All biological systems in the body interact with each other and adapt to the contexts in which a child is developing—for better or for worse. The brain and all other organs and systems in the body are like a team of highly skilled athletes, each with a specialized capability that complements the others and all of whom are dedicated to a common goal. Systems relating to brain activity, heart and lung function, digestion, energy production, fighting infection, and physical growth are all interconnected and influence each other’s development and function. Each system “reads” the environment, prepares to respond, and shares that information with the others. Each system then “signals back” to the others through feedback loops that are already functioning at birth. Therefore, the environments we create and the experiences we provide for young children and their
families affect not just the developing brain, but also many other physiological systems, including cardiovascular function, immune responsiveness, and metabolic regulation. All of these systems are responsible for our lifelong health and well-being.

**2** Excessive and persistent adversity early in life can overload biological systems and lead to long-term consequences. When stress responses are activated frequently, intensively, and persistently during early childhood, they can become set on permanent high alert—they may activate more easily and quickly and may not turn off as readily as they should. From a biological perspective, this is essential for survival. If the world is a dangerous place, the internal systems designed to protect us need to develop in a way that anticipates frequent threats. Yet over time, these repeated activations lead to greater risk for stress-associated diseases well into the adult years—conditions such as cardiovascular disease, obesity, type 2 diabetes, respiratory and immunological disorders, and a range of mental health problems. That’s the trade-off of adapting to significant early adversity. Physiological systems typically work most effectively when they operate within a well-regulated range—and significant deviations beyond either end of that range can lead to problems in physical and mental health. For example, an immune system that doesn’t react at a sufficiently high level will be unable to fight off serious infection, but one that is hyper-reactive could flood the body with disease-causing inflammation. There are many opportunities to build resilience in the face of significant adversity—poor health outcomes are not inevitable, but they are more likely if we do not adequately support children and families experiencing persistent hardships or threats, particularly in the face of structural inequities that impose enormous challenges.

**3** The brain’s developing circuits are highly sensitive to the disruptive effects of elevated stress activation. Three brain systems are particularly susceptible: (1) emotion regulation, where circuitry for fear and threat develops early in life; (2) memory systems, where circuitry for memory and simple learning begins early and continues into later childhood; and (3) executive function systems, where circuitry for focused attention, impulse control, and higher-level cognitive skills develop in the preschool period and become more refined well into the adult years.

**4** Early, frequent activation of the immune system, which defends the body against infection and a variety of toxic substances, can result in a “double hit” against lifelong health. One of the most important components of the immune system’s response is inflammation, a physiological function that attacks invading bacteria or viruses, clears out the tissue destruction they cause, and begins the repair process. Our bodies need this for survival, but over time it can put powerful inflammatory substances used to kill microbes in constant contact with multiple organs, which can eventually damage them (the first “hit”). At the same time, a constant state of activation can also make the immune system less efficient in its fight against microbes (a second “hit”). This may explain why children living in adverse environments are more susceptible to recurrent infection and more prone to develop chronic inflammatory conditions across the lifespan, including heart disease, diabetes, depression, arthritis, gastrointestinal disorders, autoimmune disorders, multiple types of cancer, and dementia, among many others.

**5** The combination of stress and inflammation is especially threatening to health and well-being through its effects on the cardiometabolic system. Extensive research has documented increased obesity and elevated blood pressure in children experiencing the stresses of poverty, racism, unsupportive caregiving, overstimulation from excessive noise and overcrowding, and sedentary behavior from living in a violent neighborhood with no safe space for playing outdoors. There is also growing evidence that inflammation contributes to that risk, and that excessive amounts of stress hormones such as cortisol, combined with chronic inflammation, can result in insulin resistance—a physiological disruption that can lead to metabolic syndrome, obesity, diabetes, and cardiovascular disease, as well as brain changes and cognitive impairment.

Next: Implications for Policy and Practice
IMPLICATIONS FOR POLICY AND PRACTICE

- **Efforts to prevent many chronic illnesses in adults need to begin in the early childhood years.** The experiences we have early in life are at least as important for the biological foundations of physical and mental health as the lifestyle choices we make as adults. Three of the most common and costly examples of chronic health impairments—cardiovascular disease, diabetes, and depression—alone account for nearly $600 billion in direct health care expenditures in the United States annually (above and beyond their indirect costs, such as lost productivity). All three share a common association with elevated inflammation, which can be traced to recurrent hardships or threats in early childhood.

- **Three science-based principles should be used to inform more effective policies and programs across sectors to protect the developing brain and other biological systems from the disruptive effects of early adversity.** These principles can guide interventions that go beyond providing learning experiences for children and information for parents and other caregivers to create conditions that will strengthen the early childhood foundations of both learning and health.
  - **Support responsive relationships:** Reliable “serve-and-return” interactions between young children and the adults who care for them help to reduce the physiological disruptions of excessive stress activation and protect developing biological systems, especially in the earliest years. Adult caregivers also need supportive relationships to reduce stress, solve problems, and share ideas.
  - **Reduce sources of stress:** Policies and programs that lessen economic and psychosocial burdens on families with young children pay off in two ways. First, they reduce chronic activation of stress systems in both adults and children. Second, they enhance adult capacity for providing responsive caregiving that facilitates healthy child development.
  - **Strengthen core life skills:** In order to provide a well-regulated caregiving environment, adults must be able to set and meet goals, manage their own behavior and emotions, establish daily routines, and facilitate social-emotional development and skill-building in young children. Well-matched programs can help both children and adults build and apply these skills through modeling, coaching, and practice.

- **Primary health care offers a key delivery channel for reaching the largest number of children at the earliest possible ages in a non-stigmatizing context.** Team-based care provided through culturally and linguistically responsive, trusted relationships offers a promising model for individualized approaches to building resilience and preventing, reducing, or mitigating the consequences of early adversity. Reducing disparities in child health outcomes at a population level, however, will require a substantial shift in professional training, current practice, and payment systems to address the following challenges.

- **There is an urgent need for more effective strategies to support young children by confronting poverty, racism, violence, housing instability, food insecurity, and other sources of chronic adversity that impose significant stresses on their families.** Services and supports must move beyond a sole focus on children and parents to an intentional, “upstream” focus on macro-level policies that systematically threaten the health and wellbeing of families affected by structural inequities and systemic racism. Science-informed thinking combined with on-the-ground expertise and the lived experiences of families raising young children under a wide variety of conditions (many of whom are typically marginalized) can be a powerful catalyst of new ideas.

- **All policies and delivery systems serving young children and families across sectors (including but not limited to medical care and early care and education) can and must measure their success by improved child outcomes in both health and learning.** Persistent attempts to increase access to services, reduce fragmentation, build integrated delivery systems, and secure sustainable funding remain important objectives. But these efforts will not produce greater impacts until the measurement of their success moves beyond serving more children and enhancing interagency collaboration and begins to focus more explicitly on key child outcomes.