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Pregnancy as a period of risk, adaptation, and resilience for mothers and infants

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Abstract

The pregnancy period represents a unique window of opportunity to identify risks to both the fetus and mother and to deter the intergenerational transmission of adversity and mental health problems. Although the maternal–fetal dyad is especially vulnerable to the effects of stress during pregnancy, less is known about how the dyad is also receptive to salutary, resilience-promoting influences. The present review adopts life span and intergenerational perspectives to review four key areas of research. The first part describes how pregnancy is a sensitive period for both the mother and fetus. In the second part, the focus is on antecedents of maternal prenatal risks pertaining to prenatal stress response systems and mental health. The third part then turns to elucidating how these alterations in prenatal stress physiology and mental health problems may affect infant and child outcomes. The fourth part underscores how pregnancy is also a time of heightened fetal receptivity to maternal and environmental signals, with profound implications for adaptation. This section also reviews empirical evidence of promotive and protective factors that buffer the mother and fetus from developmental and adaptational problems and covers a sample of rigorous evidence-based prenatal interventions that prevent maladaptation in the maternal–fetal dyad before babies are born. Finally, recommendations elaborate on how to further strengthen understanding of pregnancy as a period of multilevel risk and resilience, enhance comprehensive prenatal screening, and expand on prenatal interventions to promote maternal–fetal adaptation before birth.

Keywords

adaptation; adversity; intergenerational transmission; pregnancy; prenatal programming; resilience; stress

The prenatal period is a time of rapid development, when a multitude of psychological and physiological changes occur for both mother and fetus. Thus, pregnancy is a sensitive period when the dyad is vulnerable to the effects of adversity; however, mothers and infants also are especially receptive to salutary influences. Research has found that maternal exposure to adversity prior to conception (particularly during her childhood) can have transformative

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neurobiological and epigenetic effects that may be biologically embedded and transmitted to the fetus (Swales et al., 2018; Yehuda & Meaney, 2018). Compared to women without early-life adversity and mental health problems prior to pregnancy, pregnant women with a history of adversity and mental health problems may experience more risks to their mental health and more disruptions to their prenatal stress physiology. Therefore, their offspring may be at higher risk for developmental problems in the domains of stress regulation, mental health, cognitive development, and relationship formation (Sperlich & Seng, 2008; Yehuda & Meaney, 2018). In contrast, women's positive early-life experiences from childhood may be a source of strength and resilience and may have promotive and protective benefits for maternal and infant outcomes. Prenatal stress, mental health, and maternal wellbeing during pregnancy may therefore represent an important link between maternal early-life experiences and maternal and fetal health.

The present review focuses on the intergenerational transmission of risk and resilience during the pregnancy period, with a focus on understanding (a) antecedents of maternal prenatal mental health problems and stress rooted in maternal lifetime adversity, and (b) consequences of maternal mental health problems and stress on offspring outcomes. In this review, prenatal stress includes perceptions of stress as well as stress physiology, and mental health problems during pregnancy include depression, generalized anxiety (hereinafter referred to as anxiety) and post-traumatic stress disorder (PTSD). We focus on these three mental health problems because of their common occurrence in pregnant women, the increasing body of research specifically linking them to alterations in stress physiology during pregnancy, and the evidence that when these disorders occur during pregnancy, they are associated with fetal development.

In the United States, compared to non-pregnant women, pregnant women may experience twice the rate of depression (up to 20% vs. 10%; Center for Disease Control and Prevention (CDC), 2019b), and low-income pregnant women may experience more than three-fold rates of depression (approximately 30% to 50% vs. 10%; Choi & Sikkema, 2016; Narayan et al., 2017). Although more difficult to distinguish due to normative fears concerning pregnancy and childbirth, rates of prenatal anxiety also are higher compared to non-pregnant women (Dunkel Schetter & Tanner, 2012). Rates of PTSD, a less-studied prenatal mental health problem than depression and anxiety but an especially potent risk for women with childhood adversity, are also elevated in community samples of pregnant women compared to their non-pregnant counterparts (e.g., approximately 6%–8% compared to 4%–5%; Seng, Rauch, et al., 2010). In lower-income samples, PTSD symptoms may be clinically elevated in as many as 18%–29% of pregnant women or more, particularly if women are high-risk due to childhood adversity and pregnancy complications (Narayan et al., 2017; Narayan, Atzl, et al., 2019; Yildiz, Ayers, & Phillips, 2017). Many reasons may account for heightened rates of mental health problems during pregnancy. These include factors associated with the pregnancy (e.g., whether it was planned or wanted), support in the co-parenting relationship (e.g., whether the father of the baby provides support and wants the pregnancy), demographic and financial circumstances (e.g. socioeconomic status, access to concrete needs, number of children already in the family), and other emotional, and cognitive factors that may influence pregnant women's well-being (Narayan et al., 2019; Slade, Cohen, Sadler, & Miller, 2009; Sperlich & Seng, 2008). Physiologically, the massive hormonal

changes that occur normatively during the prenatal period may also unmask vulnerabilities in both physical (e.g., diabetes, hypertension) and mental (e.g., depression) health.

With a focus on mental health and stress during pregnancy, the current review synthesizes research that underscores pregnancy as a transformative opportunity to (a) understand how maternal mental health and stress lie at the intersection of mothers' and infants' wellbeing, and (b) harness and leverage resilience process to deter intergenerational transmission of stress and psychopathology in the next generation. In addition to a period of vulnerability when maternal mental health and stress may be exacerbated, pregnancy also is a window of possibility to nurture better mental health and promote recovery (Davis, Hankin, Swales, & Hoffman, 2018; Garcia et al., 2019; Narayan, Rivera, Bernstein, Harris, & Lieberman, 2018). Many women are motivated by the upcoming birth of a new child and optimistic for change. Women also typically have more contact with the medical system during their pregnancies, so there is greater opportunity for outreach and treatment (Davis et al., 2018; Narayan et al., 2017; River, Narayan, Galvan et al., 2019). Finally, empirical evidence points to increased plasticity in the maternal as well as the fetal brain during the prenatal period (Davis et al., 2019; Glynn, 2010, 2012; Glynn, Davis, Sandman, & Goldberg, 2016). For these reasons, understanding the antecedents and consequences of maternal mental health and stress during the prenatal period and applying life span and intergenerational perspectives are important for identifying opportunities for prevention and intervention to promote resilience.

This review is structured in four parts. The first section will provide an overview of the prenatal period as a sensitive period of development for both the fetus and the mother. The second section will focus on experiences of adversity that may be antecedents of maternal stress and mental health problems during the prenatal period. The scope of adversity includes childhood adversity, such as maltreatment and broader adverse childhood experiences (ACEs), which, in addition to maltreatment, include exposure to family/household dysfunction (i.e., parental divorce/separation, domestic violence, substance use, mental illness, and incarceration; CDC, 2019a; Felitti et al., 1998); and adulthood adversity, such as adulthood life stressors, and intimate partner violence (IPV) or other relationship conflict. The third section of the review will focus on prenatal maternal stress and mental health in relation to offspring development. The fourth section will focus on adaptation and resilience during the pregnancy period. Here, we present evidence that because maternal stress and mental health problems during pregnancy are strongly associated with fetal development, the signals that the fetus receives in the prenatal environment may promote adaptation to the postnatal world and also may be beneficial for development, growth, and survival. Finally, we discuss research and translational efforts to identify and promote resilience during the pregnancy period, arguing that pregnancy is a prime opportunity for prevention and intervention efforts designed to benefit maternal mental health and promote fetal infant development and wellbeing.

Pregnancy as a Sensitive Period for the Fetus and Mother: Biological Changes

Fetal development

The pace of fetal development far exceeds development during any other period of the life span. The dramatic transformation from a single-celled zygote to a newborn involves the formation and maturation of all major organ systems. The carefully orchestrated series of events that underlie the development of the brain are particularly complex. Brain development begins during gestation and continues into the postnatal period (Gilmore, Knickmeyer, & Gao, 2018). The pace of fetal brain maturation is particularly rapid. Neurogenesis commences as early as 42 days after conception (Stiles & Jernigan, 2010) and by the end of the second trimester, 200 billion neurons have been produced (Bourgeois, 1997). Cells migrate to their final destination where they begin to arborize and form dendritic branches (Sidman & Rakic, 1973). Synaptogenesis is present as early as the 16th gestational week, indicating communication between neurons (Bourgeois, Goldman-Rakic, & Rakic, 1994; Kostovi, Judas, Rados, & Hrabac, 2002).

Although genetic factors clearly play a central role in these maturational processes, it has become increasingly clear that environmental factors, including fetal experiences and exposures in utero, also play a critical role in shaping these developmental processes. The prenatal period is a sensitive period when the fetus is particularly susceptible to environmental influences. Experiences during the prenatal period are critical for normative processes from the closing of the neural tube to development of circuits involved in sensory processing (Burton, Hempstock, & Jauniaux, 2001; Godfrey & Barker, 2001; Moon & Fifer, 2000). The developing fetal brain additionally is particularly susceptible to harm from teratogenic factors such as toxins, infection, maternal stress including prenatal mental health problems, and other environmental exposures (Davis, Head, Buss, & Sandman 2017; Davis et al., 2019; Kim et al., 2017; Madigan et al., 2018). Less considered is the likelihood that the fetal period is also a window of opportunity when salutary experiences may exert beneficial influences. Understanding the influence of prenatal experiences, both adverse and salutary, on fetal brain development is critical because it then allows us to investigate individual differences in infants' emotional and cognitive development and their subsequent vulnerability and resilience to mental health problems.

Maternal development

Women also undergo many changes during pregnancy. Vast physiological changes support fetal growth and development but also change the maternal brain in preparation for motherhood. During gestation, maternal physiology undergoes massive changes including transformations in stress physiology and immune function, both of which likely have implications for the maternal brain (Howland, Sandman, & Glynn, 2017; Noroña, Doom, Davis, & Gunnar, 2020). For the mother, the hormonal changes of pregnancy are perhaps more dramatic than any other phase of the life span. A robust non-human animal literature documents that the experience of pregnancy is associated with neurological changes in the mother that persist throughout her life span (see Glynn et al., 2018 for review). The hormone changes associated with gestation are linked to changes in neuronal structure, signaling, and

neurogenesis (Keyser-Marcus et al., 2001; Shingo et al., 2003). Further, normative increases in pregnancy-related hormones (e.g., estrogen) not only predict maternal behavior, but experimental administration of them also elicits the onset of maternal behavior in virgin animals (Fahrbach & Pfaff, 1986; Numan, 2006; Numan, Rosenblatt, & Komisaruk, 1977). The impact of pregnancy on the female goes beyond behaviors and neural circuits directly linked to mothering. The experience of gestation also is linked to consistent alterations in both physiological and psychological stress responses.

The hypothalamic–pituitary–adrenocortical (HPA) axis undergoes profound changes during the prenatal period. The HPA axis is one of the major stress responsive systems and plays a central role in maintaining homeostasis. During the prenatal period the HPA axis plays a key role in regulation of fetal maturation and timing of delivery and directly impacts the maternal brain (Howland et al., 2017; Smith, Mesiano, & McGrath, 2002). In response to stress signals, corticotropin releasing hormone (CRH) is released from the hypothalamus. CRH binds to receptors in the pituitary leading to the production of proopiomelanocortin (POMC) which is cleaved by enzymes into adrenocorticotrophic hormone (ACTH) and other bioactive peptides. ACTH is released into the bloodstream and stimulates secretion of the glucocorticoid, cortisol, from the adrenal cortex. This system is regulated by a negative feedback loop whereby the release of cortisol feeds back to the hypothalamus and pituitary decreasing the production of CRH and ACTH. This cascade of hormones mobilizes resources to cope with stress and maintain homeostasis. During pregnancy the development of the placenta transforms the regulation of this system. The placenta, a fetal organ, produces hormones including CRH in both the maternal and fetal systems (King, Nicholson, & Smith, 2001). The CRH produced from the placenta is identical in structure and bioactivity to CRH produced from the hypothalamus (Goland, 1988). However, in contrast to the negative feedback at the level of the hypothalamus, cortisol stimulates the production of CRH from the placenta, similar to the role of cortisol in the amygdala (Robinson, Emanuel, Frim, & Majzoub, 1988). Therefore, during pregnancy, there is a positive feedback loop whereby both maternal and fetal cortisol stimulate an increase in the production of CRH from the placenta (Sandman et al., 2006; Waffarn & Davis, 2012). This HPA and placental axis represents a pathway by which environmental signals may be transmitted to the fetus and thus, shape its developmental course. During pregnancy, the maternal pituitary gland doubles in size, and cortisol levels increase 3- to 5-fold over gestation, achieving levels typically only seen in Cushing's disease (Mastorakos & Ilias, 2003; Sandman et al., 2006). Placental CRH production in the maternal circulation increases 40-fold from the end of the first trimester to term (Sandman et al., 2006; Sandman, Glynn, & Davis, 2015).

These massive changes in maternal HPA axis functioning during the prenatal period are normative and support maturation of the fetus as well as timing of parturition, but also may affect maternal mental health during the perinatal period (Glynn, 2010). During pregnancy, the HPA axis response to a variety of different stressors diminishes (de Weerth & Buitelaar, 2005). Further and in parallel to physiological changes, pregnant women also exhibit reduced psychological responses to stress (Glynn, Wadhwa, Dunkel Schetter, & Sandman, 2001, 2004). These normative responses are likely adaptive and may provide some protection to the mother–fetal dyad during pregnancy. However, elevated exposure to stressors, especially early in gestation, increase risk for preterm birth (Glynn et al., 2001). Moreover,

women who do not show the normative decrease in physiological and psychological stress responding during pregnancy are at increased risk for preterm delivery (Buss, Entringer, et al., 2009; Glynn, Dunkel Schetter, Hobel, & Sandman, 2008). The endocrine profile in pregnancy also may impact maternal sensitivity to stressors, thereby contributing to vulnerability to mental health problems during the perinatal period (Glynn, Davis, & Sandman, 2013). Prenatal stress exposure additionally increases risk for development of maternal anxiety and mood disorders (Slattery & Hiller, 2016). Prenatal hormone trajectories of the HPA and placental axis have been proposed to be one of the risk indicators for the development of postpartum depression (Glynn et al., 2013; Glynn & Sandman, 2014; Yim et al., 2009, 2010). This evidence suggests that prenatal maternal stress physiology and mental health problems during pregnancy are closely interrelated, with stress physiology potentially affecting the emergence of mental health problems, and pre-conception and prenatal mental health problems affecting stress physiology. For instance, elevated maternal PTSD symptoms during pregnancy affect cortisol concentrations during pregnancy (Seng, Low, Ben-Ami, & Liberzon, 2010). Therefore, mental health problems and stress physiology during pregnancy likely have bidirectional, transactional effects on maternal well-being during pregnancy, as well as fetal well-being, and labor, delivery, and infant outcomes.

Adversity Antecedents of Prenatal Maternal Stress and Mental Health Problems

Adversity and prenatal maternal stress physiology

During pregnancy, many women reference their childhood experiences, both negative and positive, in considering how they want to care for their new baby. Negative childhood experiences, such as maltreatment and other forms of interpersonal trauma, can have enduring effects on maternal mental health problems during pregnancy and on multiple aspects of individual and maternal–fetal stress physiology. Thus, the pregnancy period may be a particularly sensitive time for women, when prior history of adversity and unresolved trauma may render pregnant women vulnerable to re-emergence of mental health problems and stress (Slade & Cohen, 1996; Sperlich & Seng, 2008). Given the plasticity of the mother and her fetus during the prenatal period, the effects of early-life adversity may be amplified with implications for maternal and child development (Yehuda & Meaney, 2018).

Childhood adversity may contribute to maladaptive alterations in stress physiology during pregnancy, such as greater maternal HPA axis dysregulation evidenced by both elevated and suppressed concentrations of cortisol during pregnancy (Bowers & Yehuda, 2016; Schreier, Enlow, Ritz, Gennings, & Wright, 2015; Swales et al., 2018). Maternal report of childhood maltreatment is linked to elevations in hair cortisol concentrations during pregnancy (Schreier et al., 2015) and has been found to amplify the impact of women's more proximal exposure to adulthood traumatic events prior to pregnancy on prenatal hair cortisol concentrations (Swales et al., 2018). Further, childhood maltreatment also is associated with alterations in placental–fetal stress physiology, including significantly steeper increases in placental CRH across gestation (Buss et al., 2017; Moog et al., 2018). These studies point to pathways by which maternal childhood adversity may directly affect fetal stress exposure and transmit higher-than-typical cortisol and placental CRH levels. The dynamic changes in

maternal physiology during this period and the responsivity to stress signals suggests a pathway by which childhood adversity may alter maternal prenatal stress regulation and reactivity, and such dysregulation of stress physiology may, in turn, affect maternal–fetal stress transmission.

Both hypercortisolism and hypocortisolism during pregnancy are associated with negative consequences for maternal and fetal well-being (Bowers & Yehuda, 2020; Davis et al., 2017; Davis & Sandman, 2010; Yehuda & Meaney, 2018). Depending on the nature, severity, and chronicity of the childhood adversity exposure, some pregnant women who were chronically maltreated may show hypocortisolism, a pattern observed in non-pregnant, chronically maltreated individuals (Gunnar & Quevedo, 2007; Yehuda et al., 2010). This downregulation of cortisol secretion is believed to be a response to chronic elevations in cortisol and serves to protect against wear and tear on the regulatory and inflammatory systems.

Downregulation of cortisol secretion, however, may increase risk that subsequent adversity will not be met with an effective stress response and may render individuals more susceptible to mental health problems, such as PTSD (Bowers & Yehuda, 2016; Pratchett & Yehuda, 2011). Non-pregnant individuals with childhood adversity and PTSD may show blunted cortisol patterns, but it is unclear if these patterns preceded the emergence of PTSD, thereby increasing risk for it, are a direct consequence of PTSD, or are an indirect consequence from chronic or severe childhood adversity (Pratchett & Yehuda, 2011).

Key in the pathway between maternal childhood and adulthood adversity prior to pregnancy and alterations in maternal stress physiology during pregnancy are ongoing maternal mental health problems stemming from adversity. In actuality, many studies linking maternal childhood and adulthood adversity to disruptions in stress physiology do not consider the preceding and often ongoing role of mental health problems during pregnancy, which may affect and be affected by altered stress physiology (Evans, Myers, & Monk, 2008; Yehuda & Meaney, 2018). More research is needed in this area. Regardless, the dramatic multilevel changes during pregnancy increase the likelihood that the physiological consequences of early and cumulative adversity may be amplified during pregnancy, thereby impacting both the mother and fetus.

Adversity and prenatal maternal mental health problems

From a psychological standpoint, during pregnancy, women reflect back on their childhood as they consider the type of caregiving they had, and the type of parent they want to be. For women with histories of childhood adversity, such as maltreatment and other interpersonal trauma in their families of origin, the pregnancy period can be a time when women are haunted by unresolved traumatic experiences (Lieberman, Díaz, & Van Horn, 2009; Narayan, Oliver Bucio, et al., 2016; Slade et al., 2009). Physical changes and physiological sensations associated with pregnancy, such as experiencing abdominal growth, the fetus kicking, and other aches and pains, can invoke reminders of past abuse and loss of control over one's body at the hands of the abuser. Some women with histories of maltreatment may experience the growing fetus as a bodily invasion that is out of their control because it reminds them of the powerlessness of being victimized (Sperlich & Seng, 2008). Adulthood

adversity, such as stressful and traumatic life events in adulthood, including IPV, can also amplify consequences of childhood adversity and mental health problems.

Maternal experience of childhood adversity—As women prepare to become mothers, adverse experiences with their childhood caregivers may once again become especially salient and harmful. Childhood adversity more broadly, and childhood maltreatment more specifically, is associated with elevated maternal mental health problems during pregnancy, such as elevated depression, anxiety, and PTSD symptoms (Choi & Sikkema, 2016; Racine, Zumwalt, McDonald, Tough, & Madigan, 2019; Seng, 2002). A few recent studies have illuminated that specific types of childhood adversity may uniquely affect specific types of maternal mental health problems during pregnancy. For instance, retrospective report of both family dysfunction and physical and emotional abuse, but not sexual abuse, was associated with psychosocial difficulties, including depression, anxiety, perceived stress, and other social risks, during pregnancy (Racine, Madigan, et al., 2018). Of note, however, this study did not assess PTSD during pregnancy, which is a well-established consequence of childhood sexual abuse (Sperlich & Seng, 2008). Another recent study found that a history of childhood maltreatment was associated with depression and PTSD symptoms during pregnancy, but exposure to childhood family or household dysfunction was not. In addition, childhood maltreatment that was specifically reported to begin in early childhood (ages 0–5), rather than later in childhood, was associated with maternal prenatal PTSD symptoms, but not with maternal prenatal depression symptoms (Atzl, Narayan, et al., 2019). Taken together, these findings indicate that both type and timing of childhood adversity are important to consider for specific mental health outcomes during pregnancy.

Maternal experience of adversity in adulthood and cumulative lifetime adversity—Exposure to stressful life events and negative circumstances in adulthood before conception, as well as during pregnancy, may also exacerbate prenatal maternal mental health problems. Stressful life events including interpersonal trauma (e.g., physical and sexual assaults) but also those pertaining to homelessness, incarceration, and severe poverty during pregnancy are associated with higher levels of both depression and PTSD symptoms during pregnancy (Narayan et al., 2018). Women's experiences of violent trauma, such as witnessing or experiencing physical or sexual assault from a romantic partner or stranger before or during pregnancy were also robustly related to PTSD symptoms during pregnancy (Harris-Britt, Martin, Li, Casanueva, & Kupper, 2004). Studies also specifically point to the relationship dysfunction with the father of the baby as a particularly influential form of adulthood adversity for mental health during pregnancy.

Romantic relationship conflict and IPV can take multiple forms (e.g., physical, sexual, and psychological), and can become a complicated risk factor for pregnant women. For instance, for some women, the pregnancy period may represent a time of decreased risk for IPV victimization because the woman and fetus are viewed as more fragile. For other women, however, it might represent a period of increased risk, especially if the pregnancy is unplanned or the perpetrator questions the paternity (Chambliss, 2008; Jasinski, 2004; Narayan, Hagan, Cohodes, Rivera, & Lieberman, 2016). In terms of specificity of adversity and prenatal mental health problems, studies have linked physical and psychological IPV

victimization during pregnancy to women's heightened levels of prenatal depression (Flanagan, Gordon, Moore, & Stuart, 2015).

IPV victimization is more common among women who experienced childhood maltreatment and is another factor affecting PTSD during pregnancy (Pratchett & Yehuda, 2011; Seng, 2002). One study found that a history of childhood maltreatment was associated with increased rates of IPV victimization during pregnancy, and both childhood maltreatment and IPV were independently associated with prenatal PTSD symptoms. Moreover, psychological IPV victimization, as opposed to physical or sexual IPV victimization, was most strongly associated with PTSD symptoms during pregnancy (Huth-Bocks, Krause, Ahlfs-Dunn, Gallagher, & Scott, 2013), again illustrating the importance of considering specificity in the type of risk in addition to the cumulative nature of childhood and adulthood risks. Moreover, relationship-based adversity may reflect victimization that has accumulated from childhood. For instance, higher levels of relationship conflict with and lower levels of support from the baby's father partially mediated the link between childhood maltreatment and both depression symptoms and PTSD symptoms during pregnancy (River, Narayan, Atzl, Rivera, & Lieberman, 2019). These latter findings emphasize the enduring role that childhood adversity likely has on prenatal maternal mental health problems. Although many of the above studies relied on retrospective report of childhood experiences, they suggest that it is critical to consider life span experiences of pregnant women, beginning in childhood in order to understand intergenerational transmission of mental health problems through the prenatal period.

The above evidence elucidates several potential life span pathways of risk characterized by cumulative adversity, the emergence of mental health problems, and alterations in stress physiology. Specifically, maternal history of childhood adversity may portend risk for subsequent exposure to adversity or revictimization, either before or during the pregnancy period, or both. Moreover, both childhood adversity and adulthood adversity likely affect mental health problems during pregnancy (Narayan et al., 2016; Pratchett & Yehuda, 2011; Sperlich & Seng, 2008). In addition, although more research is needed, maternal exposure to adversity affects both maternal mental health problems and stress physiology during pregnancy, which in turn have bidirectional effects (Evans et al., 2008; Seng, 2002). Together, these complicated pathways pose risks into the postpartum period in the domains of postnatal maternal mental health, infant stress regulation and responsivity, and maternal–infant bonding.

Fetal Programming: Maternal Prenatal Stress Predicts Child Mental Health Problems

Maternal stress and mental health problems during the prenatal period, as discussed in the second section, likely exert profound consequences on the developing fetus as well as on the mother. The Fetal Programming or Developmental Origins of Health and Disease (DOHaD) hypothesis posits that during sensitive Windows of fetal development, the environment can exert lasting influences on health and well-being across the life span (Barker, 1998). This hypothesis was generated largely based on studies of in-utero nutritional deprivation (Barker,

2002; Gluckman & Hanson, 2004). Broadly, these studies indicate that the fetus adapts its developmental course in response to prenatal signals to prepare for survival in the postnatal world. Such adaptations, however, may have a long-term cost for morbidity and mortality. Prenatal adversity is linked to reduced fetal growth and small size at birth. Furthermore, numerous epidemiological and observational studies demonstrate that small size at birth is predictive of a range of physical and mental health outcomes throughout the life span (Barker, Eriksson, Forsen, & Osmond, 2002; Davis, Buss, et al., 2011; Kim et al., 2014). It is unlikely that small size at birth is the causal risk factor; rather, it is a marker of perturbations during the prenatal period that represent the origin of the vulnerability. These studies provide evidence that the prenatal period is a sensitive window when the fetus is particularly susceptible to environmental insults. In the sections that follow, we focus on prenatal maternal stress and mental health problems as types of prenatal adversity that impact both birth outcomes and trajectories of offspring physical and mental health. As there are many excellent reviews linking prenatal maternal psychological distress to infant, child and adolescent outcomes (Davis et al., 2018; de Weerth, 2018; Madigan et al., 2018; Robinson, Lahti-Pulkkinen, Heinonen, Reynolds, & Raikkonen, 2019; Sandman, Davis, Buss, & Glynn, 2011), we only briefly overview the links between prenatal maternal mental health and child outcomes here. We then discuss these links within the framework of adaptation and resilience.

Prenatal maternal stress and mental health, and child outcomes

Prenatal maternal stress and mental health problems are associated with persisting consequences for both the mother and her offspring (Barker, Jaffee, Uher, & Maughan, 2011; Buss et al., 2012; Davis & Pfaff, 2014; Davis & Sandman, 2012; Korhonen, Luoma, Salmelin, & Tamminen, 2012; O'Donnell, Glover, Barker, & O'Connor, 2014; Sandman, Buss, Head, & Davis, 2015). Several recent meta-analyses provide strong evidence that prenatal maternal depression is associated with preterm birth (Grigoriadis et al., 2013; Grote et al., 2010) and low birth weight (Grote et al., 2010). Further, maternal prenatal PTSD may additionally predict negative birth outcomes including disrupted growth and shorter gestation/increased risk for preterm birth (Cook, Ayers, & Horsch, 2018). A recent prospective study of 4,408 pregnancies found that prenatal PTSD predicted increased rates of preterm birth. It is widely known that shortened gestation impacts brain development (e.g., Davis, Buss, et al., 2011; Kim et al., 2014). Interestingly, fetuses that go on to be delivered preterm display reduced connectional integrity as compared to age-matched fetuses who are delivered at term (Thomason et al., 2017). The detection of connectivity differences among at-risk fetuses *prior* to birth suggests that the fetal brain is susceptible to prenatal influences and that the long-term developmental consequences of preterm birth begin in utero.

The link between prenatal maternal stress and mental health problems on development persists throughout infancy and childhood, and likely into adulthood. Most research in this area has focused on prenatal maternal stress, anxiety, and depression, with one of the most well-replicated consequences of these prenatal maternal mental health problems being increased negative emotionality in offspring. Although shared genes between the mother and her offspring clearly contribute to shared variance in mental health, evidence from studies of

in vitro fertilization or quasi-experimental natural disaster research suggests that environmental factors additionally contribute to the intergenerational transmission of mental health problems (Glynn et al., 2001; King & Laplante, 2005; Rice et al., 2009). Prospective longitudinal studies show that prenatal maternal mental health problems and stress predict greater negative emotionality and fearful temperament in the offspring, assessed by both laboratory observation and maternal report (Blair, Glynn, Sandman, & Davis, 2011; Davis et al., 2004, 2007; Huot, Brennan, Stowe, Plotsky, & Walker, 2004; Rouse & Goodman, 2014). Further, these links are not fully accounted for by postnatal exposures, as these associations remain after covarying for postnatal factors, such as maternal postpartum mental health.

The link between prenatal maternal mental health problems, stress, and child negative emotionality persists throughout childhood and is associated with the development of children's internalizing problems (Davis & Sandman, 2012; Howland, Sandman, Glynn, Crippen, & Davis, 2016). A recent prospective study with close to 2,000 mother-child dyads measured maternal stress, anxiety, and depression both during pregnancy and postnatally and showed that prenatal distress predicted child negative emotionality at 3 years and internalizing problems at 5 years after covarying postnatal maternal mental health (Hentges, Graham, Plamondon, Tough, & Madigan, 2019). Prenatal maternal stress, anxiety, and depression also predicted elevated depressive symptoms in adolescence assessed by both maternal report and child self-report (Davis et al., 2019; O'Donnell et al., 2014). The link between prenatal maternal mental health problems and offspring internalizing psychopathology is also apparent in young adulthood, as documented in several large cohort studies (Capron et al., 2015; Pearson et al., 2013; Plant, Pariente, Sharp, & Pawlby, 2015). In one study, offspring were 3.4 times more likely to have a diagnosed depressive disorder at 18–25 years of age after accounting for postnatal maternal depression and sociodemographic risk factors (Plant et al., 2015).

Prenatal maternal stress and mental health problems additionally predict child cognitive outcomes. These include associations with general cognitive function (Davis & Sandman, 2010) and perhaps more specifically with executive function (Buss, Davis, et al., 2009; Davis & Sandman, 2010). Findings from two large cohort studies (Avon Longitudinal Study of Parents and Children and Generation R) show that prenatal maternal depression predicted child attentional problems at 3 years of age after covarying for both postpartum maternal depression and paternal depression (Van Batenburg-Eddes et al., 2013). Relatedly, prenatal maternal depression predicted problems with executive functioning and attention shifting at 4 years of age (El Marroun et al., 2017) as well as increased risk for an ADHD diagnosis during childhood (Clemens et al., 2015). Additional prospective longitudinal studies have linked prenatal maternal anxiety to problems with attentional control through adolescence (Van den Bergh & Marcoen, 2004; Van den Bergh et al., 2005). These studies provide evidence for an association between prenatal maternal depression and child cognitive function.

Fetal programming of HPA axis development is one of the most frequently proposed pathways by which maternal stress and mental health are thought to impact child outcomes. Prenatal maternal stress, anxiety, and depression are linked to disruptions in children's stress responses and circadian HPA axis functioning from the neonatal period through adolescence

(Davis, Glynn, Waffarn, & Sandman, 2011; Galbally, van Rossum, Watson, de Kloet, & Lewis, 2019; O'Donnell et al., 2013; Van den Bergh, Van Calster, Smits, Van Huffel, & Lagae, 2008). For example, maternal stress during the prenatal period is associated with prolonged neonatal cortisol responses to stress (Davis, Glynn, et al., 2011) and prenatal maternal depression predicted heightened cortisol reactivity at 1 year of age (Osborne et al., 2018).

Fewer studies have evaluated the relation between maternal PTSD during pregnancy and child outcomes (Cook et al., 2018; Seng, Low, Sperlich, Ronis, & Liberzon, 2011). However, some investigators have documented that maternal PTSD during pregnancy predicts poorer infant birth outcomes, lower maternal–infant bonding, and higher levels of infant distress (Seng, 2002; Seng et al., 2013). Moreover, like depression, maternal PTSD during pregnancy also is associated with shorter gestation and lower infant birth weight (Seng et al., 2011). In terms of associations with stress physiology, following the 911 attacks, Yehuda et al. (2005) reported that mothers who developed PTSD had lower salivary cortisol levels, as did their infants. Furthermore, lower levels of salivary cortisol in infants were subsequently associated with higher levels of infants' distress (Brand, Engel, Canfield, & Yehuda, 2006). In another study, infants born to women who were pregnant during and then developed PTSD in response to an earthquake in Wenchuan County of Sichuan Province in China showed impairments in cognitive development (Cai et al., 2017). Consistent with observational human data, a mouse model of prenatal traumatic experiences showed that prenatal exposure caused an increase in anxiety-like behavior in the offspring (Osborne et al., 2018). Although the extant literature provides compelling evidence that maternal stress, anxiety, and depression during the prenatal period predict stress regulatory physiology in offspring and their developmental outcomes, more attention is needed to the specific the impact of maternal PTSD during pregnancy on child outcomes, particularly child cognition.

More studies that adopt a fully intergenerational design and link maternal and child functioning through factors during the prenatal period are also needed. For example, maternal childhood adversity or adulthood adversity prior to pregnancy likely impacts developmental outcomes in the offspring via prenatal maternal stress and mental health, yet few studies have directly documented this possibility. McDonnell and Valentino (2016) found that maternal self-report of childhood adversity predicted both prenatal maternal depression symptoms and poorer infant socioemotional functioning, suggesting that prenatal factors may contribute to the link between maternal adversity and child outcomes. Further in a sample of 907 dyads, Letourneau et al. (2019) showed that the relation between maternal ACEs and child internalizing and externalizing problems was partially mediated by prenatal maternal anxiety and depression. In addition, maternal report of ACEs predicted lower levels of infant adaptive functioning (e.g., motor, communication, and problem-solving skills) at 12 months via both maternal physical and mental health problems during the prenatal period (Racine, Plamondon, et al. 2018). These findings illustrate intergenerational pathways of risk from women's experiences to infants' development through the pregnancy period.

Adaptation and Resilience

In addition to a sensitive period of vulnerability, the pregnancy period is a window to promote adaptation and resilience in mothers and infants. Opportunities to better understand how to deter intergenerational transmission of risk include (a) identifying how maternal and environmental signals provide information to the fetus and program expectations about postnatal conditions that may promote offspring adaptation, (b) examining how links between mothers' adversity and offspring mental health problems can be ameliorated by promotive and protective factors during pregnancy, and (c) supporting resilience in pregnant women through translational prevention and intervention efforts. This section reviews each of these three areas.

Prenatal maternal stress and offspring adaptation to the postnatal environment

The links between prenatal maternal stress and fetal development are typically viewed through the lens of pathology. However, signals of maternal stress provide information to the fetus about the quality of the postnatal world that may have an adaptive benefit for survival in a given postnatal environment. The most well-documented example of this comes from nutrition. It is widely known that the prenatal period is a sensitive window when the fetus responds to nutritional deprivation with the development of a "thrifty phenotype" that promotes survival in an environment where food is scarce but is maladaptive and increases risk for metabolic disease when food is plentiful (Gluckman, Hanson & Pinal, 2005). These findings highlight the necessity of considering the larger context, including the postnatal environment, to understand the impact of prenatal stress and maternal mental health, elucidate their role in the developmental course, and identify appropriate interventions.

During pregnancy, biological stress signals, such as placental CRH, also transmit information to the fetus and shape the developmental course. The metamorphosis of the Western Spadefoot Toad illustrates the role stress hormones may play as a gestational signal that reflects the quality of the environment, affect development, and have implications for survival. This toad has a fascinating adaptive response to adversity (Denver, 1997). When its pool of water desiccates rapidly, the tadpole adapts to this harsh environment by accelerating metamorphosis into a toad that is able to survive outside of water. However, a consequence of this accelerated developmental trajectory is that the toad is both smaller and less successful at foraging and reproducing as compared to a toad that had a more optimal environment allowing for a protracted developmental course. Stress hormones play a central role in this adaptive process. If CRH receptors are blocked, the tadpole's metamorphosis will not be accelerated in the context of a rapidly evaporating pool of water, and the tadpole will not survive.

The human fetus similarly incorporates signals from the maternal host environment into its developmental trajectory. The stress signal placental CRH is similarly associated with both shortened gestation and preterm birth in humans as well as accelerated maturation (Class et al., 2008; Sandman et al., 2006; Swales et al., 2019), and these alterations may have adaptive advantages for survival; for example, stressed fetuses tend to have greater lung maturity when born preterm (Dunkel Schetter, 2009; Glynn et al., 2008). Like the toad, these

adaptations are advantageous if the fetus is born preterm, but also may have long-term costs (Davis, Glynn, et al., 2011; Stout, Espel, Sandman, Glynn, & Davis, 2015).

Prenatal adaptations made by the offspring may further impact postnatal developmental trajectories. Studies have shown that placental CRH is linked to postnatal growth trajectories. For instance, elevated placental CRH predicts accelerated increases in BMI during the first postnatal year (Stout et al., 2015). Prenatal fetal adaptations additionally may impact behavioral regulation, as elevated placental CRH in utero have been found to predict offspring's increased internalizing problems (Davis et al., 2005; Howland et al., 2016) and may have persisting consequences for brain development during childhood (Curran, Sandman, Davis, Glynn, & Baram, 2017; Sandman et al., 2018). Further, neuroimaging studies indicate that in utero exposure to adversity is associated with alterations in the functional architecture of the infant brain, most notably in limbic–prefrontal circuitry that may reflect accelerated maturation. In a study by Posner et al. (2016), 6-week old infants exposed to prenatal maternal depression demonstrated increased inverse (i.e., increased negative) resting state functional connectivity between the amygdala and bilateral dorsal prefrontal cortex and ventromedial prefrontal cortex. The authors interpret these data as consistent with the hypothesis of a more mature pattern. However, both increased and decreased connectivity have been observed in resting state and depending on the type of task that is used (Gee et al., 2013). Future research with replication and longitudinal follow-up is needed to determine whether the observation that prenatal adversity is associated with resting state functional connectivity reflects accelerated maturation. However, these data are suggestive that early experiences shape developmental trajectories in ways that may be adaptive, but also increase risk for subsequent mental health problems (Tottenham, 2020).

Moreover, as with nutrition, stress signals in the in-utero environment may set expectations for the postnatal world. The degree of concordance of maternal depression symptoms during pregnancy and postpartum predicted cognitive function during infancy. Specifically, the more consistent the pre- and postnatal periods, the better infants performed on the Bayley Scale of Mental Development (Sandman, Davis, & Glynn, 2012).

Reframing our understanding of prenatal signals as information that shape the developmental course with potential adaptive benefits for the offspring highlights the importance of considering the broader context and the potential that prenatal stress may have benefits in certain contexts. There is, however, another implication for this adaptation framework that further highlights the need for preconception and prenatal prevention and intervention efforts for the mother in order to optimize benefits. The fetal programming literature provides robust evidence that the prenatal environment is incorporated into the offspring's developmental course and is associated with profound and long-lasting sequelae. Thus, preconception and prenatal efforts that aim to promote resilience, by either leveraging existing promotive and protective factors and resources, or implementing preventive interventions, are likely to have the greatest positive long-term benefit.

Promotive and protective factors that ameliorate negative outcomes following maternal adversity, mental health problems, and stress

It is critical to understand promotive and protective factors either prior to or during pregnancy that can promote maternal and fetal resilience and positive postnatal outcomes. Although much of the extant literature focuses on risk factors for maternal mental health problems and stress during pregnancy, studies find, for example, that a history of positive childhood experiences and better current social support during pregnancy are associated with better prenatal mental health and better child outcomes. For example, a mother's report of more positive relationships with her parental figures and the presence of more affection during childhood were associated with fewer prenatal depression symptoms (Chung, Mathew, Elo, Coyne, & Culhane, 2008). In another study, pregnant women's higher numbers of reported benevolent childhood experiences (BCEs) involving supportive relationships and a positive and predictable quality of life were associated with fewer mental health problems and lower exposure to adversity during pregnancy (Narayan et al., 2018). These studies suggest that although less frequently studied, positive early-life experiences also likely have intergenerational benefits through the prenatal period. Although many of these studies rely on retrospective reports of positive childhood which may be impacted by current mental health and other factors, there is evidence for convergence between prospective and retrospective reports (e.g., Glynn et al., 2019). Further, current depression symptoms are only modestly associated with positive memories from childhood (Narayan, Ippen, Harris, & Lieberman, 2019). More research is needed to compare the relative strength of prospectively- versus retrospectively-assessed positive childhood experiences on well-being specifically in pregnant women.

In terms of proximal resources, social support during pregnancy is strongly associated with women's prenatal mental health (Dunkel Schetter, Sagrestano, Feldman, & Killingsworth, 1996; Dunkel Schetter, 2011; Sperlich & Seng, 2008). Studies that examine both high-income and low-income women across a range of ethnic groups show that higher perceived effectiveness of social support from the baby's father and other counterparts, as well as greater availability of help in general, is associated with lower levels of anxiety and depression symptoms during pregnancy (Dunkel Schetter, 2011; River, Narayan, Atzl, Rivera, & Lieberman, 2020; Séguin, Potvin, Denis, & Loiselle, 1995). Furthermore, studies that have covaried for women's histories of childhood adversity and current stressful life events continue to find that the presence of high-quality social support is associated with benefits for women's prenatal mental health (Racine et al., 2019; Séguin et al., 1995). Acknowledging the likely bidirectional nature of the association, in that women with better mental health may both experience and report better social relationships, it is important to note that high social support is one of the most robust correlates of better maternal mental health and more optimal birth outcomes.

The benefits of social support to pregnant women also extend to more positive infant outcomes. For instance, higher levels of perceived social support from the babies' fathers predicted more positive postnatal Maternal×Infant interactions through lower levels of maternal prenatal depression symptoms. Higher levels of social support also predicted infants' more effective cortisol reactivity following a stressor partially mediated by both

lower levels of prenatal depression and more positive Mother×Infant interactions (Thomas, Letourneau, Bryce, Campbell, & Giesbrecht, 2017). Another study found that when levels of maternal depression symptoms were lower or levels of general maternal prenatal social support (not specifically from the father of the baby) were higher, the associations between infants' negative temperament and their cortisol levels were attenuated, suggesting protective effects of both better prenatal mental health and greater social support (Luecken, MacKinnon, Jewell, Crnic, & Gonzales, 2015). These studies together point to the potential of social support to help promote and buffer postnatal adaptation in the infant and the mother–infant relationship, in conjunction with the additional positive effect that higher social support likely also has on alleviating prenatal depression symptoms. Few studies have examined whether social support may help to ameliorate effects of maternal prenatal PTSD on postnatal adaptation, but this is a viable area of future inquiry.

An additional consideration is that the nuances of social support and its benefits may be complicated to measure during pregnancy, particularly for women with lifelong and cumulative risks. For instance, pregnant women who have been maltreated as children often confront painful decisions about whether and to what extent they may draw from support from previously abusive caregivers when caring for their new babies (Sperlich & Seng, 2008). Relying less on social support from previously maltreating caregivers is associated with a reduction in the risk of childhood maltreatment when babies were born, even among women who continued to have elevated depression (Easterbrooks, Chaudhuri, Bartlett, & Copeman, 2011). Thus, in this case resilience may be enhanced by reducing contact with sources of childhood adversity. Furthermore, women's reports of the support they currently receive from their partner during pregnancy may be influenced by idealized views of the support they hope to receive when the baby is born. One study found that women actually had poorer mental health and higher levels of stress during pregnancy if they self-reported high levels of support from partners but were rated by trained coders to actually have low levels of support based on their open-ended descriptions of partners (River, Narayan, Atzl et al., 2019). These findings indicate that self-reports of social support, the most common strategy of assessment, are likely impacted by other factors including pregnancy related experiences and maternal mental health. Additional research is needed to assess pregnant women's social support from various counterparts using a variety of methodologies beyond self-report.

More research also is needed to identify broader promotive and protective factors that buffer against the intergenerational transmission of mental health problems and stress from mothers to babies. Given the enduring effects of childhood experiences, this may be particularly important in pregnant women with histories of childhood adversity. For instance, a recent review identified only 18 published studies on research that supported or promoted health, well-being, and resilience in pregnant women with childhood adversity, with fewer than a dozen of these specifically focused on factors that buffer against effects of maternal childhood adversity on prenatal mental health problems (Atzl, Grande, Davis, & Narayan, 2019). This review found that social support was the most widely studied resource for pregnant women with childhood adversity; however, the total number of studies on social support were still surprisingly few. This dearth of research points to an underdeveloped literature on perinatal promotive and protective factors in contexts of adversity.

Translational efforts and interventions for prenatal mental health and stress

Targeted clinical efforts, such as preventive interventions, are needed to address and reduce pregnant women's mental health and stress. Prenatal care represents an opportunity to reach and to provide support and intervention for pregnant women. Although screening for perinatal depression and anxiety is now becoming the standard of care (American College of Obstetricians and Gynecologists (ACOG), 2018), routine prenatal screening is often not sufficient. Moreover, neither symptoms of prenatal PTSD nor exposure to childhood adversity are regularly screened prenatally.

Research shows that routine prenatal care may also be fraught with barriers, especially for women with high levels of mental health problems and stress, low-income women, and women from racial and ethnic minority groups (Narayan et al., 2017; Sperlich & Seng, 2008; River, Narayan, Galvan et al., 2019). Evidence suggests that only a minority of clinically depressed women (18%) (Marcus, 2009) seek treatment during the prenatal and postpartum periods. Even when women receive appropriate referrals for mental health treatment from their providers, depression and PTSD symptoms can continue to interfere with the ability to connect with and maintain adequate healthcare alliances and interpersonal support during pregnancy (Seng, 2002). Another study showed that one third of pregnant women with clinical levels of depression and PTSD symptoms in their second or third trimester of pregnancy declined referrals for mental health services during pregnancy (Narayan et al., 2017). An additional set of barriers pertain to childhood adversity. Many pregnant women with unresolved trauma histories and resulting untreated mental health problems report feeling pressure to suppress their own needs and focus on their babies during pregnancy (Narayan et al., 2017; River, Narayan, Galvan et al., 2019; Sperlich & Seng, 2008). Because current routine screening does not typically include assessment of childhood adversity, women with trauma histories may be even less recognized as needing support.

The prenatal period represents a key opportunity to reach such underserved, high-risk populations of women with more formalized and targeted translational efforts. Many women do have both increased motivation and increased contact with the medical system during the prenatal period (Sperlich & Seng, 2008). We briefly review a sample of intervention efforts that are designed to address prenatal mental health problems and sources of adversity stemming from childhood trauma and lack of support within the romantic or co-parenting relationship.

One recent approach combines basic research with therapeutic assessment during pregnancy to represent a "foot-in-the-door" technique to connect women to services. A series of studies conducted with low-income and racially and ethnically diverse pregnant women in San Francisco and Denver revealed that pregnant women appreciate participating in focused clinical research study that assesses childhood adversity and mental health problems in conjunction with positive childhood experiences and ongoing support. This clinical research endeavor blended assessment of risks and resources to leverage existing protective factors and start a conversation about additional services and programs that may meet the needs of pregnant women. Pregnant women involved in these studies reported appreciating the opportunity to identify and process painful experiences of adversity that may be previously

unrecognized sources of mental health problems and stress, and then having the opportunity to connect to more formalized, tailored services and preventive interventions during pregnancy, depending on their needs and other priorities (Narayan et al., 2017, 2019).

The Care Project is a prenatal intervention that directly addresses barriers to mental health treatment and assesses benefits for mothers and their children (Davis et al., 2018). This project implements MomCare, a form of brief interpersonal psychotherapy (IPT) for depression during the prenatal period that is designed to meet the needs of low-income women from culturally diverse backgrounds and improve both maternal and infant outcomes. MomCare is a culturally-relevant, collaborative care intervention that provides brief IPT via approximately eight sessions after an initial engagement session (Grote et al., 2015). MomCare is efficacious with socio-economically disadvantaged pregnant women of diverse cultural backgrounds; women randomized to MomCare showed significantly higher rates of depression remission and lower depressive symptom severity as compared to controls. These effects persisted through 18 months postpartum (effect sizes = .35 for severity of depressive symptoms and .36 for depression remission) (Grote et al., 2015). Of note, MomCare is particularly beneficial for women with histories of adversity (Grote, Zuckoff, Swartz, Bledsoe, & Geibel, 2007, 2015). An important aspect of MomCare's success is that women participate in an initial engagement session to problem solve common barriers to treatment.

The goal of the Care Project specifically is to test whether reducing maternal depression affects child developmental outcomes, as the long-term benefits to offspring following prenatal interventions delivered to women remain unknown (Davis et al., 2018; Garcia et al., 2019). In the Care Project, women with elevated depression symptoms are randomly assigned to receive either MomCare or the standard of care. Mothers are followed throughout the prenatal period and mother–infant dyads are assessed from birth until the infant is 18 months of age. In addition to assessing maternal trajectories of mental health and stress, infant brain development, cognitive function and emotional regulation are evaluated throughout the postpartum period. This project tests the hypothesis that maternal intervention during the prenatal period will exert benefits for both the mother and infant. The use of random assignment in this project addresses some of the limitations of correlational research. If reducing maternal depression during the prenatal period benefits infant brain development then this would provide support for the Fetal Programming Hypothesis and underscore the importance of beginning intervention prior to birth.

Perinatal Child–Parent Psychotherapy (CPP) and MotherWise are two additional evidence-based interventions during pregnancy that address maternal childhood adversity and relationship-based adversity with the father of the baby. Perinatal CPP aims to prevent the intergenerational transmission of adversity and mental health problems from mothers to children by helping women to process and recover from unresolved trauma before babies are born, as well as increase awareness of and attunement to the fetus, and strengthen positive attributions of infants (Lieberman et al., 2009; Narayan, Oliver Bucio, Rivera, & Lieberman, 2016). MotherWise, a relationship-based program, aims to strengthen communication skills and healthy conflict resolution strategies during pregnancy using the evidence-based *Within My Reach* curriculum (Rhoades, Mazzoni, & O'Reilly Treter, 2019). It also provides support

for women to safely exit relationships that could be harmful to maternal and fetal wellbeing. MotherWise is multi-format and involves group-based workshops for pregnant women and couples, as well as individual case management, with the goal to improve birth and child outcomes, in addition to maternal wellbeing and relationship functioning (Rhoades et al., 2019). Together, all of the above intervention efforts aim to implement resources and foster resilience during the pregnancy period to promote long-term maternal, fetal, and relational wellbeing before babies are born. More translational prevention efforts that reduce mental health problems and stress dysregulation and are delivered during pregnancy or even prior to conception are needed to bolster resources and protective capacities in women before adversity occurs and mental health problems escalate.

Conclusions

There is growing awareness that maternal experiences of childhood and cumulative adversity may have intergenerational effects, making the prenatal period not only a window when the consequences of maternal adversity and resulting problems with mental health and stress physiology impact the fetus, but also a window of opportunity for resilience and intervention (Davis et al., 2018; Narayan et al., 2019; Sperlich & Seng, 2008; Yehuda & Meaney, 2018). The extant literature provides compelling evidence that the trajectory of fetal development is profoundly influenced by the intrauterine environment, including signals to the fetus that stem from maternal stress and mental health problems. However, these findings also provide support that the prenatal period is a window of opportunity to disrupt this intergenerational transmission of adversity and mental health problems from mothers to infants.

Several targeted areas of additional research are needed. Given the life span and intergenerational pathways linking maternal childhood and cumulative adversity, mental health problems before and during pregnancy, disruptions in maternal–fetal stress physiology, and negative neonatal and infant outcomes, more research needs to utilize study designs that account for as many of these variables as possible. Such studies could leverage intergenerational designs not only to better understand how the pregnancy period is a unique time of risk, but also to harness resilience processes that may promote or buffer adaptation across generations, particularly in families with maternal childhood adversity. There is a significant gap in research that examines prenatal protective factors that buffer against the effects of maternal childhood adversity on alterations in maternal–fetal stress physiology.

Research is needed to clarify whether effects of childhood adversity on maternal mental health and stress physiology during pregnancy depend on whether the adversity was measured retrospectively or prospectively. Recent research has shown that childhood adversity assessed with retrospective measurement is valid and shows similar associations to outcomes than prospective assessments (e.g., Glynn et al., 2019), although associations between retrospectively reported adversity and outcomes may be impacted by contemporaneous factors (e.g., mental state, trait negativity, ongoing stress; Reuben et al., 2016). However, prospective data on childhood adversity, such as child welfare records of documented maltreatment, also have disadvantages; official records may miss cases that either were not reported at all or did not rise to the level of attention needed for substantiation. Thus, both retrospective and prospective data on childhood adversity have

advantages and disadvantages. Their relative predictive strength for various aspects of prenatal maternal and fetal wellbeing is an important area for future research.

Finally, PTSD continues to be an understudied mental health problem in pregnant women. More research should be dedicated to antecedents of maternal prenatal PTSD, such as the role of social support and pre-conception stressors, and the interaction between maternal adversity and PTSD before and during pregnancy on maternal–fetal stress physiology. PTSD symptoms, as well as childhood adversity, should also be routinely screened in all pregnant women. Stronger and more focused empirical and translational efforts to understand pathways of intergenerational risk and resilience through the pregnancy period will extend and enhance the burgeoning literature base and continue to promote optimal health and wellbeing in mothers and children across development and over generations.

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