology was attenuated by mothers' co-occurring antisocial behavior symptoms, which were moderately correlated with depression symptoms (Sellers et al. 2014).

Other helpful information has come from intervention studies designed to change a purported mechanism and testing the support for that mechanism in the association between intervention group (active intervention versus control) and child functioning. For example, enhanced maternal sensitivity, a target of a home visiting program, mediated the association between program participation and children's later language outcomes (Neuhauser et al. 2018).

3.2.4. Exposure of offspring to childhood adversities. Findings from several studies support a link between depression in mothers and children's greater exposure to childhood adversities—that is, stressful environments even beyond harsh parenting. Whether such adversities serve as mechanisms in the transmission of risk is less clear. The association of poverty with elevated rates of depression relative to others with greater resources provides a compelling case for considering the role of poverty in terms of exposing children of depressed mothers to even more stressors than are associated with the mother's depression alone. Relatedly, mothers' depression that is recurrent has been found to be associated with their children's more chronic and episodic stress even in the absence of current depression in the children (Feurer et al. 2016). Couples' conflict is another common correlate of depression in women and, thus, an important consideration in terms of children's exposures to interparental conflict as a transmission mechanism. Emotional security theory is a helpful conceptual model in that it highlights a mediating role of children's emotional insecurity to explain how marital conflict mediates associations between mothers' depression and children's development of psychopathology (Cummings et al. 2014). Several of the papers included in Stein and colleagues' (2014) review found support for couples' conflict as at least a partial mediator of associations between perinatal depression and offsprings' later functioning.

Two studies serve as strong examples of support for stressful environments as a mechanism. One is a study in which mothers' self-reported parenting stress when their children were 12 months old mediated the association between depressive symptoms during pregnancy and the first year postpartum and children's dysregulation and externalizing problems at 18 months of age (Fredriksen et al. 2019). In a second such study, the association between mothers' depression symptom severity when the children were 1.5 years old and children's internalizing and externalizing disorders at ages 7–8 years was largely explained by greater risk factor exposure—that is, a cumulative risk factor score reflecting mothers' early parenthood, low educational attainment, and substance use or criminal history within the child's first 2 years of life (Barker et al. 2012). Thus, research findings continue to provide support for stress as a mechanism.

In terms of how stressors serve as mechanisms in the intergenerational transmission of depression, it may be that stressed, depressed mothers provide poor role models for effective coping strategies, that stressors spill over into parenting, or that stressful environments function as additional stressors in a cumulative risk model. Interventions provide important opportunities to test models of stressors as mechanisms in the transmission of depression from mothers to children. Examples include home visiting programs that aim to enhance stress management skills and minimize social isolation (Ammerman et al. 2013), parenting programs that aim to address couples' conflict (Sanders et al. 2014), and problem-solving education for mothers administered through Head Start programs (Silverstein et al. 2017). Understanding stressors as mechanisms in the intergenerational transmission of depression emphasizes that interventions solely aimed to reduce mothers' depression to alleviate risks to the children are unlikely to be successful.

3.2.5. Children's vulnerabilities as mechanisms. Consensus is emerging on an understanding of at least a few aspects of child functioning that have been reliably found to characterize children of depressed mothers even before the onset of depression in the children. These characteristics may reflect vulnerabilities to the later development of psychopathology, early signs of disorder, endophenotype of disorder (Hasler et al. 2004), or some other terminology. To be consistent with the terminology used by Goodman & Gotlib (1999), I will continue to use the word vulnerabilities while recognizing strong arguments for alternative terminology. Importantly, although these vulnerabilities are often studied as "outcomes," they are at least conceptually, if not empirically, implicated as mechanisms in developmental pathways to disorder or resilience. That is, depression in mothers increases the likelihood of children's vulnerabilities, and the vulnerabilities account for at least part of the variance in the association between mothers' depression and children's onset of depression or other disorders. Conceptually, children's vulnerabilities mediating associations between mothers' depression and children's later development of psychopathology may be explained by children's vulnerabilities setting them on a course of further developmental challenges. Alternatively, transactional models suggest that children's vulnerabilities increase mothers' depression or impose further challenges on mothers' parenting (beyond challenges from the mothers' depressive symptoms). Consistent with this model, cross-lagged paths revealed not only that parents' (predominantly mothers') depressive symptoms predicted children's levels of behavior problems a year later but that the reverse was also true: Children's higher levels of behavior problems in one year predicted higher levels of parents' depressive symptoms in the subsequent year (Bagner et al. 2013).

There are some vulnerabilities that, as suggested in several studies, both (*a*) link depression in mothers to the vulnerability and also (*b*) link the vulnerability to the later onset of depression or other disorders. These include anomalous psychobiological characteristics (e.g., poorer physiological stress or emotion regulation ability; blunted reward- or approach-related functioning; brain structure and function, e.g., less functional connectivity of the amygdala to other brain regions), temperament (e.g., low positive affectivity; high negative affectivity; effortful control) or other personal characteristics, and cognitive vulnerabilities to depression (e.g., biases, rumination) (for a review of some of this literature and a description of an ongoing test of this mediational model, see Davis et al. 2018). As one example, children's early childhood personality (higher neuroticism and lower conscientiousness and agreeableness) mediated the relationship between mothers' depression that had occurred earlier in children's lives and their later behavior problems (Allen et al. 2019). Although not specific to depression in mothers (i.e., addressing childhood adversities more broadly), McLaughlin and colleagues (2019) provided detailed support for a set of mechanisms that have empirical support as developmental processes mediating associations between adversities and children's later development of depression and other disorders, along with a proposed set of intervention targets to address those purported mechanisms.

3.3. How Mechanisms Might Work Together

Increasingly sophisticated study designs inform the understanding of how mechanisms might work together. Examples include consideration of multiple mediators in a single conceptual model and study design. One such study design that allows for direct comparison of the relative strengths of the mechanisms is tests of competing purported mechanisms (e.g., Moss et al. 2020). Furthermore, longitudinal designs enable tests of potential differential roles of mechanisms in developmental pathways or intergenerational transmission. For example, a mother's insensitive parenting may initially mediate associations between her perinatal depression and her offspring's later depression, and stressors may function as intermediate mediators.

In particular, one important consideration is related to depression being recurrent. Thus, it is not surprising that studies testing a purported mechanism, such as interparental conflict, also find a mediational role of mothers' later depression. Earlier research folded recurrence into the idea of chronicity, which is important but may mask specific knowledge to be gained from examining timing and frequency of recurrences as mechanisms. Using multilevel structural equation modeling, Moss and colleagues' (2020) study (see the previous paragraph) found that the effect of mothers' preconception depression on their children's functioning was mediated by the mothers' postbirth depression.

4. FUTURE DIRECTIONS

4.1. Research

One of the strongest messages from this overview is that research would benefit from more consideration of variability. Essentially, we must characterize our samples of depressed mothers in terms of comorbidities, correlates, and course. Greater consideration of variability also requires being sensitive to the sociocultural environmental considerations of the populations we sample (for an example, see Glover et al. 2018). Depression does not occur in a vacuum; neither can our conceptual models without imposing limitations on the progress that we need to make.

Although one might infer from the well-justified movement away from monocausal theories (Kendler 2019)—theories of causal pathways in the intergenerational transmission of depression, as is the concern of this article—that researchers should abandon depression in mothers as a focus of research, I suggest a very different conclusion: the importance of embracing notions of multiple mechanisms. We should ask not only, what can inclusion of multiple mechanisms in a single study design tell us about the relative strength of their mediational effects but also, how might multiple mechanisms work together? Ultimately, what is it that matters about depression in mothers? How? And when? Does what matters differ depending on the aspect of child functioning that is of concern? Or does it matter differently depending on when in development we are studying the mechanism or the children (i.e., moderated mediation)? That is, the timing of children's exposure to their mothers' depression seems likely to be associated with different mechanisms in the transmission of risk. Also important in terms of enhancing theory and practice is testing whether mediators have direct or indirect effects.

A related challenge for researchers is to sort out what is unique about depression in mothers in terms of transmission of risk for the development of psychopathology. Easy and important steps toward asking this question have considered depression in fathers, relative to mothers, but also stress and anxiety, relative to depression, in mothers. Use of statistical techniques to attempt to isolate effects has its limitations. Sufficiently powered studies to test moderation help to address this problem. For example, is depression associated with children's adverse functioning only in the context of particular clinical characteristics of mothers' depression, as suggested in Section 2.3.2.4? Propensity score matching can isolate depression relative to specific sets of variables that are suspected or known to play causal roles. A network of findings from such approaches would be most informative.

Another important consideration for researchers as they design their studies is to collect data that would enable tests of diathesis–stress relative to differential susceptibility (Belsky et al. 2019). That is, tests of differential susceptibility require data on a full range of not only negative but also positive experiences. In particular, a purported mechanism or moderator should include the concerning aspects as well as the positive ones. With parenting, for example, studies would include harsh and withdrawn parenting as well as warm, responsive parenting. Such findings would be particularly helpful in identifying the subgroups of children who are most at risk for intergenerational transmission.

Finally, given that not all children of depressed mothers develop depression or other disorders, a key point from a developmental psychopathology perspective is the importance of understanding individual children's pathways to resilience despite the exposure. That is, what are the alternative pathways and relevant processes (mechanisms) that facilitate resilience? An essential point from these considerations is that enhancing resilience is a promising target of interventions to prevent the intergenerational transmission of depression (Chmitorz et al. 2018). Examples based on the literature reviewed here include training children in stress response strategies, cognitive biases, and positive affect.

4.2. Policy and Practice

Although I have delved into the studies that tested the potential of mothers' treatment for depression benefiting their children, the fact remains that rates of treatment are low, particularly for psychotherapy. This has implications for research in terms of imposing limitations regarding generalizability of findings when one studies samples of depressed women in treatment. It also has implications for policy and practice. In particular, it is essential to disseminate effective prevention and treatments of depression, particularly those that have been developed with sensitivity to the special considerations of depression in women who are mothers and that have been found to be effective for those groups. Examples include the parenting interventions that have been tailored to depression in mothers (as mentioned in Section 3.2.3) and mindfulness-based cognitive therapy for the prevention of depression recurrence in perinatal women (Dimidjian et al. 2016). Task shifting—building capacity to disseminate effective treatments by training and supervising community health workers—addresses constraints related to both cost and shortages of trained providers. Other solutions involve use of computer technology (including handheld devices), such as for remotely training providers in evidence-based practices or to provide women direct access to interventions that have been translated into online tools. An essential next step in studies of intergenerational transmission of depression is developing, testing, and disseminating ways to enhance delivery of evidence-based treatments for depression, and not only for depression but also for other elements in the model of risk.

Effect sizes for associations between mothers' depression and children's functioning and for mechanisms in those associations tend to be small. Research taking multiple risks into account will likely yield larger effect sizes than have been typical. Nonetheless, even small effect sizes are clinically and practically meaningful, as discussed above (see Section 2.2) and in previous publications (e.g., Goodman et al. 2011).

From a public health perspective, an important shift occurred relatively recently from a focus on depression during the parenting of infants and young children to a consideration of depression during pregnancy. A related and emerging shift is toward consideration of preconception depression and other aspects of women's functioning in relation to intergenerational transmission of depression. Attention to preconception enables consideration of the increasingly understood roles of mothers' early adverse experiences, consistent with animal models (Bouvette-Turcot et al. 2019, Moss et al. 2020).

SUMMARY POINTS

1. The association of depression in mothers with a wide range of aspects of children's functioning, across development (i.e., from fetuses through adolescence), is a well-replicated finding.

2. Effect sizes for associations between mothers' depression and children's functioning generally are small, albeit meaningful.
3. The association of depression in mothers with children's functioning even well before the age when depression is likely to occur is important not only in indicating potential vulnerabilities to the later development of depression but also in providing insights into early-occurring challenges to offspring, the challenges these may impose for getting back on track to normative development, and the child-associated challenges to mothers.
4. Depression in adults is highly variable in numerous ways, and that variability raises important questions regarding the intergenerational transmission of depression; researchers are increasingly taking these questions into consideration in hypothesis generation, study design, and interpretation of findings.
5. A shift in emphasis to multicausality is consistent with strong support for a set of moderators of the association between depression in mothers and their children's functioning; that is, depression does not act alone.
6. Relative to Goodman & Gotlib's (1999) Developmental Model for Understanding Mechanisms of Transmission, support for the same four mechanisms remains strong, although researchers have contributed to a more sophisticated understanding of each of them: heritability; innate dysfunctional neuroregulatory mechanisms; exposure to negative maternal cognitions, behaviors, and affect; and the stressful context of children's lives.
7. Important next steps in the study of intergenerational transmission of depression include greater consideration of the variability within depression, embracing notions of multiple mechanisms, sorting out what is relatively unique about depression in mothers in terms of transmission of risk for the development of psychopathology, tests of diathesis–stress relative to differential susceptibility, and understanding individual children's pathways to resilience despite the exposure.
8. Important next steps in policy and practice regarding intergenerational transmission of depression are to enhance the workforce of providers of evidence-based interventions, both prevention and treatment, to mothers with depression and to their children, including nontraditional options for who might be the providers, how providers might get trained and supervised, and how the treatments might get delivered.

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LITERATURE CITED

Aktar E, Qu J, Lawrence P, Tollenaar M, Elzinga B, Bögels S. 2019. Fetal and infant outcomes in the offspring of parents with perinatal mental disorders: earliest influences. *Front. Psychiatry.* **https://doi.org/10.3389/fpsyt.2019.00391**

Allen T, Oshri A, Rogosch F, Toth S, Cicchetti D. 2019. Offspring personality mediates the association between maternal depression and childhood psychopathology. *J. Abnorm. Child Psychol.* 47:345–57

Ammerman RT, Putnam FW, Altaye M, Stevens J, Teeters AR, van Ginkel JB. 2013. A clinical trial of in-home CBT for depressed mothers in home visitation. *Behav. Ther.* 44:359–72

Augustyn MB, Fulco CJ, Henry KL. 2018. Intergenerational continuity in depression: the importance of time-varying effects, maternal co-morbid health risk behaviors and child's gender. *J. Youth Adolesc.* 47:2143–68

Bagner DM, Pettit JW, Lewinsohn PM, Seeley JR. 2010. Effect of maternal depression on child behavior: a sensitive period? *J. Am. Acad. Child Adolesc. Psychiatry* 49:699–707

Bagner DM, Pettit JW, Lewinsohn PM, Seeley JR, Jaccard J. 2013. Disentangling the temporal relationship between parental depressive symptoms and early child behavior problems: a transactional framework. *J. Clin. Child Adolesc. Psychol.* 42:78–90

Barker DJP. 1998. In utero programming of chronic disease. *Clin. Sci.* 95:115–28

Barker ED, Copeland W, Maughan B, Jaffee SR, Uher R. 2012. Relative impact of maternal depression and associated risk factors on offspring psychopathology. *Br. J. Psychiatry* 200:124–29

Barker ED, Kirkham N, Ng J, Jensen SKG. 2013. Prenatal maternal depression symptoms and nutrition, and child cognitive function. *Br. J. Psychiatry* 203:417–21

Beardslee WR. 1989. The role of self-understanding in resilient individuals: the development of a perspective. *Am. J. Orthopsychiatry* 59:266–78

Belsky J, Pokhvisneva I, Rema ASS, Broekman BFP, Pluess M, et al. 2019. Polygenic differential susceptibility to prenatal adversity. *Dev. Psychopathol.* 31:439–41

Beuke CJ, Fisher R, McDowall J. 2003. Anxiety and depression: why and how to measure their separate effects. *Clin. Psychol. Rev.* 23:831–48

Bouvette-Turcot A-A, Fleming AS, Unternaehrer E, Gonzalez A, Atkinson L, et al. 2019. Maternal symptoms of depression and sensitivity mediate the relation between maternal history of early adversity and her child temperament: the inheritance of circumstance. *Dev. Psychopathol.* In press. **https://doi.org/10.1017/S0954579419000488**

Brennan PA, Hammen C, Anderson MJ, Bor W, Najman JM, Williams GM. 2000. Chronicity, severity, and timing of maternal depressive symptoms: relationships with child outcomes at age five. *Dev. Psychol.* 36:759–66

Bromet E, Andrade LH, Hwang I, Sampson NA, Alonso J, et al. 2011. Cross-national epidemiology of DSM-IV major depressive episode. *BMC Med.* 9:90

Campbell SB, Cohn JF, Meyers T. 1995. Depression in first-time mothers: mother-infant interaction and depression chronicity. *Dev. Psychol.* 31:349–57

Chmitorz A, Kunzler A, Helmreich I, Tüscher O, Kalisch R, et al. 2018. Intervention studies to foster resilience—a systematic review and proposal for a resilience framework in future intervention studies. *Clin. Psychol. Rev.* 59:78–100

Cicchetti D, Rogosch FA. 1996. Equifinality and multifinality in developmental psychopathology. *Dev. Psychopathol.* 8:597–600

Colich NL, Kircanski K, Foland-Ross LC, Gotlib IH. 2015. HPA-axis reactivity interacts with stage of pubertal development to predict the onset of depression. *Psychoneuroendocrinology* 55:94–101

Collishaw S, Hammerton G, Mahedy L, Sellers R, Owen MJ, et al. 2016. Mental health resilience in the adolescent offspring of parents with depression: a prospective longitudinal study. *Lancet Psychiatry* 3(1):49–57

Connell AM, Goodman SH. 2002. The association between psychopathology in fathers versus mothers and children's internalizing and externalizing behavior problems: a meta-analysis. *Psychol. Bull.* 128:746–73

Conradt E, Adkins DE, Crowell SE, Monk C, Kobor MS. 2018. An epigenetic pathway approach to investigating associations between prenatal exposure to maternal mood disorder and newborn neurobehavior. *Dev. Psychopathol.* 30:881–90

This paper provided bases for researchers studying depression in mothers to turn attention to depression occurring during pregnancy.

Essential concepts for understanding the breadth of children's outcomes associated with depression in mothers and their being multiply determined.

Cuijpers PC, Weitz E, Karyotaki E, Garber J, Andersson G. 2015. The effects of psychological treatment of maternal depression on children and parental functioning: a meta-analysis. *Eur. Child Adolesc. Psychiatry* 24:237–45

Cummings EM, Cheung RYM, Koss K, Davies PT. 2014. Parental depressive symptoms and adolescent adjustment: a prospective test of an explanatory model for the role of marital conflict. *J. Abnorm. Child Psychol.* 42:1153–66

Davis EP, Hankin BL, Swales DA, Hoffman MC. 2018. An experimental test of the fetal programming hypothesis: Can we reduce child ontogenetic vulnerability to psychopathology by decreasing maternal depression? *Dev. Psychopathol.* 30:787–806

Derose LM, Shiyko M, Levey S, Helm J, Hastings PD. 2014. Early maternal depression and social skills in adolescence: a marginal structural modeling approach. *Soc. Dev.* 23:753–69

Dieter JNI, Emory EK, Johnson KC, Raynor BD. 2008. Maternal depression and anxiety effects on the human fetus: preliminary findings and clinical implications. *Infant Ment. Health J.* 29:420–41

Dimidjian S, Goodman SH, Felder J, Gallop R, Brown A, Beck A. 2016. Staying well during pregnancy and the postpartum: a pilot randomized trial of mindfulness-based cognitive therapy for the prevention of depressive relapse/recurrence. *J. Consult. Clin. Psychol.* 84:134–45

Dipietro JA, Kivlighan KT, Costigan KA, Rubin SE, Shiffler DE, et al. 2010. Prenatal antecedents of newborn neurological maturation. *Child Dev.* 81:115–30

Dipietro JA, Voegtline KM, Pater HA, Costigan KA. 2018. Predicting child temperament and behavior from the fetus. *Dev. Psychopathol.* 30:855–70

Duan C, Hare MM, Staring M, Deligiannidis KM. 2019. Examining the relationship between perinatal depression and neurodevelopment in infants and children through structural and functional neuroimaging research. *Int. Rev. Psychiatry* 31:264–79

Evans J, Heron J, Patel R, Wiles N. 2007. Depressive symptoms during pregnancy and low birth weight at term: longitudinal study. *Br. J. Psychiatry* 191:84–85

Evans J, Melotti R, Heron J, Ramchandani P, Wiles N, et al. 2012. The timing of maternal depressive symptoms and child cognitive development: a longitudinal study. *J. Child Psychol. Psychiatry* 53:632–40

Feurer C, Hammen CL, Gibb BE. 2016. Chronic and episodic stress in children of depressed mothers. *J. Clin. Child Adolesc. Psychol.* 45:270–78

Fisher SD, Wisner KL, Clark CT, Sit DK, Luther JF, Wisniewski S. 2016. Factors associated with onset timing, symptoms, and severity of depression identified in the postpartum period. *J. Affect. Disord.* 203:111–20

Foley DL, Pickles A, Simonoff E, Maes HH, Silberg JL, et al. 2001. Parental concordance and comorbidity for psychiatric disorder and associate risks for current psychiatric symptoms and disorders in a community sample of juvenile twins. *J. Child Psychol. Psychiatry* 42:381–94

An important reminder of the need for, and potential benefits from taking, an international perspective on intergenerational transmission.

Foster CE, Webster MC, Weissman MM, Pilowsky DJ, Wickramaratne PJ, et al. 2008. Course and severity of maternal depression: associations with family functioning and child adjustment. *J. Youth Adolesc.* 37:906–16

Fredriksen E, von Soest T, Smith L, Moe V. 2019. Parenting stress plays a mediating role in the prediction of early child development from both parents' perinatal depressive symptoms. *J. Abnorm. Child Psychol.* 47:149–64

Glover V, O'Donnell KJ, O'Connor TG, Fisher J. 2018. Prenatal maternal stress, fetal programming, and mechanisms underlying later psychopathology—a global perspective. *Dev. Psychopathol.* 30:843–54

Provided a comprehensive model for understanding intergenerational transmission of depression; newer evidence provides further support, albeit with a more nuanced understanding of risk.

Goodman SH, Brogan D, Lynch ME, Fielding B. 1993. Social and emotional competence in children of depressed mothers. *Child Dev.* 64:516–31

Goodman SH, Cullum KA, Dimidjian S, River LM, Kim CY. 2018. Opening windows of opportunities: evidence for interventions to prevent or treat depression in pregnant women being associated with changes in offspring's developmental trajectories of psychopathology risk. *Dev. Psychopathol.* 30:1179–96

Goodman SH, Garber J. 2017. Evidence-based interventions for depressed mothers and their young children. *Child Dev.* 88:368–77

Goodman SH, Gotlib IH. 1999. Risk for psychopathology in the children of depressed mothers: a Developmental Model for Understanding Mechanisms of Transmission. *Psychol. Rev.* 106:458–90

Goodman SH, Rouse MH, Connell A, Broth M, Hall C, Heyward D. 2011. Maternal depression and child psychopathology: a meta-analytic review. *Clin. Child Fam. Psychol. Rev.* 14(1):1–27

A comprehensive review of depression in mothers being associated with a range of functioning in children.

Goodman SH, Tully EC. 2009. Recurrence of depression during pregnancy: psychosocial and personal functioning correlates. *Depress. Anxiety* 26:557–67

Gruhn MA, Dunbar JP, Watson KH, Reising MM, McKee L, et al. 2016. Testing specificity among parents' depressive symptoms, parenting, and child internalizing and externalizing symptoms. *J. Fam. Psychol.* 30:309–19

Guintivano J, Manuck T, Meltzer-Brody S. 2018. Predictors of postpartum depression: a comprehensive review of the last decade of evidence. *Clin. Obstet. Gynecol.* 61:591–603

Gustafsson H, Grieve P, Werner E, Desai P, Monk C. 2018. Newborn electroencephalographic correlates of maternal prenatal depressive symptoms. *J. Dev. Orig. Health Dis.* 9(4):381–85

Hammen C. 2002. Context of stress in families of children with depressed parents. In *Children of Depressed Parents: Mechanisms of Risk and Implications for Treatment*, ed. SH Goodman, IH Gotlib, pp. 175–202. Washington, DC: Am. Psychol. Assoc.

Hankin BL, Mermelstein R, Roesch L. 2007. Sex differences in adolescent depression: stress exposure and reactivity models. *Child Dev.* 78:279–95

Hasler G, Drevets WC, Manji HK, Charney DS. 2004. Discovering endophenotypes for major depression. *Neuropsychopharmacology* 29:1765–81

Heron J, O'Connor TG, Evans J, Golding J, Glover V. 2004. The course of anxiety and depression through pregnancy and the postpartum in a community sample. *J. Affect. Disord.* 80:65–73

Hishinuma ES, Chang JY, McArdle JJ, Hamagami F. 2012. Potential causal relationship between depressive symptoms and academic achievement in the Hawaiian High Schools Health Survey using contemporary longitudinal latent variable change models. *Dev. Psychol.* 48:1327–42

Horowitz JL, Garber J. 2003. Relation of intelligence and religiosity to depressive disorders in offspring of depressed and nondepressed mothers. *J. Am. Acad. Child Adolesc. Psychiatry* 42:578–86

Jacobs N, van Os J, Derom C, Thiery E, Delespaul P, Wichers M. 2011. Neuroticism explained? From a non-informative vulnerability marker to informative person–context interactions in the realm of daily life. *Br. J. Clin. Psychol.* 50:19–32

Jarde A, Morais M, Kingston D, Giallo R, MacQueen GM, et al. 2016. Neonatal outcomes in women with untreated antenatal depression compared with women without depression: a systematic review and meta-analysis. *JAMA Psychiatry* 73:826–37

Kendler KS. 2019. From many to one to many—the search for causes of psychiatric illness. *JAMA Psychiatry* 76:1085–91

Essential reading for understanding the need to move away from monocausal models.

Kendler KS, Gardner CO, Neale MC, Prescott CA. 2001. Genetic risk factors for major depression in men and women: similar or different heritabilities and same or partly distinct genes? *Psychol. Med.* 31:605–16

Kessler RC, Berglund P, Demler O, Jin R, Koretz D, et al. 2003. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA* 289:3095–105

Kessler RC, Zhao S, Blazer DG, Swartz M. 1997. Prevalence, correlates, and course of minor depression and major depression in the National Comorbidity Survey. *J. Affect. Disord.* 45:19–30

Kinsella MT, Monk C. 2009. Impact of maternal stress, depression and anxiety on fetal neurobehavioral development. *Clin. Obstet. Gynecol.* 52:425–40

Klein DN, Allmann AE. 2014. Course of depression: persistence and recurrence. In *Handbook of Depression*, ed. IH Gotlib, CL Hammen, pp. 64–83. New York: Guilford. 3rd ed.

Kovacs M, Akiskal HS, Gatsionis C, Parrone PL. 1994. Childhood-onset dysthymic disorder: clinical features and prospective naturalistic outcome. *Arch. Gen. Psychiatry* 51:365–74

Latendresse G, Wong B, Dyer J, Wilson B, Baksh L, Hogue C. 2015. Duration of maternal stress and depression: predictors of newborn admission to neonatal intensive care unit and postpartum depression. *Nurs. Res.* 64:331–41

Letourneau N, Tramonte L, Willms JD. 2013. Maternal depression, family functioning and children's longitudinal development. *J. Pediatr. Nurs.* 28:223–34

Lewinsohn PM, Rohde P, Seeley JR, Klein DN, Gotlib IH. 2003. Psychosocial functioning of young adults who have experienced and recovered from major depressive disorder during adolescence. *J. Abnorm. Psychol.* 112:353–63

Lewis G, Neary M, Polek E, Flouri E, Lewis G. 2017. The association between paternal and adolescent depressive symptoms: evidence from two population-based cohorts. *Lancet Psychiatry* 4:920–26

Lewis G, Neary M, Polek E, Flouri E, Lewis G. 2018. Paternal and maternal depression and offspring risk: additive effects or worse?—Authors' reply. *Lancet Psychiatry* 5:108

Lieb R, Isensee B, Hofler M, Pfister H, Wittchen H-U. 2002. Parental major depression and the risk of depression and other mental disorders in offspring. *Arch. Gen. Psychiatry* 59:365–74

Lovejoy MC, Graczyk PA, O'Hare E, Neuman G. 2000. Maternal depression and parenting behavior: a meta-analytic review. *Clin. Psychol. Rev.* 20:561–92

Malm H, Brown AS, Gissler M, Gyllenberg D, Hinkka-Yli-Salomäki S, et al. 2016. Gestational exposure to selective serotonin reuptake inhibitors and offspring psychiatric disorders: a national register-based study. *J. Am. Acad. Child Adolesc. Psychiatry* 55:359–66

Mayes LC, Bornstein MH. 1997. *Attention Regulation in Infants Born at Risk: Prematurity and Prenatal Cocaine Exposure*. New York: Guilford

McLaughlin KA, DeCross SN, Jovanovic T, Tottenham N. 2019. Mechanisms linking childhood adversity with psychopathology: learning as an intervention target. *Behav. Res. Therapy* 118:101–9

Mineka S, Vrshek-Schallhorn S. 2014. Comorbidity of unipolar depressive and anxiety disorders. In *Handbook of Depression*, ed. IH Gotlib, CL Hammen, pp. 84–102. New York: Guilford. 3rd ed.

Moffitt TE, Harrington H, Caspi A, Kim-Cohen J, Goldberg D, et al. 2007. Depression and generalized anxiety disorder: cumulative and sequential comorbidity in a birth cohort followed prospectively to age 32 years. *JAMA Psychiatry* 64:651–60

Monti JD, Rudolph KD. 2017. Maternal depression and trajectories of adolescent depression: the role of stress responses in youth risk and resilience. *Dev. Psychopathol.* 29:1413–29

Moss KM, Loxton D, Dobson AJ, Slaughter V, Mishra GD. 2020. Testing competing mediators of the association between pre-conception maternal depression and child health-related quality of life: the MatCH study. *Arch. Women's Ment. Health* 23:53–62

Murray L, Arteche A, Fearon P, Halligan S, Goodyer I, Cooper P. 2011. Maternal postnatal depression and the development of depression in offspring up to 16 years of age. *J. Am. Acad. Child Adolesc. Psychiatry* 50:460–70

Naicker K, Wickham M, Colman I. 2012. Timing of first exposure to maternal depression and adolescent emotional disorder in a national Canadian cohort. *PLOS ONE* 7(3):e33422

Natsuaki MN, Shaw DS, Neiderhiser JM, Ganiban JM, Harold GT, et al. 2014. Raised by depressed parents: Is it an environmental risk? *Clin. Child Fam. Psychol. Rev.* 17:357–67

Netsi E, Pearson RM, Murray L, Cooper P, Craske MG, Stein A. 2018. Association of persistent and severe postnatal depression with child outcomes. *JAMA Psychiatry* 75:247–53

Neuhauser A, Ramseier E, Schaub S, Burkhardt SC, Lanfranchi A. 2018. Mediating role of maternal sensitivity: enhancing language development in at-risk families. *Infant Ment. Health J.* 39:522–36

NICHD (Natl. Inst. Child Health Hum. Dev.) Early Child Care Res. Netw. 1999. Chronicity of maternal depressive symptoms, maternal sensitivity, and child functioning at 36 months. *Dev. Psychol.* 35:1297–310

Nolen-Hoeksema S, Girgus J. 1994. The emergence of gender differences in depression during adolescence. *Psychol. Bull.* 115:424–43

Nomura Y, Davey K, Pehme PM, Finik J, Glover V, et al. 2019. Influence of in utero exposure to maternal depression and natural disaster-related stress on infant temperament at 6 months: the children of Superstorm Sandy. *Infant Ment. Health J.* 40:204–16

Nomura Y, Wickramaratne PJ, Pilowsky DJ, Newcorn JH, Bruder-Costello B, et al. 2007. Low birth weight and risk of affective disorders and selected medical illness in offspring at high and low risk for depression. *Compr. Psychiatry* 48:470–78

O'Connor EE, Langer DA, Tompson MC. 2017. Maternal depression and youth internalizing and externalizing symptomatology: severity and chronicity of past maternal depression and current maternal depressive symptoms. *J. Abnorm. Child Psychol.* 45:557–68

O'Donnell KJ, Meaney MJ. 2017. Fetal origins of mental health: the developmental origins of health and disease hypothesis. *Am. J. Psychiatry* 174:319–28

Olfson M, Blanco C, Marcus SC. 2016. Treatment of adult depression in the United States. *JAMA Intern. Med.* 176:1482–91

Patton GC, Coffey C, Carlin JB, Olsson CA, Morley R. 2004. Prematurity at birth and adolescent depressive disorder. *Br. J. Psychiatry* 184:446–47

Pawlby S, Hay D, Sharp D, Waters CS, Pariante CM. 2011. Antenatal depression and offspring psychopathology: the influence of childhood maltreatment. *Br. J. Psychiatry* 199:106–12

Pearson RM, Evans J, Kounali D, Lewis G, Heron J, et al. 2013. Maternal depression during pregnancy and the postnatal period: risks and possible mechanisms for offspring depression at age 18 years. *JAMA Psychiatry* 70:1312–19

Posner J, Cha J, Roy A, Peterson B, Bansal R, et al. 2016. Alterations in amygdala–prefrontal circuits in infants exposed to prenatal maternal depression. *Transl. Psychiatry* 6:e935

Price JL, Drevets WC. 2009. Neurocircuitry of mood disorders. *Neuropsychopharmacology* 35:192–216

Prinzie P, Stams GJ, Dekovic M, Reijntjes AH, Belsky J. 2009. The relations between parents' Big Five personality factors and parenting: a meta-analytic review. *J. Pers. Soc. Psychol.* 97:351–62

Psychogiou L, Russell G, Owens M. 2020. Parents' postnatal depressive symptoms and their children's academic attainment at 16 years: pathways of risk transmission. *Br. J. Psychol.* 111(1):1–16

Qiu A, Shen M, Buss C, Chong Y-S, Kwek K, et al. 2017. Effects of antenatal maternal depressive symptoms and socio-economic status on neonatal brain development are modulated by genetic risk. *Cereb. Cortex* 27:3080–92

Reuben JD, Shaw DS. 2015. Resilience in the offspring of depressed mothers: variation across risk, domains, and time. *Clin. Child Fam. Psychol. Rev.* 18:300–27

Rice F, Harold G, Boivin J, van den Bree M, Hay D, Thapar A. 2010. The links between prenatal stress and offspring development and psychopathology: disentangling environmental and inherited influences. *Psychol. Med.* 40:335–45

Richards D. 2011. Prevalence and clinical course of depression: a review. *Clin. Psychol. Rev.* 31:1117–25

Rifkin-Graboi A, Bai J, Chen H, Hameed WBR, Sim LW, et al. 2013. Prenatal maternal depression associates with microstructure of right amygdala in neonates at birth. *Biol. Psychiatry* 74:837–44

Rouse MH, Goodman SH. 2014. Perinatal depression influences on negative affectivity: timing, severity, and co-morbid anxiety. *Infant Behav. Dev.* 37:739–51

Salisbury AL, Wisner KL, Pearlstein T, Battle CL, Stroud L, Lester BM. 2011. Newborn neurobehavioral patterns are differentially related to prenatal maternal major depressive disorder and serotonin reuptake inhibitor treatment. *Depress. Anxiety* 28:1008–19

Sanders MR, Kirby JN, Tellegen CL, Day JJ. 2014. The Triple P-Positive Parenting Program: a systematic review and meta-analysis of a multi-level system of parenting support. *Clin. Psychol. Rev.* 34:337–57

Sandman CA. 2010. Human fetal heart rate: a unique opportunity to assess the fetal programming hypothesis. *Infant Child Dev.* 19:76–79

Sawyer KM, Zunszain PA, Dazzan P, Pariante CM. 2019. Intergenerational transmission of depression: clinical observations and molecular mechanisms. *Mol. Psychiatry* 24:1157–77

Scher CD, Ingram RE, Segal ZV. 2005. Cognitive reactivity and vulnerability: empirical evaluation of construct activation and cognitive diatheses in unipolar depression. *Clin. Psychol. Rev.* 25:487–510

Segal ZV, Williams JMG, Teasdale J. 2018. *Mindfulness-Based Cognitive Therapy for Depression*. New York: Guilford. 2nd ed.

Sellers R, Harold GT, Elam K, Rhoades KA, Potter R, et al. 2014. Maternal depression and co-occurring antisocial behaviour: testing maternal hostility and warmth as mediators of risk for offspring psychopathology. *J. Child Psychol. Psychiatry* 55:112–20

Silveira PP, Pokhvisneva I, Parent C, Cai S, Rema ASS, et al. 2017. Cumulative prenatal exposure to adversity reveals associations with a broad range of neurodevelopmental outcomes that are moderated by a novel, biologically informed polygenetic score based on the serotonin transporter solute carrier family C6, member 4 (SLC6A4) gene expression. *Dev. Psychopathol.* 29:1601–17

Silverstein M, Diaz-Linhart Y, Cabral H, Beardslee W, Hegel M, et al. 2017. Efficacy of a maternal depression prevention strategy in Head Start: a randomized clinical trial. *JAMA Psychiatry* 74:781–89

Stein A, Pearson RM, Goodman SH, Rapa E, Rahman A, et al. 2014. Effects of perinatal mental disorders on the fetus and child. *Lancet* 384:1800–19

A comprehensive review of associations between depression in mothers and functioning in children, focusing on moderators or confounding variables.

Teti DM, Gelfand DM, Messinger DS, Isabella R. 1995. Maternal depression and the quality of early attachment: an examination of infants, preschoolers, and their mothers. *Dev. Psychol.* 31:364–76

Thomason M, Hect JL, van den Heuvel MI, Marshall NA, Waller R, et al. 2017. High stress in pregnant mothers is associated with reduced global brain efficiency in the fetus. *Biol. Psychiatry* 81(10 Suppl.):S298–99

Tryon WW. 2018. Mediators and mechanisms. *Clin. Psychol. Sci.* 6:619–28

Essential paper for understanding limits of tests of mediation for informing mechanisms.

van Batenburg-Eddes T, Brion M, Henrichs J, Jaddoe V, Hofman A, et al. 2013. Parental depressive and anxiety symptoms during pregnancy and attention problems in children: a cross-cohort consistency study. *J. Child Psychol. Psychiatry* 54:591–600

van der Waerden J, Galéra C, Larroque B, Saurel-Cubizolles M-J, Sutter-Dallay A-L, Melchior M. 2015. Maternal depression trajectories and children's behavior at age 5 years. *J. Pediatr.* 166:1440–48.e1

Vigod SN, Villegas L, Dennis CL, Ross LE. 2010. Prevalence and risk factors for postpartum depression among women with preterm and low-birth-weight infants: a systematic review. *BJOG* 117:540–50

Viktorin A, Meltzer-Brody S, Kuja-Halkola R, Sullivan PF, Landén M, et al. 2016. Heritability of perinatal depression and genetic overlap with nonperinatal depression. *Am. J. Psychiatry* 173:158–65

Weissman MM, Berry OO, Warner V, Gameroff MJ, Skipper J, et al. 2016. A 30-year study of 3 generations at high risk and low risk for depression. *JAMA Psychiatry* 73:970–77

Weissman MM, Gammon D, John K, Merikangas KR, Warner V, et al. 1987. Children of depressed parents: increased psychopathology and early onset of major depression. *Arch. Gen. Psychiatry* 44:847–53

Yan N. 2016. Children's resilience in the presence of mothers' depressive symptoms: examining regulatory processes related to active agency. *Child. Youth Serv. Rev.* 61:90–100

Zimmerman M, Ellison W, Young D, Chelminski I, Dalrymple K. 2015. How many different ways do patients meet the diagnostic criteria for major depressive disorder? *Compr. Psychiatry* 56:29–34