DEVELOPMENT OF AN EVIDENCE-BASED EARLY CHILDHOOD DEVELOPMENT STRATEGY

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About the Center for Child Health Policy and Advocacy at Texas Children’s Hospital

The Center for Child Health Policy and Advocacy at Texas Children’s Hospital (PACT), a collaboration between the Baylor College of Medicine Department of Pediatrics at Texas Children’s Hospital and the American Academy of Pediatrics (AAP), delivers an innovative, multi-disciplinary, and solutions-oriented approach to child health in a vastly evolving health care system and market place. PACT is focused on serving as a catalyst to impact legislative and regulatory action on behalf of vulnerable children at local, state, and national levels. This white paper is written for the Episcopal Health Foundation (EHF), which aims to transform the people, institutions, and places in Texas to create healthy communities. Early childhood development is listed as one of EHF’s seven strategies to enhance community health through positive interventions with long-term impacts.

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EXECUTIVE SUMMARY

Background
Advances in developmental biology and neuroscience are building a strong evidence base that supports new approaches to population health centered on the early experiences and exposures in the first three years of life. Positive early experiences and exposures foster optimal brain development. Conversely, negative experiences and exposures impair brain development through cumulative damage over time or impaired development of the brain architecture during sensitive developmental periods. Pathways identified by a large body of research include three broad domains - prenatal, social, and physical. The downstream impact of what occurs along these pathways may include cognitive impairment and behavioral disorders, both of which influence lifelong achievement, economic productivity, and responsible citizenship. Recognition of these pathways has major implications for informing investments into basic science, preventive care, community-based interventions, and health policy. Increasingly, stakeholders from diverse sectors acknowledge there is a window of opportunity early in life in which the brain is particularly susceptible to effective interventions with measurable long-term benefits. The fundamental question for stakeholders is how best to allocate limited resources to produce transformative and sustainable changes. This white paper was undertaken with the principal purpose of setting priorities for investment in early childhood brain development.

Methods
The methodological approach consisted of a systematic review of the literature and key informant interviews with both local and national experts in brain and early childhood development. For the systematic review, the authors conducted an extensive review of scientific articles with key search terms relevant to brain development and early childhood development along the prenatal, social, and physical pathways. Concurrently, the authors conducted key informant interviews to gain perspectives from experts in the field. Local experts were interviewed to facilitate an environmental scan of the landscape in the 57 counties of the Episcopal Diocese of Texas. National experts were additionally interviewed to gain insights on how brain and early childhood development are understood and addressed in different settings across the country. The findings from the systematic review and key informant interviews were synthesized to develop a framework to inform strategies.

Framework
While many factors impact brain development in children aged 0-3 years, parent/caregiver-child relationships are key in nurturing brain development and mitigating negative factors. “Serve and return” interactions in the context of these relationships shape brain architecture. When parents or caregivers are sensitive and responsive to a young child’s signals and needs, they provide an environment rich in “serve and return” experiences. A framework for understanding early childhood development should include the family as the central pillar with relationships to other factors – learning and stimulation, nutrition, health services, environmental toxins – all occurring in the broad context of the community. The application of this model in the EHF region would result in investments into the community infrastructure and into evidence-based programs that strengthen and support the family unit.
Recommendations
As there are numerous evidence-based interventions aimed to improve early childhood development, implementation into real-world settings should be the focus of efforts. Recommendations were developed along three spheres: Intervention Focus, Investment Strategies, and Future Explorations.

Intervention Focus
Focus should be made on prevention as it demonstrates the highest return on investment. There are three potential stages at which foundations could intervene: the preconception stage, prenatal stage, and birth to age three stage. Intervening at earlier stages increases the likelihood of preventing or mitigating potential developmental harms. Strategies for investments should rely on proven interventions supported by data. Currently, limited data is available on the preconception stage, thus the prenatal stage is the earliest stage supported by evidence. Intervening at the level of the prenatal environment would not only address adverse intrauterine exposures, but also mitigate downstream exposures, such as maternal depression and stress, that may occur once the child is born. Additionally, there is a plethora of data supporting interventions that encourage positive parent-child experiences during the 0-3 year age span. Therefore, efforts should also focus on the parent-child interaction because this relationship is the most significant influence on brain development during the 0-3 year age span.

Investment Strategies
As there are limitations to philanthropic support, foundations must pursue multi-pronged strategies that effectively bridge research, community programming, and policy in order to ensure sustainability over time. In order to maximize impact, foundations should seek to pool resources with other foundations similarly invested in improving early child development. Efforts should be made to develop relationships with scientists studying brain development and provide seed funds to propel promising research. Support of community organizations should be contingent on use of evidence-based curricula to improve early childhood brain development. Partnerships with academic institutions may provide a mechanism for more rigorous data collection, analysis, and program evaluation for community programs given foundation support.

Future Explorations
The ultimate goal is to intervene at the most proximal domains of influence, therefore further exploration of possibilities for intervention during the preconception stage is warranted. Currently, there is little research on the preconception stage as it relates to brain and early childhood development.

Additionally, innovative funding strategies should be considered, such as a venture capital model to invest in nonprofit organizations supporting early childhood development. This would enable foundations to support emerging nonprofit organizations focused on early childhood development at the earliest stages of their organizational development.

Lastly, this project provides an overview of the various pathways that impact brain development. As a next step, we recommend engaging experts and stakeholders in the development of innovative strategies specifically for the EHF region. This engagement could be in the form of a working group, advisory board, or a one-day retreat to guide efforts. In terms of specific interventions, efforts should be directed towards developing implementation strategies to imbed evidence-based programs into communities.
INTRODUCTION

Children comprise a significant portion of our country, with 73.6 million children estimated in the U.S. in 2014. Approximately 7 million of those children live in Texas and 25% live in poverty (Lee 2015). The vitality of a nation depends, in part, on the aptitude of the next generation. Science demonstrates that intellectual and cognitive potential is determined by how the brain develops during the first few years of life. The brain controls the biological effects of all the other organ systems and influences cognition, intelligence, learning, coping and adaptive skills, and behavior. Because the brain controls these different aspects of human life, impaired brain function leads to impaired physical, mental, and emotional health and decreased functioning in society. Therefore, investments in early childhood to support healthy brain development help to reduce societal costs in remediation, health care, mental health services, and increased rates of incarceration.

Brains are built over time in a hierarchal fashion. During the first few years of life, new neuronal synapses are formed at the rate of 700 new connections per second. Simple circuits are developed first, and then more complex circuits build upon the simple ones. A combination of genes and early childhood experiences affect the nature and quality of the circuits developed and maintained. Neuronal connections are modified over time to make brain circuits more efficient. However, there is a critical window from birth to age 2-4 years during which the brain is most susceptible to significant and irreversible modifications (Johnson 2005). Neurons that remain inactive or are rarely active due to lack of stimulation are eliminated and those that are stimulated by experience are strengthened and maintained (Edelman 1987; Greenough 1987; Black 1998; Belsky 2011; Eagleman 2015). Therefore, the environment in which a child grows can either promote abundant, strong neuronal connections or a paucity of neuronal connections, and the prenatal to age four timeframe is the period during which a child’s brain is most susceptible to external influence.

There are many external factors that positively and negatively influence brain development during the critical window in childhood. These factors can be categorized into three groups: 1) prenatal pathways, 2) social pathways, and 3) the physical environment. The assessment of whether a brain is properly developing is often done by measures of cognition, language, intelligence, and social, emotional, psychological, and behavioral skills. Cognition is defined as a complex set of higher mental functions that include attention, memory, thinking, learning, and perception (Bhatnagar 2001). This paper will focus on using these outcome measures as indicators for optimal or adverse brain development.

Overall, this paper provides a brief overview of the pathways that influence brain development in early childhood between the ages of 0-3 years and discusses the impact of the pathways on brain outcome measures, with the primary purpose of priority setting. We also highlight interventions that mitigate harms to brain development and provide recommendations for prioritization of investment strategies.
The quality of the environment in which a fetus is exposed shapes cognitive and behavioral functioning (Richetto 2014). Fetal brain development is a complex and sensitive process that involves a variety of external maternal factors. These factors can alter the course of fetal brain maturation, thereby predisposing the individual to the development of multiple conditions early in life. Below we review prenatal factors critical to brain development.

**Prenatal Depression**

Prenatal depression has been estimated to affect upwards of 38% of women in the U.S. (Records 2007). It may frequently go undiagnosed because symptoms of depression are attributed to physical and hormonal changes typical of pregnancy (Bowen 2006). Risk factors for prenatal depression include a history of depression, lack of a partner, marital distress, lack of social support, poverty, increased life stress, substance abuse, previous abortions, unplanned pregnancy, ambivalence towards the pregnancy, and anxiety about the fetus.

Scientists have postulated that prenatal depression may result in programming effects on the hypothalamic-pituitary-adrenal (HPA) axis in both mother and child (Sohr-Preston 2006). The HPA axis controls stress hormones, and dysregulation in depression may elevate maternal concentrations of these hormones, particularly cortisol. Prenatal exposure to maternal cortisol may program the fetus’ hormonal axis to be more reactive to stress, which results in children becoming more easily over-aroused to non-threatening situations, including learning environments. Frequent fetal HPA axis activation may interfere with children’s development of learning, memory consolidation, and executive function.
The effects of prenatal depression on early child development, mediated through changes in the HPA axis, are manifested from birth through childhood. At birth, prenatal depression results in shorter gestation (Diego 2009; Field 2004). This result is concerning because children born prematurely face a higher risk of developing cognitive and behavioral problems (Larroque 2008). Prenatal depression has also been associated with a higher prevalence of infant sleep disturbances (Diego 2009; Field 2010), which have been associated with childhood behavioral conditions including depression, Attention Deficit/Hyperactivity Disorder (ADHD), difficult temperament, and neurodevelopmental disorders (Gruber 2000; Stores 2001). Taken as a whole, the findings reviewed indicate that maternal depression during pregnancy can alter a fetus’ HPA axis secondary to elevated maternal stress hormones in the intrauterine environment. Fetal dysfunction of the HPA axis puts the child at risk for cognitive delays after birth.

**Maternal Stress**

Stress is an encompassing term that includes a diverse range of exposures that may be acute or chronic (Kingston 2015; Glover 2014). Different types of maternal stress include maternal anxiety, daily hassles, bereavement, and distress from an unhealthy relationship. As with depression, maternal stress may lead to HPA axis alterations in the fetus that cause over-arousal after birth. This over-arousal can have short- and long-term impact on cognitive development (Lupien 2009). Moreover, infants of prenatally stressed mothers have less positive interactions with their mothers (Field 1985), are highly reactive (Davis 2004), have shown worse regulation of attention (Huizink 2003, 2004), and poorer language abilities (Laplante 2004). Maternal stress has also been associated with difficult temperament, sleep disorders, lower cognitive performance, and increased fearfulness among infants and toddlers. Additionally, pre-school children of mothers with prenatal stress have decreased attention spans, hyperactivity, behavioral and emotional problems, and bad behavior (Van den Bergh 2005).
Maternal Substance Abuse

Maternal use of illicit substances represents a significant public health problem with impact on child brain development. Cocaine has effects on the brain architecture important for the development of brain circuitry and human learning (Cregler 1986; Mayes 1991). Cocaine has significant effects on cognitive development at two years of age, with cocaine-exposed children twice as likely to have significant delay (Singer 2002). Additionally, alcohol has significant effects on brain development. Alcohol exposure leads to significant differences in brain size and shape (Archibald 2001), which result in developmental delay, learning disabilities, and hyperactivity. Despite declining rates of smoking during pregnancy, exposure to nicotine during pregnancy remains a significant problem. Prenatal nicotine exposure has been associated with altered brain structure and function in children (Tiesler 2014). Structural changes in the fetal or postnatal period include smaller volumes of the cerebellum and lateral ventricular system and a smaller frontal lobe. Such changes can lead to development delay in cognitive function. Prenatal nicotine exposure has been linked to impaired reading performance, increased risk of language impairment, and poor performance on language tests (Cho 2013; Eicher 2013). Nicotine exposure has also been associated with ADHD (Linnert 2003).

Maternal Physical Health

Dietary habits have substantial effects on the physiology and metabolism of fetuses (Modgil 2014). Growth and development of the fetus relies on nourishment provided by the maternal system. Furthermore, deficiency or excess of any nutrient results in long-term consequences to the fetus. Iron deficiency during gestation alters brain architecture, chemistry, and development (Lozoff 2006). This impacts development between 6-24 months of age. Infants with iron deficiency anemia test lower in cognitive, motor, social-emotional, and neurophysiologic development (Lozoff 2006). Among infants and toddlers, differences persist even after treatment with iron (Lozoff 2006).

Prenatal Vitamin B-12 deficiency has been shown to adversely affect the nervous system in the fetus, increasing the risk of neurodegenerative disease (Finkelstein 2015). Separately, Vitamin D status during pregnancy has been associated with improved neuropsychological development in children, including language, motor, and psychomotor outcomes (Morales 2015). In addition to vitamins, fatty acids are also important to brain development. The
fatty acids act as essential dietary nutrients, with docosahexaenoic acid (DHA) serving a major role in the growth and function of brain tissue (Innis 2007). There is a positive association between DHA status and neurodevelopmental outcomes in children (Hibbeln 2007, Oken 2008). Long-term studies suggest positive effects from increasing DHA nutrition on mental and motor skill development in early childhood (Helland 2003). Overall, efforts to improve maternal intake of critical nutrients during pregnancy can have a significant impact on brain development at a very low cost.

Physical Environment

Maternal exposure to toxins in the physical environment during pregnancy can impact the brain development of the child. Heavy metals, pesticides, air contaminants, and toxic pollutants pervade the environment (Modgil 2014). Heavy metals pose significant risks to fetuses. For instance, various metals, including lead and mercury, have been linked to memory difficulty in the child (Bose-O’Reilly 2010). Pesticides, including insecticides, herbicides, and fungicides, also pose significant risk to brain development. Pesticides have been linked to the loss of brain architecture and cognitive impairment (Modgil 2014). Additionally, prenatal pesticide exposure is associated with a higher risk of a developmental disorder at two years of age (Eskenazi 2007). Moreover, prenatal exposure to insecticides, such as chlorpyrifos, leads to developmental delay during the first three years of life (Rauh 2006). Lastly, air pollutant exposure results in slower brain processing speeds and ADHD (Peterson 2015).

Interventions

Screening for prenatal risk factors represents a core strategy for addressing brain development given the high return on investment from preventive care. As indicated by a large body of research, many risk factors go undetected secondary to inadequate screening by clinicians. Screening for factors such as depression, nutrition, and environmental exposures may facilitate implementation of evidence-based solutions. Evidence-based programs are being implemented in Texas and other cities to reduce maternal stress and depression and equip expectant mothers for parenthood. For example, the Health District in San Antonio offers prenatal educational classes focusing on prenatal care, nutrition, stress management, and labor/postpartum care for pregnant women and those who are considering becoming pregnant.

Peer support and psychotherapy group interventions have been shown to reduce prenatal depression and cortisol levels (Field 2013). Listening to music, relaxation, and cognitive behavioral therapy has been shown to reduce maternal stress (Field 2010), and maternal music exposure during pregnancy has led to higher scores for cognitive function in infants (Arya 2012). Also, yoga during pregnancy was found to reduce stress (Newham 2014, Battle 2015). Locally, the Motherhood Center offers prenatal and “mommy and me” yoga classes. Additionally, Houston Pregnancy Massage and Doula Care offers pre- and postnatal maternal massages, childbirth classes, and infant massage, all of which reportedly help alleviate maternal and family stress. However, these programs are often costly and therefore are only available to higher income families.
SOCIAL PATHWAYS

The social factors have the largest impact on the modification of neuronal connections during the brain's critical window in childhood. As described above, stimulating environments promote the development of strong neuronal connections, however the absence of such environments causes termination of the neuronal connections that are critical for cognition, intelligence, and overall functioning in society.

The Parent/Caregiver and Child Relationship

The development of healthy brain architecture depends on responsive, positive relationships with parents and caregivers. Nine key characteristics of effective relationships that optimize brain development have been identified in the literature: attunement/engagement, responsiveness, clear communication, managing communication breakdowns, emotional openness, understanding one's own feelings, empowerment and strength building, moderate stress and challenges to minimize toxic stress (Shonkoff 2010), and building coherent narratives (Moore 2007). Positive relationships between parents/caregivers and children are critical for the development of optimal brain architecture because of the dependency of neuronal connections on this interaction. The caregiver’s response to the child's verbal or nonverbal communication, often called “serve and return”, shapes which connections remain and which ones are eliminated (National Scientific Council on the Developing Child 2004). An example of a positive “serve and return” scenario is a caregiver or parent's attentive response to a young child's cries or attention-seeking through eye contact, addressing the child, and meeting the child’s need. This type of positive interaction creates neural connections that support the development of communication and social skills. Responsive looks and smiles from caregivers trigger the release of pleasurable neurochemicals that help the infant’s brain to grow. Positive neurochemicals from supportive relationships can even protect young infants from the negative effect of toxic neurochemicals that result from adverse childhood experiences, such as poverty or violence, and toxic stress (Moore 2007).

In the absence of supportive relationships, the likelihood of poor outcomes in cognition and physical and mental health increases for a child as the severity or number of adverse childhood experiences accumulates. Moreover, as the child’s “serves” go unreturned, impairment of the child's brain architecture will occur. In the most extreme scenarios, children who suffer from severe neglect or child maltreatment (i.e. physical, sexual, or emotional abuse) in the first years of life experience excessive termination of several important synapses in the brain. This results in permanent damage to the developing brain, and these children have been shown to have a smaller head size, less gray and white matter volume, abnormal brain structure, brain hypo-activation, increased incidence of mental illness, and a lower IQ (Perry 2002; Mehta 2009; Eluvathingal 2006; Belsky 2011; Eagleman 2015). Even in less extreme home environments where children are not mistreated or neglected, the parent-child relationship can be affected by external factors that decrease the number of “serve and return” interactions between the parent/caregiver and child. Below we discuss potentially modifiable factors that have been identified as having an impact on the parent/caregiver-child relationship.
Below we discuss potentially modifiable factors that have been identified as having an impact on the parent-child relationship:

**Postnatal Depression**

Postnatal depression can negatively affect the ability of the mother to interact positively and responsively to her child. The emotions that are common with postnatal depression, such as sadness, loneliness, tiredness, fatigue, lack of motivation, and volatile emotions, interfere with the mother’s ability to be responsive to her child. Thus, the “serve and return” relationship between mother and child is negatively affected. Maternal depression has been associated with deprivation of the child’s basic needs, such as food and nutrition, which leads to poor growth and has been associated with adverse behavior outcomes in children (Avan 2010). Moreover, children whose mothers are depressed are more likely to have language and cognitive delays (Stein 2008; Singla 2015), and low socioeconomic status (SES) puts children at a higher risk for the negative impacts of caregiver depression (Stein 2008).

Unfortunately, mental health disorders are the second leading cause of hospitalization of women of childbearing age (15-44 years) in Harris County and across Texas. In 2012, approximately 100,000 Texas women were hospitalized with a mental disorder, with mood disorders accounting for nearly 60% of the diagnoses. It is estimated that 69-79,000 Texas women experience postpartum depression each year, with 12-15,000 of these women living in Harris County (Van Horne 2014).

**Maternal Stress**

Not surprisingly, maternal stress can also interfere with the “serve and return” interaction between mother and child. There are many factors that contribute to maternal stress, such as poverty, food insecurity, and neighborhood violence. Yet, intimate partner violence is one of the most significant sources of maternal stress. It is estimated that 15.5 million children in the U.S. reside in households in which interpersonal violence is recurrent. Mothers who experience intimate partner violence report increased stress levels and difficulty responding positively to their children (Herman-Smith 2013). Thus, the impact of intimate partner violence on brain development is significant. Further, maternal stress has been strongly associated with increased DNA methylation, a signaling tool to mediate gene expression and inactivate cells, in the child (Phillips 2008). Erroneous inactivation of cells in young childhood leads to disease in adulthood and adverse brain development (Essex 2013), as well as impaired cognitive and socio-emotional development when the children become school-aged (Kingston 2012).

**Parenting**

Parenting includes discipline, monitoring, autonomy granting, as well as emotional components of warmth, acceptance, and responsiveness (Frick 1994; Stouthamer-Loeber 1986; Maccoby 2000; McLeod 2007). There is a constitutional right, as
interpreted by the U.S. Supreme Court, for parents to generally raise their children as they see fit. The assumption is that the “natural bonds of affection lead parents to act in the best interests of their children” (Parham v. J.R.). Therefore, for many, how parents interact with their children is a private matter unless the state has an overwhelming right to intervene (i.e. child abuse). However, research demonstrates that parents’ interaction with their child, whether positive or negative, has a significant impact on their child’s brain development and can have a long-lasting effect on that child’s cognition and physical, mental, and behavioral health (Merz 2015; Moore 2007). For low-income children, parental responsiveness was identified as a significant predictor of both current cognitive skills as well as future literacy, math, and emotion knowledge (Merz 2015). In the same at-risk population, positive parenting was found to mitigate other adverse events (Flouri 2015). Unfortunately many parents, especially those who are considered high-risk (i.e. low socioeconomic status or teen parents), are unaware of the importance of responsive parenting (Singla 2015). Thus, many parental interventions focus on educating parents and building their capacity to engage in the responsive parenting that is required for the “serve and return” interaction with their children.

**Adverse Childhood Experiences (ACEs) and Toxic Stress**

Adverse childhood experiences (ACEs) and the resulting toxic stress can cause disruptions in the developing brain and body that affect health, school readiness, learning, and behavior. Specifically, ACEs such as physical or sexual abuse, physical and emotional neglect, poverty, parental psychopathology, parental stress, and conflict between parents have been linked to structural changes in the parts of a child’s brain that control executive functioning, emotion, memory, mood, and behavior (Chartier 2010; Chapman 2004; Gunnar 2009).

The impact of ACEs on the brain and body is caused by the prolonged, elevated physiologic stress response that these situations initiate in a child’s body. This prolonged, unrelenting physiologic stress response, is often called “toxic stress”. Normally, the body responds to stress through a series of hormonal interactions, and then when the stressor is gone or buffered, the hormones are no longer released. However, unmitigated external stressors cause constant release of stress hormones, which alters neuronal growth and neural circuits in the brain and results in a prolonged release of stress hormones even when the external stressor is no longer present (Cohen 2006; Seckfort 2008; Heim 2010; Frodl 2013; Palmer 2013). This toxic stress occurs when there is an absence of a supportive, “serve and return” caregiver-child relationship to buffer the child’s exposure to ACEs. Risk factors for toxic stress are extreme poverty, significant under-nutrition, recurrent emotional or physical abuse, chronic neglect, severe maternal depression, parental substance abuse, and exposure to violent conflicts (Britto 2013). Toxic stress leads to long-term behavioral and emotional problems that increase the risk for mental and physical health disorders in adulthood (Gunnar 2009). Andy Gardner, MD, describes toxic stress as the “key intergenerational transmitter of social and health disparities”.

Adverse childhood experiences are not limited to a certain ethnic, racial or economic group, as evidenced by The Adverse Childhood Experiences Study, which evaluated over 17,000 middle class, middle-aged Americans and found associations between ACEs
such as household dysfunction, abuse, neglect, and negative mental and physical health outcomes (Felitti 1998). More than half of the participants in this study reported at least one ACE, and one-fourth reported more than 2 ACEs (Felitti 1998). This study found a positive correlation between number of ACEs and health and behavioral diseases as an adult (Felitti 1998). For instance, children who had four or more ACEs had a significant increase in alcoholism, drug abuse, depression, smoking, greater than 50 sexual partners, sexually transmitted diseases and severe obesity (Felitti 1998). Thus, there is a cumulative effect of ACEs on child cognitive and behavioral outcomes, with number of ACEs correlating to a higher risk of poor academic performance, adult depression, and poor adult health outcomes (Sameroff 2000).

In addition to child abuse and parental neglect, poverty is a major ACE that negatively impacts brain development. Poverty in early childhood has been associated with smaller white and cortical gray matter and hippocampal and amygdala volumes in school age children. However, these changes in brain structure are ameliorated by positive caregiver relationships (Luby 2012, 2013). Thus, experts hypothesize that it is not poverty itself that adversely affects brain development, but rather the effect poverty has on the parent/caregiver relationship with the child. Studies demonstrate that low-income children have less optimal home and childcare environments, both of which provide less cognitive stimulation (Eamon 2002). Additionally, children in low-income families have been shown to watch more TV, have limited access to books, and read less frequently with their parents (Kumanyika 2006; Duke 2000; Newman 2011). Children in low-income families also have limited access to optimal nutrition, a higher incidence of chronic health conditions, and increased exposure to environmental toxins (Krassner 1986; Schürch 1995; Bloom 2009; Bellinger 2008; Hillemeier 2011).

In addition, toxic stress may occur as a result of living in poverty. Two major risk factors for toxic stress are: 1) inadequate supply of affordable housing for low-income families, which decreases their ability to pay for other necessities such as food, medical, and/or dental care, and 2) the increasing spatial segregation of households by income and the development of physically and socially deteriorated neighborhoods that are not perceived as being safe (Anderson 2002). Neighborhood characteristics cause toxic stress that impairs caregivers’ ability to have optimal, supportive relationships with children (Jutte 2015). In addition to caregivers’ toxic stress, children may independently experience toxic stress from their neighborhoods. Studies have shown that neighborhood quality is an independent factor that influences child brain development (Vanderbilt-Adriance 2008). Dangerous neighborhoods negatively impact child development through increasing the child’s exposure to stress (Hackman 2012). Further, exposure to community adversity influences gene expression and brain development (Jutte 2015). Therefore, the effects of poverty on brain development are compounded through its effects on both caregivers and their children.
Interventions

An important focus of all early child development interventions should be to promote attuned and responsive relationships and secure attachments between parents/caretakers and children that will maximize “serve and return” interactions and minimize toxic stress. Additionally, interventions should include a component dedicated to increasing the child’s exposure to external stimulation, which will provide the foundations for socio-emotional language and cognitive skills (Moore 2007; Garner 2013). Moreover, parents and/or caretakers should be engaged and involved in the interventions, which are called “two-generation” programs, to optimize the well-being of both the parents and the child (Shonkoff 2013). Finally, interventions that focus on prevention or early identification of risk factors for negative outcomes should be prioritized, as these efforts are more cost effective than intervening after the injury has already occurred, and have greater long-term effects on population-based early brain development (Chapman 2004; Doyle 2009; Heckman 2011, Thompson 2014). Types of programs that meet these criteria are parenting education programs, home visitation programs, and maternal mental health and support. We highlight the following as examples of each.

Parenting Education Programs

Tiered evidence-based parenting programs have been consistently identified as one of the most cost effective evidence-based public policy solutions for child welfare (Mercy 2009; Lee 2012). The lowest tier usually involves public health campaigns on positive parenting and universal education through pediatric offices, community centers, and/or churches. Higher tiers include more intensive programming for high-risk families or for families with a history of child maltreatment. Tiered programs provide support for individual families who are in greatest need (i.e. families with greatest risk), as well as provide an upstream solution for improving parenting skills and relationships between parents and children, and preventing child abuse and neglect. An example of a successful parenting program is the U.S. Triple P System Population Trial (TPSPT), which took place in 18 counties in South Carolina. A meta-analysis of Triple P-Positive Parenting Programs found consistent evidence that this program positively changes parental skills, child behavioral problems, and parental wellbeing (Nowak 2008).

Home Visitation Programs

Home visitation programs have been shown to positively impact health outcomes and brain development in early childhood. These programs provide high-risk parents with education on parenting, health, nutrition, normal child development, and resource availability through regular home visits by a nurse or other professional. The data on home visitation programs are mixed; some trials show positive effects on infant health and development and reduced child maltreatment, while other studies do not. This is thought to be due to the heterogeneity in program quality and study design. One example of a successful home visitation program is the Nurse Home Visiting Partnership (NHVP). This program targets high-risk pregnant women who have at least two of the following risk factors: unemployed, unmarried, or less than 12 years of education.
Women are enrolled at less than 29 weeks gestation and are followed until their child is two years old. A certified nurse with formal training goes out to the house regularly and teaches parents what to expect during and after pregnancy. They also provide parenting education, which includes how to play with the baby to promote healthy cognitive development, and encourage healthy behaviors such as good nutrition and avoiding tobacco, alcohol, and other drugs. The NHVP has undergone randomized evaluations at three sites in the U.S., and children of mothers enrolled in this program had fewer health problems, fewer encounters for injuries and toxic ingestions, and were more likely to be breastfed. These children also had higher GPAs at age nine compared to the children whose parents did not receive the NHVP intervention (Olds 2006, Mercy 2009; Currie 2015). Evidence-based home visitation programs are somewhat limited by their high cost, although they can be cost-effective over time.

**Maternal Mental Health Support/Social Support for Mothers**

Perceived positive support and the development of active, effective coping strategies can promote maternal psychological wellbeing and decrease the negative impact of maternal depression on the mother-child relationship. Mothers with positive support from spouses, family members, and/or the community report fewer depressive symptoms and better bonding with their infants (Singla 2015).

Mothers with depression also need access to mental health care services. Screening women for depression and referring to appropriate services, as well as increasing access to mental health providers, are all important policy initiatives that will result in better maternal mental health. Good maternal mental health is critical to the development of the optimal “serve and return” parent-child relationship. Therefore, incorporating mental health support services into early childhood interventions, such as parenting education, home visitation programs, and early childhood education programs, is an attractive strategy (Sohr-Preston 2006; Moore 2007).

Any intervention that provides women with an opportunity to form social networks and a support system will likely reduce toxic maternal stress and increase maternal self-confidence (Ruel 2013). One example of such an intervention is the concept of group well-child visits. Similar to the group prenatal care visits described above, group well-child visits usually bring together 2-10 children and their caregivers to see the health professional at the same time. Anticipatory guidance is provided in a conversational format in the group setting, which provides time for an extended interaction between the provider and the families while also promoting informal bonds between participating families (Rushton 2013).

Overall, the social pathways have the most significant, long-lasting impact on brain development in childhood, and the most influential factor is the parent/caregiver and child relationship. Therefore, interventions to maximize this factor and minimize the negative factors in this pathway will optimize child brain development.
Toxins

Toxins, such as lead, pesticides, and air pollution, can harm a child’s brain development because they interfere with the normal physical processes of the brain and nervous system. For instance, children of agricultural workers demonstrate short-term memory and attention loss when exposed to pesticides such as organophosphates (Rauh 2006). Additionally, children living in areas with high nitrogen dioxide (NO2) concentration have poor cognition and white matter changes in the brain (Calderón-Garcidueñas 2008).

However, the most common environmental toxin impacting brain development is lead. Childhood lead poisoning is a preventable illness that impedes the cognitive and behavioral development of children. The CDC defines lead poisoning as blood levels of lead greater than 10 ug/dL. However, due to the nervous system’s rapid growth during the earliest years of life, even very small doses of lead can cause injury to the brain in children ages 0-3 years (Jedrychowski 2009). Even in children ages 3-5, much lower lead levels have caused impairment in brain functioning. Thus, a safe lead level in children has yet to be determined (Evens 2005).

Lead poisoning occurs through the ingestion of lead, and is more common in children because a child’s intestinal lining is more permeable to lead than an adult’s. Children also engage in behaviors, such as playing in the dirt, teething, mouthing toys, etc., that increase the risk of lead exposure. Lead is found in dirt, household dust, lead paint, imported toys, and ceramics. Public health measures to reduce lead poisoning - such as removing lead paint, educational messaging, and lead testing in children - have had some positive impact, but lead poisoning continues to be a problem (Evens 2005). The challenge with lead poisoning is that children with elevated blood levels have no overt symptoms, and symptoms that are exhibited, such as tiredness or eating poorly, are often behaviors that occur normally between the ages of 18-28 months. Lead can cause a decrease in IQ of a child by 5 points, which is enough to shift a child from gifted and talented to normal intelligence, and those with normal intelligence to special education. The areas of the brain that control impulse control and physical movement are also affected. For instance, children with lead poisoning between the ages of 1 and 3 demonstrate greater hyperactivity, distractibility, and lower frustration tolerance (Mendelsohn 1998). Additional deficits in reaction time, visual-motor integration, and attention have also been discovered.

The impact of lead on brain development may not be limited to the direct effects on the brain. Studies have found that higher lead levels in mom and child are associated with lower maternal perceptions of being able to discipline their children, which may contribute to poorer parenting and family interactions (Kordas 2011). Parent-child interactions have a significant impact on brain development in young children, thus lead’s impact on this interaction compounds the physical impediments to brain development.
Living conditions

The environment in which children live can negatively impact their brain development. Below we list three living conditions - noise, crowding and chaos - that can impact brain development in childhood.

Noise

The exact mechanism in which noise impacts brain development is not clear, however research has shown that children who are exposed to chronic noise have cognitive deficits that impact their reading, and deficits in the brain’s speech function and auditory processing (Kujala 2009; Evans 2006). Additionally, children appear to adapt to chronic noise exposure by ignoring or tuning out auditory stimuli. Yet, an unintended consequence of this coping strategy is indiscriminate filtering of auditory stimuli, including speech - a fundamental building block of reading (Cohen 1973; Evans 1997; Hygge 2002; Moch-Sibony 1984). The impact of chronic noise on a child’s speech function and cognition may be the result of an indirect effect. Rather than a direct impact on the brain itself, noise may interfere with caregiving behaviors. Caregivers may talk less to their children, be less responsive, and not read aloud in noisy settings (Ferguson 2013). Decreased caregiver interaction interferes with the “serve and return” model upon which the brain architecture is formed.

Crowding

The U.S. Census considers more than one person per room as a crowded living environment, and this index has been shown critical to human wellbeing (Baum 1987; Evans 2001). The negative effect of crowding on brain development becomes apparent at 18 and 24 months of age (Gottfried 1984). Moreover, research demonstrates that children who live in a crowded environment have verbal, perceptual, quantitative, and language deficits at the ages of 30-42 months. Additionally, residential crowding was shown to be negatively associated with the IQ scores of children at 30 months (Wachs 1978).

These cognitive deficits may be due to crowding’s interference with the “serve and return” relationship between children and their caretakers. Parents are less responsive to young children in more crowded homes, starting in infancy, irrespective of social class (Bradley 1984; Bradley 1994; Evans 1999; Wachs 1989; Wachs 1991). These children often exhibit social withdrawal, which may be a coping mechanism to their parent’s decreased responsiveness. Moreover, there is reduced parental monitoring of children in crowded homes (Gove 1983; Hassan 1977; Mitchell 1971), and parents talk less to their infants (Wachs 1979, 1991) and use less sophisticated speech from infancy to two and a half years of age (Evans 1999). Even after controlling for SES, both children and their parents report more strained, negative familial interactions in crowded homes (Baldassare 1981; Bartlett 1998).
The impact of crowding can possibly be mitigated by increased access to the outdoors. Children prefer outdoor settings, particularly those in nature (Chawla 2002; Hart 1978; Korpela 2002; Moore 1989). One reason for this may be the wider array of motoric and social play opportunities and greater independent mobility afforded by such spaces (Heft 1988; Kyttä 2002, 2004). Nearby nature may also enhance attention (Wells 2000) and buffer some of the ill effects of chronic stressor exposure among children (Wells 2003).

**Chaos/housing**

Children ages 3-4 that live in chaotic homes demonstrate more deficits in cognitive development compared to their peers (Petrill 2004). The effect of chaos on brain development may be indirect, as parents of infants in more chaotic homes, regardless of SES, are less responsive and offer fewer stimulating learning opportunities (Corapci 2002). In contrast, families in households with structured routines are more cohesive, happier, and have less conflict (Jensen 1983). Thus, most of the explanations for the adverse impacts of chaotic early childhood settings have focused primarily on parent-child relationships and on self-regulatory ability.

Housing environments also have potential developmental consequences. Several adverse child outcomes are related to residence in economically impoverished neighborhoods, even when the study controlled for individual-level SES (Leventhal 2000). Because housing, chaos and crowding are all related, and have a relationship with low SES, it is difficult to ascertain the direct impact of any of these factors. Though, most of the studies controlled for SES and found that each of these factors was an independent variable.
Nutrients provide the building blocks that play a critical role in DNA synthesis, neurotransmitter and hormone metabolism, and are important components of enzyme systems in the brain (Nyaradi 2013). Adequate nutrition is critical to normal brain development during pregnancy and up to age two years old (Ngure 2014). Inadequate nutrition affects brain development directly, and the window of opportunity to correct the impact of inadequate nutrition closes after two years of age (Alderman 2014). Several studies have demonstrated persistent cognitive deficits, including lower IQ and poorer academic achievement, despite correction of malnutrition and a complete catch-up in physical growth by the end of puberty (Galler 2012). Notably, their teachers reported a striking 4-fold increase (60% vs. 15%) in the prevalence of attention problems relative to healthy children (Galler 2013).

An essential mineral to brain development is iron. Iron is a vital part of forming the covering (i.e. myelination) around nerves that facilitate transmission of information. Also, iron may affect oxygen transport/storage, which is important for brain function (Wang 2013). Infants with iron deficiency demonstrate attentiveness defects such as ADHD that manifest as they get older (Galler 2012). Further, infants with iron-deficiency anemia performed 6 to 15 points lower on their mental development test compared to infants without anemia (Lozoff 2006). Though, interestingly, some diet-induced brain deficits may be ameliorated by positive child/caregiver experiences (Galler 2013).

Breastfeeding has been shown to improve cognitive development, with some studies showing an increase in IQ of 2 to 5 points in children who were breastfed (Nyaradi 2013). Breastfeeding provides adequate nutritional support for the developing brain, but also increases maternal-child bonding. Therefore, it is difficult to ascertain whether the improvement in intelligence and cognition is due to breast milk alone, or the “serve and return” interaction that breastfeeding encourages.

Interventions

The physical environment can impact a child’s brain development through direct interference of the brain’s normal processes, and through its influence on the “serve and return” model that is critical for the development of the brain’s architecture. Little is known about the cumulative effects of these factors or the threshold at which little harm occurs if exposed to these factors. It seems evident that some factors, such as lead, have a negative impact even at the smallest levels of exposure, especially between the ages of 0 to 3 years. However other factors, such as chaos and noise, appear to require a chronic, sustained exposure. Interestingly, in both the toxins that physically damage the brain and social conditions that indirectly affect the brain, the positive caregiver-child interaction can mitigate that harm. Additionally, the interventions directed at obviating these harms all involve educating families to avoid certain conditions and improving
housing/living conditions. For lead in particular, interventions focus on removing sources of lead through remediation of housing, educating families on keeping children away from possible lead sources, increasing calcium intake, and screening (Evens 2005). In Harris County, approximately 300 children are diagnosed with lead poisoning annually. However, only 20% of children in Harris County receive lead testing; therefore the number of actual lead poisoning cases could be much larger. The Houston Health Department received $6 million to provide lead remediation for at-risk families, and efforts to increase screening and awareness of lead poisoning are underway.

Inadequate nutrition is another modifiable factor that can impede brain development. Organizations like Healthy Living Matters (HLM), which is a local public-private partnership consisting of a multi-sector group of local leaders, have formed as an initiative to curb childhood obesity in Houston/Harris County (up to 34% of Harris County children are overweight or obese). A major focus of HLM is improving access to good nutrition in local low-income neighborhoods (21% of households with children are food insecure) as well as improving the built environment to provide a safe, stimulating place to play, which encourages more physical activity and also reduces toxic stress.

Lastly, increasing children’s access to outdoors may mitigate poor living conditions. An example of an innovative local program working to improve the built environment and reduce toxic stress is the Children and Nature Network. They provide children and families with outdoor experiences in neighborhoods and early childcare environments that have a strong emphasis on experiences in nature, such as gardening and playgrounds. Data shows that access to a high-quality park with programming increases cognitive stimulation and decreases family toxic stress. Interaction with nature and exercise are positive coping mechanisms that reduce toxic stress. Moreover, high-quality parks have been shown to increase neighborhood sense of pride and safety.
There are many factors that can negatively impact brain development in children aged 0-3 years. However, there is one main factor that positively impacts brain development during this time period, and also has the ability to mitigate adverse effects from other factors - parent/caregiver-child relationships. These relationships are key to the “serve and return” interaction vital for proper brain development during the sensitive periods of 0-3 years. Moreover, positive relationships are key to the development of resilience in the child to adapt to adverse childhood events. On the other hand, negative “serve and return” interactions can create irreversible changes in the brain that adversely affect the child's brain architecture and impede the child's ability to adapt to other external adversities.

We developed a model (Figure 1) that depicts the significance of the family - defined as the core caregiver-child relationship, including parents, extended family, adoptive parents, etc. - and its relationship to the other major factors in early childhood development. The family shown in the model also includes factors that affect maternal health, which influences the child's brain prenatally and beyond. Each factor interacts and influences the child's development in the family unit, but also impacts the child's development independent of the family relationships. Additionally, the model depicts the importance of strong social and community supports, which can buffer the adverse effects of stressors on the family through provision of resources, social support, education programs, economic mobility, and positive modeling of parenting behaviors by other community members or organizations. In addition to family support, the community infrastructure involves housing, access to nutritious foods, addressing toxins, and access to health care services. Thus, strong communities have the ability to address factors that adversely affect brain development such as living conditions, neighborhood violence, exposure to toxins, and access to resources in their neighborhoods. This model also reflects the prioritization of factors. The predominate center circle reflects the most influential factor, family relationships, and the smaller external circles reflect less influential factors.

The application of this model in the EHF region would result in investments into the community infrastructure and into evidenced-based programs that strengthen and support the family unit. Such programs include community parenting education programs, initiatives to integrate screening and treatment of maternal stress, prenatal classes, efforts to improve housing for families as that will reduce crowding and chaos - which interfere with parent-child interactions, and exposure to lead and other toxins in the home.
For foundations wishing to invest in early childhood development, there are multiple pathways to strategically achieve this goal. Strategies may include supporting research through existing relationships with researchers, supporting new or established community programs, or allocating funds towards requests for proposals. Foundations may work alone or in partnership with other foundations. The Pritzker Children’s Initiative and The Bridgespan Group recently released a report outlining numerous early childhood investment opportunities that both public and private sector investors can make immediately to improve brain development. This report emphasized five categories of investment: strengthen public systems of early care and education; scale health and developmental screenings to connect parents to resources; improve the training, continuing education, professional development, and compensation of early childhood educators; support greater access to high-quality, evidence-based programs for families; and promote ongoing program innovation and improvement.

As there is no single path towards the outcome of improving early child development, philanthropic organizations must make strategic decisions based on resources, existing relationships with stakeholders, the context of their communities, and opportunities that may arise. Foundations must also consider strategies by which their efforts can be translated into policy since philanthropic resources are limited and cannot assure success alone. Two examples of how foundations invest in early childhood development are described below.

**Bezos Foundation**

The Bezos Family Foundation in Seattle supports evidence-based, inspiring learning environments for young people. The Foundation views early childhood as a critical window for brain architecture. It therefore supports brain research, programs that support families, and community interventions that enrich learning environments for children. The Foundation initiated its commitment to early brain development by financially supporting the Institute for Learning and Brain Sciences (I-LABS) at the University of Washington. Specific mechanisms included partial support of an Endowed Chair and capital investment in the infrastructure for I-LABS, which required matching funds by the University of Washington. To further support research, the Foundation has developed relationships for direct investment towards specific scientists and recommendations of other scientists. The Foundation has established a team of scientific advisors who receive small funds to support promising work that can be leveraged into larger grant funding. The Foundation also funds specific national programs such as the Frontiers of Innovation at the Center on the Developing Child at Harvard University and ParentCorps at New York University. While some of these methods are traditional for foundations, the Bezos Family Foundation has taken an innovative approach towards funding community-based nonprofit organizations. Furthermore, the Foundation has implemented a venture capital approach to seed early-stage, nonprofit organizations.
Through a nonprofit venture philanthropy fund, the Bezos Foundation has been able to identify organizations at a flex point in their development and provide support for critical activities such as building a business model and developing a board. Understanding the limits of philanthropy to support early child development, the Bezos Foundation’s ultimate goal is to bridge research, practice, and policy.

**Oregon Parenting Education Collaborative**

The mission of the Oregon Parenting Education Collaborative (OPEC) is to support delivery of evidence-based parenting education programs and to support collaborative efforts to strengthen regional parenting education systems through coordination and planning. Its mission is to ensure that Oregon parents have access to high quality, proven parenting education programs that support them in their critical role as their children’s teachers. Regional parenting education “hubs” work with community partners to deliver parenting education services, while building stronger and more coordinated parenting education systems in their regions. OPEC is a partnership between four of Oregon’s largest foundations - The Oregon Community Foundation, The Ford Family Foundation, Meyer Memorial Trust and The Collins Foundation - and Oregon State University. Prior to the formation of OPEC, the different foundations worked independently to fund early childhood development interventions in their communities. They frequently invited each other to their sponsored conferences on early childhood development. Recognizing the overlap in their goals, these foundations made the decision to pool their resources to more substantially address early childhood development in Oregon with the eventual aim to inform and impact policy. OPEC was designed as the coordinating organization for their efforts. OPEC funds community grants along 36 counties in Oregon. The funders of OPEC partnered with Oregon State University (OSU) to develop a systematic approach to support the initiative through evaluation, professional development, and technical assistance. OSU has developed tools specific to the OPEC initiative, allowing collection of common outcomes across programming efforts. Evaluation efforts are facilitated through use of the OSU-developed online reporting system, which allows grantees to maintain a role in the evaluation process. In addition to the online reporting system, OSU collects data through interviews, focus groups, and surveys. The evaluation process lays a quantifiable foundation for continual improvement of the initiative. Through rigorous data collection and partnership with academia, the foundations are well positioned to influence policy on early child development.
Both the systematic review and key informant interviews demonstrated that numerous evidence-based interventions directed at early childhood development exist. Consequently, the next critical step in addressing early childhood development is implementation of evidence-based programs into real world settings. As this work evolved, three major categories for recommendations emerged consisting of Intervention Focus, Investment Strategy, and Future Explorations. Below we outline our recommendations according to each category.

**Intervention Focus**

The opportunity to use financial investments to impact brain development in early childhood can be viewed on a continuum of possibilities. Research demonstrates that the highest return for investment occurs with preventative strategies. It is more expensive long-term to treat children, who later become adults, for the social, emotional, cognitive and behavioral deficits that result from impaired brain development. Thus, prevention is the best, most cost-effective strategy. Figure 2 depicts the stages at which interventions can optimize brain development and minimize harms.

The preconception stage is the time period before a woman becomes pregnant, and is the most upstream possibility for prevention. In fact, the CDC views the preconception stage as potentially having the most impact on preventing unfavorable brain development. Theoretically, investments in ensuring women are financially, relationally, physically, and emotionally prepared for a child would better position the woman for pregnancy and motherhood and lessen the risk of maternal depression, maternal stress, and adverse social circumstances. However, this is a new field and minimal research exists to determine whether interventions during the preconception stage are effective.

Alternatively, investments into the prenatal period are supported by solid evidence of intervention effectiveness. Evidence-based interventions during pregnancy and after birth are promising. As depicted in the Early Childhood Development (ECD) model, the family unit is the most influential factor in a child’s brain development. Therefore,
mother during pregnancy, help to reduce current stressors (i.e. prenatal classes, yoga, etc.), prepare her and her partner for parenthood, screen for depression and optimize maternal health, and provide opportunities for economic mobility through community investments should be financially supported.

Additionally, family relationships also have the most significant impact on brain development after birth to three years of age. Thus, investments supporting the parent/caregiver-child interaction will yield the highest return during this stage. There are several evidence-based parenting programs that demonstrate positive brain development outcomes that could be implemented in the EHF region. Of particular interest may be remote coaching programs, as they provide the same service (electronically) at a lower cost. Though parenting programs are effective, at-risk families cannot thrive in isolation. Individual or group parenting programs do not address the fundamental cause of parental stress - depression, poverty, poor housing, etc. Interventions that support and increase community capacity to provide resources to families, opportunities for economic mobility, parent and child support, and positive modeling would provide a more sustainable change and a greater impact in the community overall.

**Investment Strategy**

As there are numerous areas in need of financial support, investment strategy is key. To achieve long-term impact, foundations should develop a strategy to bridge basic science, practice, and policy. Pooling of resources, as was done in the OPEC initiative, creates additional opportunities to advance policies on a local and state level that support early childhood development. Therefore, we recommend a funding strategy that seeks opportunities to pool resources with other local foundations invested in improving early brain and child development. This strategy will foster a more collaborative approach to advancing child development and increase the potential for impact through pooled resources. As demonstrated by the Bezos Foundation, development of a scientific advisory board of researchers in brain science presents another important strategy. The foundation can work with the academic institutions of these scientists to leverage matching funds, thereby increasing the magnitude of available financial support. Lastly, we recommend partnerships with academic institutions to increase the rigor of data collection
and analysis for programs supported by the foundation, with the ultimate goal of only funding interventions that are supported by evidence.

**Future Explorations**

Given the impetus to intervene as early as possible on adverse exposures and experiences, the preconception period represents a consideration in future work. According to a report on preconception care by the World Health Organization (2012), there is increasing recognition that a gap exists in the continuum of care. A growing body of evidence is demonstrating that preconception care may improve child health outcomes. However, there is a scarcity of data regarding the effectiveness of interventions during the preconception phase on brain development. Logistical implementation of such strategies may also be a challenge as identifying who is going to become pregnant and incentivizing this group to participate in an intervention may prove difficult. Overall, there is no global consensus on preconception care as part of an overall strategy to improve brain development. A conference or stakeholder meeting on preconception care and brain development may elucidate more specific directions in this area.

An increasing number of companies exist that connect foundations to emerging nonprofit organizations. Many have termed this the venture capital model. We recommend consideration of using the venture capital model of investing to support emerging nonprofit organizations focused on early brain and child development. Such investments will support innovative nonprofit organizations at the earliest stage of their formation. Lastly, we recommend engaging experts and stakeholders in the discussion of developing a needs assessment for interventions in early childhood development in the EHF region, and to develop innovative, targeted solutions for implementation of evidence-based programs. This paper should be the first step of many to ensuring that investments into early childhood development are strategic, evidence-based, innovative, effective, and sustainable.
SUMMARY

With the growing acknowledgement that early exposures and experiences have both direct and indirect impact on brain development and early childhood development, there is an urgent need for investors, both private and public, to develop strategies to meet the needs of young children. Early investments will influence lifelong achievement, economic productivity, and responsible citizenship. Based on our work, we identified three pathways critical to brain development and early childhood development: prenatal, social, and environment. Targeting these pathways is essential to transforming the future of young children in the U.S. For those invested in improving brain development and early childhood development, it is important to consider strategies along three spheres: intervention focus, investment strategy, and future explorations. This approach will provide a multi-dimensional action plan that will influence research, practice, and ultimately, policy.

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