Maternal depression affects both mother and child and has significant long-term negative effects on infant development and child mental health risk (Goodman et al., 2011). The risks conferred by maternal depression experienced during the postpartum period have long been recognized; indeed mental health interventions have been developed to reduce postpartum maternal depression and, in turn, mitigate risk to child development. In contrast, the unique impact of depression experienced during the prenatal period on offspring development has only recently been understood. The potential positive effects that reducing prenatal depression could have on infant and child development are important to understand as they can set children on an early positive developmental trajectory. In addition, such interventions may be more economically efficient and more likely to reduce personal and societal burden than managing psychological symptoms and problematic behaviors after they arise. In this article, we review the deleterious effects of prenatal depression on fetal development as it relates to risk for later child psychopathology, describe an evidence-based psychosocial intervention for prenatal depression, and discuss how interventions to reduce maternal depression during pregnancy are uniquely situated to have cascading positive effects for

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both mother and child. Throughout the article we will use a composite case study of “Melissa,” a 24-year-old pregnant, Latina, single mother of a 5-year-old boy “Max,” to illustrate this idea.

Depression During Pregnancy

Depression is one of the most common prenatal complications. Studies suggest that rates of depression are as high or higher during pregnancy as compared to the postpartum period (Evans, Heron, Francomb, Oke, & Golding 2001). During pregnancy, an estimated 8.5 to 11% of women meet diagnostic criteria for major or minor depression (Gaynes et al., 2005), and even more women report elevated levels of prenatal depressive symptoms (Marcus, Flynn, Blow, & Barry, 2003). Rates of depression among high-risk samples of pregnant women, such as those exposed to contextual risk factors (e.g., poverty, racism, and violence), may be as high as 25% (Hobfoll, Ritter, Lavin, Hulsizer, & Cameron, 1995). Examples of psychosocial stressors experienced by pregnant women include lack of access to material resources, unfavorable employment conditions, heavy family and household responsibilities, low levels of social support, strain in intimate relationships, and medical complications. Some women, particularly those working lower status jobs, may find it difficult to attend prenatal appointments because of employer demands. The overlap of some depressive symptoms with pregnancy-related physical symptoms, such as sleep and appetite disturbances and fatigue, may be particularly burdensome for some women and may result in depressive symptoms being incorrectly attributed to pregnancy. Further, depressive symptoms are related to poor health behaviors in pregnant women including inadequate weight gain and substance use (Zuckerman et al., 1989), which further jeopardize the health of mother and child.

During a prenatal appointment in her first trimester, Melissa disclosed to her doctor that her current pregnancy was unplanned and she was experiencing conflict with, and receiving little support from, the father of her baby, who had wanted her to terminate the pregnancy. She reported depressed mood, excessive guilt, and crying spells, which she tried to hide from her son, and she had reduced interest in her usual activities, although she felt pressure to “put on a smile” for her son. She was unemployed and had missed recent job interviews as well as her prior prenatal appointment because she was struggling to get going and get out of the house in the morning. She was fatigued, spent much of the day napping, and struggled to make herself eat regular meals. Indeed, her doctor noted her failure to gain expected weight.

How Does Prenatal Depression Impact Offspring?

Development is more rapid during the prenatal period as compared to any other stage of life. The Fetal Programming and Developmental Origins of Disease models suggest that during periods of rapid fetal development or change, the fetus is particularly susceptible to environmental influences; these effects are thought to have persisting consequences for health and disease risk across the lifespan (Barker, 1998). In this way, prenatal depression may influence risk processes for subsequent psychopathology in offspring. Prenatal depression is linked to numerous, immediate adverse physical outcomes such as preterm birth (Fransson, Åden, Blennow, & Lagercrantz, 2011; 1.56 greater odds) and low birth weight (Grote et al., 2010), both of which have long-lasting implications for baby’s developmental course. In fact, the initial fetal programming studies illustrated that low birth weight predicted a range of physical and mental health outcomes including heart disease, diabetes, attention-deficit/hyperactivity disorder, and anxiety (Barker, Eriksson, Forsén, & Osmond, 2002; Class et al., 2014; Sømhovd, Hansen, Brok, Esbjørn, & Greisen, 2012). The consequences of prenatal depression on preterm birth and low birth weight appear to be greater for disadvantaged women (Alder, Fink, Bitzer, Hösl & Holzgreve, 2007).

Melissa experienced depression while pregnant with her son, Max. Max was born at 34 weeks gestation and he spent 2 weeks in the neonatal intensive care unit. She was very motivated to do what she could to carry her new baby to term, not feel incapacitated due to her depression, and avoid another neonatal intensive care unit stay for her new baby.

According to the Fetal Programming hypothesis, alterations to developing brain systems may be one of the key processes underlying the link between prenatal depression and offspring vulnerability to psychopathology. In addition, fetal exposure to maternal stressful negative life events (e.g., job loss, conflict with family), chronic psychosocial stress (e.g., experienced racism and homelessness), and stress hormones during the prenatal period continue to influence brain development, regulation of stress and emotion, and cognitive functioning throughout development and may contribute
to the development of psychopathology (Huizink, Robles de Medina, Mulder, Visser, & Buitelaar 2003; Talge, Neal, Glover et al., 2007). It is important to note that these effects persist after considering postpartum influences (Bergman, Sarkar, O’Connor, Modi, & Glover, 2007). Prenatal depression may impact the offspring, and thus confer risk for later psychopathology, through four key pathways including alteration of brain development, physiological stress systems, negative emotionality, and cognitive control.

Brain Development
The exceptionally rapid pace of fetal brain development renders it susceptible to various influences. Neurogenesis, migration, axon and dendrite formation, as well as a multitude of other processes occur at an extraordinary pace throughout gestation. The brain of a full-term newborn has 100 billion neurons. Studies have revealed that prenatal depressive symptoms predict aspects of brain structure and function during infancy that pose risk for later psychopathology. For example, elevated prenatal depressive symptoms are associated with differences in amygdala functioning and structure as well as increased connectivity between prefrontal and limbic areas of the brain (Posner et al., 2016; Qiu et al., 2015). The impact of prenatal depressive symptoms on brain structure and function extends into childhood. Affected neural regions are related to greater child stress and emotional reactivity (Davis, Sandman, Buss, Wing, & Head, 2013; Sandman et al., 2018) and may contribute to risk for the development of psychopathology, particularly anxiety and depression (Lupien et al., 2011; Pérez-Edgar et al., 2007; Price & Drevets, 2010). For example, Sandman and colleagues (Sandman, Buss, Head, & Davis, 2015) found that prenatal depressive symptoms predicted decreased child cortical thickness at 6–9 years old, predominantly in frontal and temporal regions.

Stress Physiology
The hypothalamic-pituitary-adrenal (HPA) axis is one of the body’s primary stress regulatory systems and contributes to mental health. The prenatal environment is thought to affect the development of the offspring’s HPA axis (Davis, Glynn, Waffarn, & Sandman, 2011). Infants of mothers with prenatal depression demonstrate higher baseline cortisol concentrations (Field et al., 2004) and greater cortisol reactivity to stressors as compared to infants of mothers without prenatal depression (Brennan et al., 2008). Cortisol is a stress hormone that acts to mobilize the body’s resources to support the fight or flight response; short-term increases in cortisol are necessary to manage stress or challenge, but chronic elevations in cortisol may exert damaging effects. These effects of prenatal depression on dysregulated HPA-axis functioning, including a larger cortisol awakening response (Vánská et al., 2016) and heightened cortisol reactivity in response to stress (Fernandes et al., 2014; Tollefson, Beijers, Jansen, Riksen-Walraven, & de Weerth, 2011), continue into childhood (Guerry & Hastings, 2011; Lopez-Duran, Kovacs, & George, 2009).

Offspring Psychopathology: Early Links With Prenatal Depression
Prospective studies demonstrate a link between prenatal depression, at diagnostic and subclinical levels, and offspring psychopathology outcomes, including anxiety, depression, and attention deficit/hyperactivity disorder later in adolescence and adulthood over and above the effects of postnatal maternal depression (Barker, Jaffee, Uher, & Maughan, 2011; Clements et al., 2015; Korhonen, Luoma, Salmelin, & Tamminen, 2012; Luoma et al., 2001). In a study of psychopathology outcomes in adult offspring, offspring exposed to maternal depression prenatally were 3.4 times more likely to meet criteria for major depressive disorder after accounting for postnatal maternal depression (Plant, Pariante, Sharp, & Pawlby, 2015).
Implementing depression screening early in pregnancy can have a multitude of cascading positive effects for both mother and child.

When Max was a baby, Melissa had trouble soothing him when he began to cry, and her mother said he was a “fussy” baby. As Max grew up, she noticed that he often reacted to new situations or frustration by crying or having a temper tantrum. He had greater difficulty calming down when upset, compared to her cousins’ children. Max also had difficulty distracting himself after something upsetting had happened. His teachers noted that Max had difficulty following instructions, modulating his activity level to match his peers, and also had weeks when he became “moody” and withdrawn. Melissa wondered if his difficulties were related to the stress and depression she had experienced while pregnant with him. She worried that her new baby might have similar problems, which fueled her motivation to reduce her current levels of stress and depression.

In summary, prenatal depression may exert effects on early fetal development that influence fetal brain and physiological stress reactivity systems. These effects may subsequently place the offspring at risk for a broad range of later psychopathology through intermediate risk mechanisms such as HPA-axis dysregulation, negative emotionality, and poor cognitive control that may be observed as early as infancy and toddlerhood. The evidence that the effects of prenatal depression persist after accounting for postpartum depression suggests the importance of looking to reduce maternal depression during the prenatal period in order to maximally decrease offspring risk for psychopathology. Further, the prevalence of prenatal depression and its unique contribution to offspring risk highlight the importance of addressing prenatal depression for professionals interested in child development and welfare.

Is Pregnancy an Optimal Time to Intervene on Maternal Depression?

During the prenatal period, women are better connected to the health care system because they have regular prenatal medical appointments, may be more receptive to guidance from a skilled professional (Battle, Salisbury, Schofield, & Ortiz-Hernandez, 2013; Dimidjian & Goodman, 2014), and may have more time relative to the postpartum period when they have a newborn for whom to care. Further, prenatal depression is a strong predictor of postpartum depression (O’Hara & Swain, 1996). For these reasons, the prenatal period provides a unique and opportune time to help women connect to mental health services.

Benefits of Prenatal Intervention for Mothers

Recommendations for prenatal care made by the American College of Obstetricians and Gynecologists include administration of a depression screener, for example the Edinburgh Postnatal Depression Screener (Cox, Holden, & Sagovsky, 1987), during the perinatal period. A few states (currently New Jersey, Illinois, and West Virginia) have adopted perinatal depression screenings as part of their health care policy. Such screenings put pregnancy health care providers in a unique position to be aware of their patients’ mental health and assist in connecting them to resources important for both mother and child (Rhodes & Segre, 2013). However, only West Virginia and Illinois specifically advocate screening during pregnancy. Implementing depression screening early in pregnancy can have a multitude of cascading positive effects for both mother and child. Having well-managed or remitted depression and established connections to mental health care benefits maternal mental health and fetal development and reduces the risk of postpartum depression (Grote et al., 2015). Establishing treatment during the prenatal period can help prepare the mother for the stressful and demanding postpartum period and ease adjustment to motherhood for first-time mothers (Collins, Dunkel-Schetter, Lobel, & Scrimshaw, 1993; Zlotnick, Johnson, Miller, Pearlstein, & Howard 2001). Sustained connection to a therapist throughout pregnancy and into the postpartum period allows for a quicker increase in support in response to resurgent depressive symptoms and socioeconomic stressors.

Despite the stressors Melissa experienced, she prioritized attending her prenatal appointments and was receptive to her midwife’s advice. Melissa’s midwife administered the Edinburgh Postnatal Depression Screener at her first prenatal visit and, based on her elevated score, discussed treatment options with her. Melissa was open to pursuing therapy because she was motivated to feel better and recognized that she would need greater support after the baby arrived.

Advantages of Prenatal Intervention for Child Outcomes

A small number of randomized control trials (RCTs) have shown that reducing a woman’s postpartum maternal depressive symptoms via intervention can impact her children’s psychopathological symptoms (for meta-analysis see Cuijpers, Weitz, Karyotaki, Garber, & Andersson, 2015). For example, in one RCT, psychotherapy for maternal depression showed reductions in child self-reported depressive symptoms at a 9-month follow-up (Swartz, Williamson, & Hariri, 2015).
Few research studies, to date, have tested the effect of reducing maternal depression prenatally on infant and child neuro-developmental outcomes (O’Connor, Monk, & Burke, 2016). Given the strong correlation between prenatal depression and a range of child developmental outcomes, intervention to reduce prenatal depression may be the most effective way to mitigate these early risks, including disrupted brain development, heightened stress reactivity, and negative emotionality, during a time of rapid development when these systems are most susceptible to environmental influences. Few studies have examined the effects of a psychotherapy intervention for prenatal depression on offspring psychological risk factors. As one example, 9-month-old infants of mothers whose prenatal depression was treated with cognitive–behavioral therapy evidenced less mother-reported reactivity to stress and negative affect compared to infants of mothers in the control group (Milgrom et al., 2015).

Interventions for Prenatal Maternal Depression

We focus on psychotherapy interventions for prenatal depression. Patients report enhanced preference for psychotherapy as compared to medication (Cuijpers, Cristea, Karyotaki, Reijnders, & Huibers, 2016). Also there is considerable debate regarding the safety of antidepressant medication usage during pregnancy for the developing fetus and later child outcomes (Udechuku, Nguyen, Hill, & Szego, 2010). There is a strong evidence base for the efficacy of psychotherapy for reducing prenatal depression (Grote et al., 2015; O’Mahen, Himie, Fedock, Henshaw, & Flynn, 2013; Spinelli, Endicott, & Goetz, 2016). In particular, adaptations of cognitive–behavioral therapy and interpersonal psychotherapy (IPT) have most often been tested. For example, evidence-based IPT that has been modified in order to engage and retain pregnant women of socioeconomically disadvantaged backgrounds in mental health treatment decreases depression during pregnancy relative to usual care (Grote et al., 2015).

Overview of Brief IPT and Its Application to Pregnant Women

Prenatal depression is strongly related to lack of social support, particularly from the spouse or partner (O’Hara & Swain 1996), which makes an interpersonal approach to the treatment of prenatal depression highly relevant. In fact, maternal social support during pregnancy has been linked to higher birth weight, positive birth outcomes, and child developmental outcomes (Feldman, Dunkel-Schetter, Sandman, & Wadhwa, 2000).

A brief version of IPT, consisting of 8 weekly individual sessions, has been developed (Swartz et al., 2004), and it received empirical support in a number of studies of pregnant women with depression (Grote et al., 2015; Swartz et al., 2004). It retains the core features of standard IPT, such as strengthening social supports, building on patient strengths and coping strategies, and resolving interpersonal problems. At the same time, brief IPT offers several advantages over standard IPT. First, it reduces the treatment burden for overwhelmed, pregnant, or parenting women with multiple acute and chronic stressors. Second, to promote a quicker treatment response, brief IPT techniques have been expanded to include behavioral activation strategies (Jacobson, Martell, & Dimidjian, 2006) that can be shared with family members or friends and assigned as weekly homework with an interpersonal focus. Treatment is focused on reducing symptoms and improving functioning in one of four possible interpersonal problem areas most closely linked with the onset of their depression. The problem areas are: (a) Role Transition, a life upheaval such as geographic move or becoming physically ill; (b) Role Dispute, a conflict with a significant other; (c) Complicated Grief, the death of a loved one; or (d) Complicated Pregnancy. Complicated Pregnancy addresses myriad difficulties women may experience navigating this life transition, including conflict with the father of the baby, medical issues related to the pregnancy, and unplanned nature of the pregnancy (Spinelli & Endicott, 2003).

Adaptations of MOMCare for Socioeconomically Disadvantaged Pregnant Women

MOMCare uses brief IPT to treat depression within a collaborative care model (Katon, 2003). The collaborative care model helps patients become active participants in their depression treatment, which is provided within the primary care setting by at least a masters-level mental health provider, supervised by a mental health team (e.g., can include an experienced IPT therapist and a prescribing medical doctor such as psychiatry or obstetrician).

MOMCare has been enhanced to be culturally relevant to pregnant, economically disadvantaged, racially/ethnically diverse women with depression (Grote, Swartz, & Zuckoff, 2008). MOMCare’s cultural enhancements are designed to be relevant to the culture of race/ethnicity (Brown, Abe-Kim, & Barrio, 2003) and the culture of poverty (Belle, 2007). First, MOMCare includes a pre–treatment engagement session prior to beginning therapy (Grote, Zuckoff, Swartz, Bledsoe, & Geibel, 2007). The engagement session is designed (a) to address the woman’s ambivalence about, and commitment to, treatment and (b) to identify and attempt to resolve her unique practical, psychological, and cultural barriers to care, including finances, child care, transportation, scheduling problems, previous negative experiences with treatment, the stigma of depression, or fear of being misunderstood by a therapist of a different background. In the engagement session, psychoeducation about depression and treatment options are also provided. Respect for the woman’s cultural preferences regarding treatment options, her goals, cultural resources, and strengths are incorporated throughout treatment.

In addition, to address unique needs of economically disadvantaged women, a case management component is integrated into brief IPT to assist them in applying for jobs and in finding safe housing, food, and baby supplies. To increase treatment accessibility, therapy sessions can be conducted over the
telephone. The therapist also engages in intensive outreach to retain patients in treatment, with telephone calls, texting, email, showing up at the patient’s non-stigmatizing public health setting, or meeting in coffee shops.

Melissa began treatment with a MOMCare therapist using brief IPT. She identified transportation and child care as significant barriers to treatment. She also shared that her mother had told her “being depressed is not something mothers have time for” and that these cultural views of depression as a mental weakness had prevented her from seeking treatment in the past. Melissa and her therapist decided to focus first on addressing her Complicated Pregnancy due to the unplanned nature of her pregnancy, little support from the father of the baby, and her financial stressors. Melissa and her therapist also worked on improving her communication with friends and family members who might be able to provide support during her pregnancy and as she prepared for birth.

Results from a randomized collaborative care trial of MOMCare showed that socioeconomically disadvantaged women with major depression, 58% of whom identified as a racial or ethnic minority, reported significantly greater improvement in depression severity and remission rates from before birth to 12 months postpartum, compared to intensive public health Maternity Support Services (Grote et al., 2015). Women with co-morbid posttraumatic stress disorder demonstrated the greatest improvements in depression (Grote et al., 2016). MOMCare also mitigated the risk of postpartum depressive symptoms and impaired functioning among women who experienced both prenatal depression and adverse birth events, such as preterm birth (Bhat et al., 2016), and was shown to be cost effective (Grote et al., 2017). In sum, findings from the MOMCare study suggest that a cost-effective collaborative care model reduces prenatal depression and could be integrated into obstetrics/gynecology clinics for pregnant women. Given the strengths of the MOMCare intervention model at reducing prenatal depression and addressing the unique challenges faced by disadvantaged pregnant women, MOMCare could be an optimal treatment to benefit both the mother and baby.

The Care Project: Does Reducing Prenatal Maternal Depression Improve Infant Outcomes?

Reducing postnatal maternal depression has positive effects on child development and may reduce risk for offspring psychopathology. Efficacious treatments exist to reduce prenatal depression (Grote et al., 2015; Spinelli et al., 2016). Yet at present, it is not known whether decreasing prenatal depression will positively impact fetal neurodevelopment and, in turn, mitigate infant risk for later psychopathology. Our current RCT, the Care Project, uses the MOMCare model to test whether reducing maternal depression during the prenatal period, a time of rapid fetal development, will reduce known risk factors in the offspring related to prenatal depression and, thus, reduce the likelihood that these offspring will develop subsequent psychopathology (Davis, Hankin, Swales, & Hoffmann, 2018). We are measuring maternal depression at numerous times beginning in pregnancy through 18 months postpartum and assessing infant risk mechanisms (see Figure 1). We measure infant risk mechanisms including structural brain development using MRI, stress reactivity via cortisol concentrations in infant hair and saliva, and negative emotionality and cognitive control.
from maternal report, electroencephalography, and standardized laboratory temperament tasks.

Summary and Conclusions

In sum, prenatal maternal depression has unique negative effects on infant and child development, including higher risk for offspring psychopathology, beyond the risk conferred by postpartum maternal depression. Intervening on prenatal depression has several unique advantages. Reducing prenatal depression may not only benefit maternal well-being but is an optimal window for promoting neurodevelopment of the offspring. Reducing prenatal depression may promote offspring adaptive brain development, HPA-axis regulation, and cognitive control, and may lessen negative emotionality. In addition, practical concerns make the prenatal period an opportune time to connect women to mental health services. However, additional research is needed to ascertain whether intervening on prenatal depression does in fact have the suggested positive effects on offspring mental health.

For women who initiate services during pregnancy, continued care at appropriate intervals maximizes the chance of maintaining remission of depressive symptoms across pregnancy and throughout the postpartum period. First-time mothers and mothers from high-risk backgrounds may be especially vulnerable to emergent stressors during the postpartum period. Sustained connections to mental health providers are likely to be more immediately effective than renegotiating barriers to care and reinitiating services at various points throughout the postpartum period. In sum, evidence-based intervention for prenatal depression, particularly culturally sensitive models designed to be effective for women at greatest risk for prenatal depression, have the potential to have a significant, positive, and long-lasting impact on both the mother and child.

Reducing prenatal depression may not only benefit maternal well-being but is an optimal window for promoting neurodevelopment of the offspring.

First-time mothers and mothers from high-risk backgrounds may be especially vulnerable to emergent stressors during the postpartum period.

Sarah E. Garcia, PhD, is a postdoctoral researcher at the University of Denver. She is interested in the early detection of risk for depression and anxiety in children and adolescents and the intergenerational transmission of internalizing psychopathology. She is also interested in how knowledge of differences in risk processes for internalizing disorders may allow better understanding of which treatments might work particularly well for certain individuals. She currently is a postdoctoral researcher and serves as a MOMCare therapist on the Care Project.

Nina E. Lillehei is a research assistant in the Neurodevelopment Research Project at the University of Denver. Nina graduated from the University of Denver with a bachelor of arts in psychology and sociology. She is interested in understanding intergenerational transmission of risk and resilience across families. She currently works as a recruiter and study coordinator for the Care Project.

Eleza R. Valente is a research assistant in the Neurodevelopment Research Lab at the University of Denver. She graduated from the University of Arizona with a bachelor of science in nutritional science and biochemistry. She has participated in clinical research with socially disadvantaged individuals and is interested in understanding how sleep influences physical and mental health. She currently works as a recruiter for the Care Project and is involved in assessment of biological processes in pregnant women.

Nancy K. Grote, PhD, MSW, is a research associate professor, emerita, at the School of Social Work, University of Washington. Dr. Grote has received national and local funding for adapting evidence-based models of depression care to be relevant both to the culture of poverty and to the culture of race/ethnicity and for disseminating culturally relevant, evidence-based treatments for perinatal depression in socioeconomically disadvantaged women in obstetrics/gynecology clinics, public health systems, and sites where pregnant and postpartum women addicted to drugs and alcohol receive treatment services. She is the creator of MOMCare and collaborator on the Care Project described in this report.

Benjamin L. Hankin, PhD, is the Kanfer Professor of Psychology at the University of Illinois. He is a developmental psychopathologist interested in understanding the etiology and trajectories of depression and related internalizing problems over the lifespan, and in conducting randomized clinical trials...
to reduce emotional distress and risk mechanisms in parents and youth. He currently is co-principal investigator of the Care Project.

Elysia Poggi Davis, PhD, is a professor of psychology at the University of Denver and is on the faculty in the Department of Psychiatry at the University of California, Irvine. Her program of research, supported by the National Institutes of Health, evaluates the way that biological and behavioral processes during the prenatal period influence developmental trajectories. Her research has demonstrated the prenatal maternal distress impacts neurodevelopment with consequences for mental health in the offspring. She currently is co-principal investigator of the Care Project.

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