

Adverse Childhood Experiences, Outcomes, and Interventions



Rachel Gilgoff, MD, CCTP^a, Leena Singh, DrPH, MPH^b,
Kadiatou Koita, MD, MH-GHS, MS-GHS^a, Breanna Gentile, PhD^{a,*},
Sara Silverio Marques, DrPH, MPH^c

KEYWORDS

- Adverse childhood experiences • Toxic stress • Pediatric stress • ACEs
- Pediatric trauma • Stress outcomes • Pediatric interventions

KEY POINTS

- Adverse childhood experiences (ACEs) are stressful or potentially traumatic events that children experience before age 18 years.
- In children and adolescents, numerous studies have linked exposure to ACEs and negative health, and developmental and behavioral outcomes.
- Screening in pediatric medical settings provides a clear opportunity for early detection, intervention, and treatment of children at risk for accumulating ACEs.
- Providing anticipatory guidance helps patients/caregivers understand ACEs and toxic stress and be attuned to the types of situations that may be causing stress for a child.
- Because ACEs are a risk factor for health conditions, it is incumbent on pediatric medical providers to screen and intervene.

INTRODUCTION

Adverse childhood experiences (ACEs) are stressful or potentially traumatic events that children experience before age 18 years. The term ACEs was coined in 1998 following the publication of the Adverse Childhood Experiences study (ACE study). ACEs are grouped into 3 domains: abuse, neglect, and household dysfunction, and include 10 categories of adverse experiences.^{1,2}

^a Clinic + Research, Center for Youth Wellness, 3450 Third Street, Building 2, Suite 201, San Francisco, CA 94124, USA; ^b National Pediatric Practice Community, Center for Youth Wellness, 3450 Third Street, Building 2, Suite 201, San Francisco, CA 94124, USA; ^c Center for Youth Wellness, 3450 Third Street, Building 2, Suite 201, San Francisco, CA 94124, USA

* Corresponding author.

E-mail address: bgentile@centerforyouthwellness.org

HISTORY AND BACKGROUND

Numerous studies have shown that ACEs, such as abuse, neglect, and household dysfunction, are common and associated in a dose-dependent manner with worse health outcomes.^{1,3,4} Exposure to these ACEs without a positive adult relationship as buffer can lead to a toxic stress response in children, leading to higher risk for health and behavioral problems. The toxic stress response, characterized by a chronic dysregulation of the neuroendocrine and immune system via the hypothalamic-pituitary axis (HPA), leads to multisystemic alterations, resulting in changes to the body's metabolic and epigenetic functioning, and onset of diseases.⁵ Exposure to adversity early in life, particularly during sensitive periods of child and adolescent development, is especially problematic because of enhanced sensitivity and likelihood of permanent and long-term integration into regulatory biological processes⁶ (Fig. 1).

EPIDEMIOLOGY AND OTHER DATA

In adults, ACEs have been found to have a strong, dose-response association with cardiovascular disease, chronic lung disease, cancer, diabetes, headaches, autoimmune disease, sleep disturbances, early death, obesity, smoking, general poor health, depression, posttraumatic stress disorder (PTSD), anxiety, substance abuse, sexual risk taking, mental ill health, and interpersonal and self-directed violence.^{7,8}



Fig. 1. The 3 types of adverse childhood experiences. (From The Truth About ACEs. Robert Woodson Foundation. Available at: <https://www.rwjf.org/en/library/infographics/the-truth-about-aces.html>. Copyright 2013. Robert Wood Johnson Foundation. Used with permission from the Robert Wood Johnson Foundation.)

In children and adolescents, numerous studies have linked exposure to ACEs and negative health, developmental and behavioral outcomes, including asthma, recurrent infections, cognitive and developmental delays, obesity, failure to thrive, and sleep disturbance,⁹ as well as delinquent behavior, bullying, physical fighting, dating violence, and weapon carrying.^{10–14} Researchers in the field continue to explore the relationship between other early childhood events and circumstances on children's health. Some of these adversities include hardship, serious illness, and death in the household.¹⁵

At the population level, the Behavioral Risk Factors Surveillance System (BRFSS), which has been collecting abuse and household dysfunction data in up to 42 states and District of Columbia, found that about two-thirds of the US population have been exposed to 1 or more ACEs. The data found ACEs to be associated with the following negative outcomes: traumatic injuries, depression, anxiety, suicide, PTSD, unintended pregnancy, pregnancy complications, fetal death, HIV, sexually transmitted diseases, cancer, diabetes, alcohol and drug abuse, unsafe sex, low educational level (noncompletion of high school), unemployment, and household poverty.¹⁶ Like the ACE Study findings, the BRFSS data showed a graded dose-response relationship indicating that the risk of negative outcomes increased with the number of ACEs. This demonstrates that most people, irrelevant of socioeconomic, racial, and cultural background, are affected by some level of ACEs. This widespread exposure is why public health leaders and child advocates have called the unaddressed exposure to ACEs a public health crisis.

ROLE OF THE PEDIATRICIAN

The vast majority of children in the United States will see a pediatric provider 15 times for well child visits during the first 5 years of their life (Bright Futures/AAP Recommendations for Preventive Pediatric Health Care [Periodicity Schedule]). This time period is considered a valuable teaching opportunity for health care providers to support caregivers in promoting healthy practices for optimal child development. The case for the role of pediatric providers in addressing one of the most serious and consequential early life circumstances—that of exposure to childhood adversity has been established.^{17,18} This dire public health issue is met with promise, but also precaution due to lack of provider training and time. Even so, pediatric providers are invested in exploring how they can improve the long-term trajectory of children's lives through screening and treatment. This written perspective highlights actionable next steps for pediatric providers in pursuit of science-informed clinical practices to address child adversity and toxic stress and focuses on ACEs as risk factors for toxic stress.

The perspective in this article is provided in 3 sections: (1) ACEs screening in pediatrics, (2) anticipatory guidance and domains of intervention, and (3) resources and referrals.

Adverse Childhood Experiences Screening in Pediatrics

Screening in pediatric medical settings provides a clear opportunity for early detection, intervention and treatment of children at risk for accumulating ACEs.¹⁹ An ACEs screen is not designed to be an in-depth assessment of child abuse but, rather, to provide an assessment of a child's risk for developing neuroendocrine and immune dysregulation, referred to as a toxic stress response. This provides the health care provider and team with valuable information that can help inform clinical management of illness.

Although initial ACE research pointed to the associations between ACEs and adult health, more recent research demonstrated child behavioral and health outcomes associated with ACEs, making screening in pediatrics essential to curb further disease.^{9,20} In addition, the substantial individual variability in how early adversity and toxic stress manifests over the life course, and the varied presentations of toxic stress physiology, make universally screening all pediatric patients for risk of toxic stress essential—even for those who may not be obviously symptomatic.⁶

Published studies show that caregivers are receptive to ACEs screening and feel comfortable discussing ACEs with their pediatricians as long as there is a trusting relationship.^{15,21} Parents find the topic of ACEs to be of value to their child's care and are also largely unaware that ACEs can have lasting health impacts from exposure under the age of 5 years (CYW Market Research, 2017. Unpublished data).

Screening also provides an opportunity for clinicians to support parents and caregivers to be buffers for their children, especially those with high exposure to adversity. This is critical as the evidence suggests that one effective intervention in preventing the negative outcomes associated with ACEs is a caring supportive adult.^{22,23} By exploring the protective and risk factors that are affecting the health of patients and families in the primary care setting, medical providers can help tap into existing sources of resilience, promote parent-child attachment, and enhance the protective factors known to help prevent toxic stress even for those patients with high doses of adversity.

Although there is no standardized method to screen for ACEs, the experience of this article's authors has pointed to the value of universal and routine screening. ACEs screening can be integrated into the standard clinical workflow similar to other pediatric screening tools. The screen is commonly administered by medical staff, reviewed by the medical provider, and the patient is referred to follow-up as appropriate. Various intervention strategies for responding to ACEs are outlined below.

Anticipatory Guidance and Domains of Intervention

Anticipatory guidance

The question remains of what medical providers can do to support the needs of patients and families after they screen for ACEs. A key intervention strategy includes patient/family education and targeted anticipatory guidance. Anticipatory guidance has been shown to be effective in improving child and family functioning in a variety of ways, including violence prevention,²⁴ sleep, and parent-child interactions.^{25,26} Anticipatory guidance is already part of standard pediatric practice, and usually includes education to patients/caregivers about what to expect, or anticipate, over the next few months or years with their child. Recommendations are specific to a child's age at the time of a visit.

Providing anticipatory guidance helps patients/caregivers understand ACEs and toxic stress and be attuned to what types of home, school, or other situations may be causing stress for a child. It gives them information to be able to identify potential symptoms of toxic stress early (eg, difficulty focusing, weight gain/loss, poor control of asthma, poor sleep, anxiety). Anticipatory guidance can also increase a caregiver's understanding of their role as a buffer to children's stress and can help provide tools that caregivers can use to build their children's resilience against adversity.

Anticipatory guidance should always be given with developmentally appropriate knowledge of trauma-informed principles, healing-centered and strengths-based approaches, and cultural humility and implicit bias awareness.^{27–30} One of the goals of anticipatory guidance about ACEs should include decreasing blame and shame given that patients and caregivers experiencing trauma-related symptomatology are exhibiting normal physiologic and biological reactions to abnormal, traumatic situations.

Domains of anticipatory guidance for toxic stress

Anticipatory guidance and interventions can focus on the following domains that have specifically been shown to aid in addressing stress and improving some aspects of neuroendocrine and immune function and health outcomes: healthy relationships, sleep, exercise, nutrition, mindfulness, and nature.³¹

Healthy relationships Numerous studies have demonstrated the protective role of caregivers, secure attachment, and their positive influence on children's development.^{32–34} Conversely, lack of social integration and/or social support have been shown to be a greater risk factor for mortality in adults than smoking, alcohol consumption, and physical activity levels.^{35,36} Just as ACEs have been found to have a dose-dependent negative impact on health, social integration has been found to have a dose-dependent protective effect on health.³⁷

It is important to note that parental ACEs and mental health are linked with intergenerational or epigenetic transmission, higher risk of parental stress response dysregulation, lack of coregulation by the caregiver, and lack of modeling self-regulation tools, all leading to greater risk of their children being exposed to adversity in higher doses without a buffer or internal self-regulation skills.^{38–41} Safe, stable, and nurturing relationships can break the intergenerational cycle of abuse.⁴² A caregiver can modulate the stress-related emotional and physiologic arousal for the child and calm the child's threat response system.

Medical providers should note the nature of the caregiver-child relationship at every visit and offer support when needed. Attention to relational health for both child and caregiver should start in the prenatal period and extend throughout the lifespan. Medical providers can support the caregiver to tend to their own physical and mental health and well-being such that the caregiver can be a buffer to their child. Self-care for caregivers involves managing their own stress levels through healthy relationships, nutritious meals, adequate sleep, physical activity, mindfulness, and tending to their own mental health.

Sleep Reduced sleep duration and poor sleep quality have been linked to many diseases and even death in both adults and children.^{43–45}

A child's bedtime routine, reading books, and limiting screen time before bed to promote sleep hygiene are most often part of standard patient education and anticipatory guidance given by medical providers.⁴⁶

However, if there is instability in a household or in the child's environment, this may impact a child's ability to sleep, leading to the need for an additional anticipatory guidance and stress management tools. Medical providers can encourage caregivers to talk with their child about stressors that may be keeping their child awake and remind them about their role in soothing the threat response system. Studies have also looked at meditation as a sleep tool as well as physical activities and found improvement in sleep quality.^{47–49} Detailing medications for sleep in the pediatric population is beyond the scope of this article. Generally, behavioral techniques and sleep hygiene education are first-line interventions.⁵⁰ Pediatric medical providers can further review the use of medications, such as melatonin in other review articles on sleep.^{50,51}

Nutrition The threat response involves activation of the sympathetic nervous system (SNS) and the HPA axis. Generally, SNS activation involves decreasing appetite and gut mobility and metabolizing energy stores to aid in quick escape. Activation of the HPA axis and cortisol release tends to involve longer-term survival strategies, such as increasing desire for high-calorie, high-fat food to increase reserves for

the next stressor.^{52–54} Thus, depending on the individual, the adversity they experience, and the length of time over which that adversity has occurred, both the SNS and the HPA axis activation can impact weight gain or loss due to stress. Anticipatory guidance on the biology of stress and its impact on weight may help reduce blame and shame surrounding obesity and offer biologically based tools to intervene.

Knowing that stress can lead to craving high-fat, high-energy foods, medical providers can work with caregivers to identify healthy forms of high-fat, high-energy foods, such as nuts, yogurt, fish, and avocados. Knowing that toxic stress can lead to inflammation and a dysregulated immune system, medical providers can offer education promoting anti-inflammatory foods, such as fruits, vegetables, turmeric, and omega-3 fatty acids and discuss avoiding proinflammatory foods, such as fast food and overly processed foods.^{55–59} Gut bacteria may impact the stress response and cognitive functioning, and future research may point to specific probiotics as helpful interventions for stress management.^{52,55,60}

Food can also be a core component of culture and relationship across the lifespan, including supporting healthy nutrition for pregnant mothers,^{53,56,61} breastfeeding practices, and responsive feeding practices,^{53,54,57,62} and eating meals together as a family and with community.

Exercise Adult and animal studies show that physical activity improves brain health, including tests of cognitive functioning and neurogenesis and affects endocrine and immune functioning.^{55,63–65} Fewer studies have evaluated the impact of physical activity on children’s neuroendocrine and immune function. A few studies have shown a positive association between physical activity and academic performance in elementary school-age children and adolescents⁶⁵ and a lower risk of respiratory infections in children.^{55,58,63,66} Given the comorbidity risk with obesity, exercise may help with weight loss and cardio-pulmonary function, including asthma management improvement.^{56,59,64,67} In addition, physical activity may improve other domains of wellness, including sleep and psychological functioning.⁴⁹

Activation of the threat response system is associated with changes in metabolic factors, including insulin and glucose.⁴³ Children who experience an acute stressor but must sit still in the classroom setting or stay inside at home due to fear of community violence, may not have an outlet to metabolize the extra energy released into their bloodstream. Exercise can help metabolize that energy and regulate the stress response for children and families.^{57,60,65,68} Programs that couple physical activity with character development, such as martial arts or mindfulness practices, such as yoga, may lead to more improvements in executive functioning.^{58,61,66,69}

Medical providers can discuss the stress-related health benefits of physical activity with caregivers, create treatment plans that include fun physical activities for both the child and their caregiver, and connect families with community resources offering physical activity programs.

Mindfulness Mindfulness and meditation have been defined and evaluated in various ways with varying specificity, making research into their impact on physiology and health complicated.^{59,60,62,63,67,68,70,71} A frequently used definition of mindfulness by Kabat-Zinn identifies core components, including nonjudgmental, open-hearted, moment-to-moment awareness, and attention in the present moment.^{59,61,62,64,67,69,70,72}

Although limitations in definitions and evaluation techniques exist, research on adults suggests that mindfulness-based interventions, including meditation, yoga,

Tai Chi, and Qi Gong can improve a wide range of social, emotional, behavioral and physiologic outcomes.^{47,62–67,70–75}

Studies in children suggest that yoga, mindfulness, and meditation programs may improve symptoms of behavioral mental health.^{65–70,73–78} Mindfulness programs may also help foster resilience and decrease parental stress^{68,71,76,79} and can be used by providers as potential interventions to manage stress for children and caregivers to improve outcomes. Medical providers can direct patients and families to books with scripts,^{69,72,77,80} picture books for younger children,^{70,73,78,81} and online tools and applications, including Sesame Workshop.^{71,72,74,75,79,80,82,83} In addition, mindfulness practices can enhance other domains of wellness. For example, Progressive Muscle Relaxation and other meditations can help worried children fall asleep.

Nature Ongoing research suggests that spending time in nature may reduce stress and improve health by lowering heart rate, reducing blood pressure, altering cortisol levels, and improving cognitive functioning.^{73,76,81,84} Exposure to nature may also help indirectly by increasing physical activity and social contact.^{74,77,82,85}

Medical providers can improve access to nature through park prescriptions, partnering with local parks and organizations, and providing families with directions. Park prescriptions were found to increase park visits, decrease perceived stress and loneliness, increase physical activity, decrease cortisol levels, and increase resilience.^{75,76,78,79,83,84,86,87}

Overall, when discussing and offering anticipatory guidance and interventions for toxic stress with children and families, a hopeful approach is critical. Although primary care medical providers are not expected to be social workers, psychologists, or psychiatrists, ACEs impact health and are, therefore, within the domain of anticipatory guidance to help mitigate and heal toxic stress. For example, telling patients that all of their tests are normal and that therefore their presenting symptoms are not medical is neglecting the limits of our current scientific knowledge on toxic stress and available testing at nonresearch-based labs. In addition, this type of communication strips the patient of hope and empowerment. Thought changes biology. Research has found that thought alone can lead to changes in the immune response and neuroplastic change.^{55,77,80} Avoiding the nocebo effect^{78,79,81,82,85,86,88,89} and helping patients and families recognize their own strength in overcoming and healing from ACEs is critical to their success. Providers must maintain a close working relationship with their families, support caregivers to be caring and buffering adults, and offer hope for healing, which can include specific intervention tools on sleep, nutrition, physical activity, mindfulness, and nature.

Resources and Referrals

For children with symptoms of toxic stress dysregulation or higher ACE scores, the medical provider may need to refer the child to additional services and supports. The type of referral will vary depending on variables, such as the prominent presenting issue, financial resources, time bandwidth, and geographic location to services. Integrated behavioral health, including care coordination, psychotherapy, and psychiatry may offer support to medical providers in a busy practice. Pediatric office-based and external interventions are essential to meet the more specific needs of patients.

Several research studies have shown that mental health interventions impact physiologic outcomes. Slopen and colleagues⁹⁰ conducted a systematic review of interventions to improve cortisol regulation in children.^{80,83,87} They found 18 articles that supported evidence for mental health focused interventions lowering cortisol levels. For example, Carlson and Earls⁹¹ implemented a social and

educational enrichment program for children for 13 months and found that the intervention group had lower noontime cortisol compared with controls.^{81,84,88,91} In addition, support programs and psychological interventions have been shown to improve health outcomes, such as lowering blood pressure and improving diabetes management.^{82,83,85,86,89,90,92,93}

Integrated behavioral health models: These models combine medical and behavioral health services to more fully address the spectrum of problems that patients bring. The goal is to treat both behavioral and physical problems in the most acceptable and effective way to yield the best results for the patient.

Care coordination: The core elements shared among care coordination models include assessment, case management, and referral to social services. Pediatric clinics should highly consider employing non-physician(s) to assist with education and care coordination.

Critical aspects of coordinated care in pediatrics include a tailored, partnership-based approach to the patient's condition and the family's situation, well-defined goals, and a single care coordinator assigned to the family who is in regular contact with them and various health care professionals involved in their care.^{84,87,91,94} Patient- and family-centered care coordination can help problem-solve around social determinants of health, including ACEs, and connect families to external resources and referrals.^{85,88,92,95}

Psychotherapy: There are a variety of evidence-supported treatments and promising practices that share core principles of culturally competent, trauma-informed therapy that are appropriate for children and families from diverse cultural backgrounds. These may include:

- Child parent psychotherapy^{86,89,93,96}
- Parent-child interaction therapy^{87,88,90,91,94,95,97,98}
- Trauma-focused cognitive behavioral therapy^{89,92,96,99}
- Dialectical behavioral therapy^{90,93,97,100}
- Cue-centered therapy^{91,94,98,101}
- Eye movement desensitization and reprocessing^{92,95,99,102}
- Biofeedback and neurofeedback^{93,94,96,97,100,101,103,104}

Psychiatry: Psychiatrists may be a critical part of the integrated health team depending on the severity of the presenting symptoms. It is important to identify psychiatrists who (1) understand the biology and physiology of trauma, (2) recognize developmental trauma disorder,^{95,98,102,105} and do not over diagnose or inadvertently misdiagnose children exposed to ACEs with other conditions, such as oppositional defiant disorder or attention deficit hyperactivity disorder, and (3) are cognizant of issues surrounding over medication and polypharmacy use especially with foster youth.^{96,99,103,106}

Flora Traub and Renée Boynton-Jarrett¹⁰⁷ offer insightful recommendations to pediatric practices to improve resilience to ACEs, including: (1) train all staff in trauma-informed care, (2) screen risk and protective factors, (3) employ non-physicians to help with screening, education, and care coordination, (4) create a medical home, (5) create an integrated behavioral health program, (6) offer group-based parenting support and education, (7) offer peer-based education, (8) customize health care to the needs of the family, (9) identify local resources, and (10) be aware of barriers to engagement.^{97,100,104,107} In addition, the American Academy of Pediatrics offers a Trauma Guide, which includes "Trauma Toolbox for Primary Care,"¹⁰⁸ "Helping Foster and Adoptive Families Cope With Trauma: A Guide for Pediatricians,"^{98,101,105,108,109} and additional resources.

SUMMARY

The ACE study demonstrates that adversity is common and impacts a wide range of health outcomes.¹ Increasing research is highlighting the physiologic and biological mechanisms, often encapsulated by the theory of toxic stress, which lead to these behavioral, mental, and physical outcomes.^{5,6,18,23}

Because ACEs are a risk factor for health conditions, such as depression, anxiety, asthma, obesity, diabetes, and heart disease, it is incumbent on pediatric medical providers to screen and intervene. Primary care is the ideal setting for ACEs screening because interacting with children and their families at regular intervals can allow patients and providers to develop a trusting relationship and address common misconceptions, which can facilitate the disclosure of ACEs and provides an opportunity for education and continued monitoring. Providers can advance the health and well-being of children and families affected by ACEs by (1) identifying children and families in need through ACEs screening, (2) offering empathetic and science-based anticipatory guidance, including expanded education and interventions related to healthy relationships, sleep, nutrition, physical activity, mindfulness, nature, and mental health, and (3) providing trauma-focused and human-centered resources and referrals when needed.

DISCLOSURE

The authors have nothing to disclose.

REFERENCE

1. Felitti VJ, Anda RF, Nordenberg D, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: the Adverse Childhood Experiences (ACE) Study. *Am J Prev Med* 1998;14:245–58.
2. Robert Wood Johnson Foundation. *The truth about ACEs*. Princeton (NJ): Robert Wood Johnson Foundation; 2013.
3. Gilbert R, Widom CS, Browne K, et al. Burden and consequences of child maltreatment in high-income countries. *Lancet* 2009;373:68–81.
4. Felitti VJ. Adverse childhood experiences and adult health. *Acad Pediatr* 2009;9:131–2.
5. Bucci M, Marques SS, Oh D, et al. Toxic stress in children and adolescents. *Adv Pediatr* 2016;63:403–28.
6. Johnson SB, Riley AW, Granger DA, et al. The science of early life toxic stress for pediatric practice and advocacy. *Pediatrics* 2013;131:319–27.
7. Kalmakis KA, Chandler GE. Health consequences of adverse childhood experiences: a systematic review. *J Am Assoc Nurse Pract* 2015. <https://doi.org/10.1002/2327-6924.12215>.
8. Hughes K, Bellis MA, Hardcastle KA, et al. The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. *Lancet Public Health* 2017;2:e356–66.
9. Oh DL, Jerman P, Silvério Marques S, et al. Systematic review of pediatric health outcomes associated with childhood adversity. *BMC Pediatr* 2018;18.
10. Burke NJ, Hellman JL, Scott BG, et al. The impact of adverse childhood experiences on an urban pediatric population. *Child Abuse Negl* 2011;35:408–13.
11. Duke NN, Pettingell SL, McMorris BJ, et al. Adolescent violence perpetration: associations with multiple types of adverse childhood experiences. *Pediatrics* 2010;125:e778–86.

12. Enlow MB, Egeland B, Blood EA, et al. Interpersonal trauma exposure and cognitive development in children to age 8 years: a longitudinal study. *J Epidemiol Community Health* 2012;66(11):1005–10.
13. Strathearn L, Gray PH, O'Callaghan MJ, et al. Childhood neglect and cognitive development in extremely low birth weight infants: a prospective study. *Pediatrics* 2001;108:142–51.
14. Richards M, Wadsworth MEJ. Long term effects of early adversity on cognitive function. *Arch Dis Child* 2004;89:922–7.
15. Koita K, Long D, Hessler D, et al. Development and implementation of a pediatric adverse childhood experiences (ACEs) and other determinants of health questionnaire in the pediatric medical home: A pilot study. *PLoS One* 2018; 13:e0208088.
16. Behavioral risk factor surveillance system ACE Data |Violence Prevention|Injury Center|CDC. 2019. Available at: <https://www.cdc.gov/violenceprevention/childabuseandneglect/acestudy/ace-brfss.html>. Accessed April 18, 2019.
17. Bethell CD, Newacheck P, Hawes E, et al. Adverse childhood experiences: assessing the impact on health and school engagement and the mitigating role of resilience. *Health Aff (Millwood)* 2014;33:2106–15.
18. Garner AS, Shonkoff JP, Committee on Psychosocial Aspects of Child and Family Health, Committee on Early Childhood, Adoption, and Dependent Care, Section on Developmental and Behavioral Pediatrics. Early childhood adversity, toxic stress, and the role of the pediatrician: translating developmental science into lifelong health. *Pediatrics* 2012;129:e224–31.
19. American Academy of Pediatrics. The medical home approach to identifying and responding to exposure to trauma 2014. Available at: https://www.aap.org/en-us/Documents/ttb_medicalhomeapproach.pdf https://www.aap.org/en-us/Documents/ttb_medicalhomeapproach.pdf. Accessed June 20, 2019.
20. Franke HA. Toxic stress: effects, prevention and treatment. *Children* 2014;1: 390–402.
21. Goldstein E, Athale N, Sciolla AF, et al. Patient preferences for discussing childhood trauma in primary care. *Perm J* 2017;21:16-055.
22. Merrick MT, Leeb RT, Lee RD. Examining the role of safe, stable, and nurturing relationships in the intergenerational continuity of child maltreatment—introduction to the special issue. *J Adolesc Health* 2013;53:S1–3.
23. Shonkoff JP, Garner AS, Committee on Psychosocial Aspects of Child and Family Health, Committee on Early Childhood, Adoption, and Dependent Care Section on Developmental and Behavioral Pediatrics. The lifelong effects of early childhood adversity and toxic stress. *Pediatrics* 2011;129:e232.
24. Sege RD, Hatmaker-Flanigan E, Vos ED, et al. Anticipatory guidance and violence prevention: results from family and pediatrician focus groups. *Pediatrics* 2006;117:455–63.
25. Nelson CS, Wissow LS, Cheng TL. Effectiveness of anticipatory guidance: recent developments. *Curr Opin Pediatr* 2003;15:630–5.
26. Hsu H-C, Lee S-Y, Lai C-M, et al. Effects of pediatric anticipatory guidance on mothers of young children. *West J Nurs Res* 2018;40:305–26.
27. Marsac ML, Kassam-Adams N, Hildenbrand AK, et al. Implementing a trauma-informed approach in pediatric health care networks. *JAMA Pediatr* 2016; 170:70–7.
28. Ginwright S. The future of healing: shifting from trauma informed care to healing centered engagement. Alexandria (VA): Kindship Carers Victoria/Grandparents Victoria; 2018.

29. Boynton-Jarrett R, Flacks J. Strengths-based approaches to screening families for health-related social needs in the healthcare setting. New York: Center For The Study Of Social Policy; 2018.
30. Derrington SF, Paquette E, Johnson KA. Cross-cultural interactions and shared decision-making. *Pediatrics* 2018;142:S187–92.
31. Harris NB. *The deepest well: healing the long-term effects of childhood adversity*. Boston (MA): Houghton Mifflin Harcourt; 2018.
32. Blum D. *Love at Goon Park: Harry Harlow and the science of affection*. New York: Basic Books; 2002.
33. Meaney MJ, Szyf M. Maternal care as a model for experience-dependent chromatin plasticity? *Trends Neurosci* 2005;28:456–63.
34. Lieberman AF, Padrón E, Horn PV, et al. Angels in the nursery: the intergenerational transmission of benevolent parental influences. *Infant Ment Health J* 2005;26:504–20.
35. Holt-Lunstad J, Smith TB, Layton JB. Social relationships and mortality risk: a meta-analytic review. *PLoS Med* 2010;7:e1000316.
36. Holt-Lunstad J. Why social relationships are important for physical health: a systems approach to understanding and modifying risk and protection. *Annu Rev Psychol* 2018;69:437–58.
37. Yang YC, Boen C, Gerken K, et al. Social relationships and physiological determinants of longevity across the human life span. *Proc Natl Acad Sci* 2016;113:578–83.
38. Lyons-Ruth K, Holmes BM, Sasvari-Szekely M, et al. Serotonin transporter polymorphism and borderline or antisocial traits among low-income young adults. *Psychiatr Genet* 2007;17:339–43.
39. Schore AN. The right brain is dominant in psychotherapy. *Psychotherapy* 2014;51:388–97.
40. Gunnar MR, Donzella B. Social regulation of the cortisol levels in early human development. *Psychoneuroendocrinology* 2002;27:199–220.
41. Sroufe LA. Attachment and development: a prospective, longitudinal study from birth to adulthood. *Attach Hum Dev* 2005;7:349–67.
42. Jaffee SR, Bowes L, Ouellet-Morin I, et al. Safe, stable, nurturing relationships break the intergenerational cycle of abuse: a prospective nationally representative cohort of children in the United Kingdom. *J Adolesc Health* 2013;53:S4–10.
43. McEwen BS. Physiology and neurobiology of stress and adaptation: central role of the brain. *Physiol Rev* 2007;87:873–904.
44. Itani O, Jike M, Watanabe N, et al. Short sleep duration and health outcomes: a systematic review, meta-analysis, and meta-regression. *Sleep Med* 2017;32:246–56.
45. Gallicchio L, Kalesan B. Sleep duration and mortality: a systematic review and meta-analysis. *J Sleep Res* 2009;18:148–58.
46. Owens JA. The practice of pediatric sleep medicine: results of a community survey. *Pediatrics* 2001;108:E51.
47. Black DS, O'Reilly GA, Olmstead R, et al. Mindfulness meditation and improvement in sleep quality and daytime impairment among older adults with sleep disturbances: a randomized clinical trial. *JAMA Intern Med* 2015;175:494–501.
48. Nagendra RPM, Maruthai NMP, Kutty BMMP. Meditation and its regulatory role on sleep. *Front Neurol* 2012;3:54.
49. Lang C, Brand S, Feldmeth AK, et al. Increased self-reported and objectively assessed physical activity predict sleep quality among adolescents. *Physiol Behav* 2013;120:46–53.

50. Badin E, Haddad C, Shatkin JP. Insomnia: the sleeping giant of pediatric public health. *Curr Psychiatry Rep* 2016;18:47.
51. Abdelgadir IS, Gordon MA, Akobeng AK. Melatonin for the management of sleep problems in children with neurodevelopmental disorders: a systematic review and meta-analysis. *Arch Dis Child* 2018;103:1155–62.
52. Romeo J, Warnberg J, Gómez-Martínez S, et al. Neuroimmunomodulation by nutrition in stress situations. *Neuroimmunomodulation* 2008;15:165–9.
53. Wardle J, Gibson EL. Chapter 55 - diet and stress: interactions with emotions and behavior. In: Fink G, editor. *Stress: concepts, cognition, emotion, and behavior*. Cambridge (MA): Academic Press; 2016. p. 435–43. <https://doi.org/10.1016/B978-0-12-800951-2.00058-3>.
54. Sims R, Gordon S, Garcia W, et al. Perceived stress and eating behaviors in a community-based sample of African Americans. *Eat Behav* 2008;9:137–42.
55. Shaffer J. Neuroplasticity and clinical practice: building brain power for health. *Front Psychol* 2016;7:1118.
56. Aubry AV, Khandaker H, Ravenelle R, et al. A diet enriched with curcumin promotes resilience to chronic social defeat stress. *Neuropsychopharmacology* 2019;44:733.
57. James A, Abramson M. Fast food and asthma and allergy: be afried, be deeply afried? *Respirology* 2018;23:881–2.
58. Kiecolt-Glaser JK, Glaser R, Christian LM. Omega-3 fatty acids and stress-induced immune dysregulation: implications for wound healing. *Mil Med* 2014;179:129–33.
59. Holt EM, Steffen LM, Moran A, et al. Fruit and vegetable consumption and its relation to markers of inflammation and oxidative stress in adolescents. *J Am Diet Assoc* 2009;109:414–21.
60. Dinan TG, Cryan JF. Regulation of the stress response by the gut microbiota: Implications for psychoneuroendocrinology. *Psychoneuroendocrinology* 2012;37:1369–78.
61. Vohr BR, Davis EP, Wanke CA, et al. Neurodevelopment: the impact of nutrition and inflammation during preconception and pregnancy in low-resource settings. *Pediatrics* 2017;139:S38–49.
62. Yousafzai AK, Rasheed MA, Bhutta ZA. Annual research review: improved nutrition—pathway to resilience. *J Child Psychol Psychiatry* 2013;54:367–77.
63. Diamond MC. Response of the brain to enrichment. *An Acad Bras Ciênc* 2001;73:211–20.
64. Russell VA, Zigmund MJ, Dimatelis JJ, et al. The interaction between stress and exercise, and its impact on brain function. *Metab Brain Dis* 2014;29:255–60.
65. Voss MW, Vivar C, Kramer AF, et al. Bridging animal and human models of exercise-induced brain plasticity. *Trends Cogn Sci* 2013;17:525–44.
66. Jedrychowski W, Maugeri U, Flak E, et al. Cohort study on low physical activity level and recurrent acute respiratory infections in schoolchildren. *Cent Eur J Public Health* 2001;9:126–9.
67. Lucas JA, Moonie S, Hogan MB, et al. Efficacy of an exercise intervention among children with comorbid asthma and obesity. *Public Health* 2018;159:123–8.
68. Sylow L, Kleinert M, Richter EA, et al. Exercise-stimulated glucose uptake - regulation and implications for glycaemic control. *Nat Rev Endocrinol* 2017;13:133–48.
69. Diamond A. Effects of physical exercise on executive functions: going beyond simply moving to moving with thought. *Ann Sports Med Res* 2015;2:1011.

70. Van Dam NT, van Vugt MK, Vago DR, et al. Mind the hype: a critical evaluation and prescriptive agenda for research on mindfulness and meditation. *Perspect Psychol Sci* 2018;13:36–61.
71. Nash JD, Newberg A. Toward a unifying taxonomy and definition for meditation. *Front Psychol* 2013;4.
72. Kabat-Zinn J. Mindfulness meditation: health benefits of an ancient Buddhist practice. In: Goleman D, Gurin J, editors. *Mind/Body Medicine*. Washington, DC: Consumer Reports Books. American Psychological Association; 1993. p. 144–56.
73. Black DS, Semple RJ, Pokhrel P, et al. Component processes of executive function—mindfulness, self-control, and working memory—and their relationships with mental and behavioral health. *Mindfulness* 2011;2:179–85.
74. Roemer L, Lee JK, Salters-Pedneault K, et al. Mindfulness and emotion regulation difficulties in generalized anxiety disorder: preliminary evidence for independent and overlapping contributions. *Behav Ther* 2009;40:142–54.
75. Tolahunase MR, Sagar R, Faiq M, et al. Yoga- and meditation-based lifestyle intervention increases neuroplasticity and reduces severity of major depressive disorder: a randomized controlled trial. *Restor Neurol Neurosci* 2018;36:423–42.
76. Chimiklis A, Dahl V, Spears AP, et al. Yoga, mindfulness, and meditation interventions for youth with ADHD: systematic review and meta-analysis. *J Child Fam Stud* 2018;27:3155–68.
77. Kallapiran K, Koo S, Kirubakaran R, et al. Review: effectiveness of mindfulness in improving mental health symptoms of children and adolescents: a meta-analysis. *Child Adolesc Ment Health* 2015;20:182–94.
78. Dunning DL, Griffiths K, Kuyken W, et al. Research review: the effects of mindfulness-based interventions on cognition and mental health in children and adolescents - a meta-analysis of randomized controlled trials. *J Child Psychol Psychiatry* 2019;60:244–58.
79. Bethell C, Gombojav N, Solloway M, et al. Adverse childhood experiences, resilience and mindfulness-based approaches: common denominator issues for children with emotional, mental, or behavioral problems. *Child Adolesc Psychiatr Clin N Am* 2016;25:139–56.
80. Snel E. *Sitting still like a frog: mindfulness exercises for kids (and their parents)*. Boulder (CO): Shambhala Publications; 2013.
81. MacLean KL. *Moody cow meditates*. New York: Simon and Schuster; 2009.
82. Weekly T, Walker N, Beck J, et al. A review of apps for calming, relaxation, and mindfulness interventions for pediatric palliative care patients. *Children* 2018; 5:16.
83. Oades-Sese GV, Cohen D, Allen JWP, et al. Building resilience in young children the sesame street way. In: Prince-Embury S, Saklofske DH, editors. *Resilience interventions for youth in diverse populations*. New York: Springer; 2014. p. 181–201. https://doi.org/10.1007/978-1-4939-0542-3_9.
84. Kondo MC, Jacoby SF, South EC. Does spending time outdoors reduce stress? A review of real-time stress response to outdoor environments. *Health Place* 2018;51:136–50.
85. Kondo MC, Fluehr JM, McKeon T, et al. Urban green space and its impact on human health. *Int J Environ Res Public Health* 2018;15 [pii:E445].
86. Razani N, Morshed S, Kohn MA, et al. Effect of park prescriptions with and without group visits to parks on stress reduction in low-income parents: SHINE randomized trial. *PLoS One* 2018;13:e0192921.

87. Razani N, Niknam K, Wells NM, et al. Clinic and park partnerships for childhood resilience: a prospective study of park prescriptions. *Health Place* 2019;57: 179–85.
88. Bingel U. Avoiding nocebo effects to optimize treatment outcome. *JAMA* 2014; 312:693–4.
89. Colloca L, Finniss D. Nocebo effects, patient-clinician communication, and therapeutic outcomes. *JAMA* 2012;307:567–8.
90. Slopen N, McLaughlin KA, Shonkoff JP. Interventions to improve cortisol regulation in children: a systematic review. *Pediatrics* 2014;133:312–26.
91. Carlson M, Earls F. Psychological and neuroendocrinological sequelae of early social deprivation in institutionalized children in Romania. *Ann N Y Acad Sci* 1997;807:419–28.
92. Harkness E, Macdonald W, Valderas J, et al. Identifying psychosocial interventions that improve both physical and mental health in patients with diabetes: a systematic review and meta-analysis. *Diabetes Care* 2010;33:926–30.
93. Ahmadpanah M, Paghale SJ, Bakhtyari A, et al. Effects of psychotherapy in combination with pharmacotherapy, when compared to pharmacotherapy only on blood pressure, depression, and anxiety in female patients with hypertension. *J Health Psychol* 2016;21:1216–27.
94. Moreno MA. Pediatric care coordination. *JAMA Pediatr* 2019;173:112.
95. Kuo DZ, McAllister JW, Rossignol L, et al. Care coordination for children with medical complexity: whose care is it, anyway? *Pediatrics* 2018;141:S224–32.
96. Lieberman AF, Ippen CG, Hernandez Dimmler M. Assessing and treating youth exposed to traumatic stress. Washington, DC: American Psychiatric Pub; 2018.
97. Funderburk BW, Eyberg S. Parent–child interaction therapy. In: *History of psychotherapy: continuity and change*. 2nd edition. Washington, DC: American Psychological Association; 2011. p. 415–20. <https://doi.org/10.1037/12353-021>.
98. Vanderzee KL, Sigel BA, Pemberton JR, et al. Treatments for early childhood trauma: decision considerations for clinicians. *J Child Adolesc Trauma* 2018. <https://doi.org/10.1007/s40653-018-0244-6>.
99. Cohen JA, Mannarino AP, Deblinger E. Treating trauma and traumatic grief in children and adolescents. 2nd edition. New York: Guilford Publications; 2016.
100. Steil R, Dittmann C, Müller-Engelmann M, et al. Dialectical behaviour therapy for posttraumatic stress disorder related to childhood sexual abuse: a pilot study in an outpatient treatment setting. *Eur J Psychotraumatol* 2018;9:1423832.
101. Carrion VG, Kletter H, Weems CF, et al. Cue-centered treatment for youth exposed to interpersonal violence: a randomized controlled trial. *J Trauma Stress* 2013;26:654–62.
102. Shapiro F, Maxfield L. Eye movement desensitization and reprocessing (EMDR): information processing in the treatment of trauma. *J Clin Psychol* 2002;58: 933–46.
103. Fisher SF. Neurofeedback in the treatment of developmental trauma: calming the fear-driven brain. New York: W. W. Norton & Company; 2014.
104. Fisher SF, Lanius RA, Frewen PA. EEG neurofeedback as adjunct to psychotherapy for complex developmental trauma-related disorders: case study and treatment rationale. *Traumatology* 2016;22:255–60.
105. van der Kolk BA. The body keeps score: approaches to the psychobiology of posttraumatic stress disorder. In: *Traumatic stress: the effects of overwhelming experience on mind, body, and society*. New York: Guilford Press; 1996. p. 214–41.

106. Naylor MW, Davidson CV, Ortega-Piron DJ, et al. Psychotropic medication management for youth in state care: consent, oversight, and policy considerations. *Child Welfare* 2007;86:175–92.
107. Traub F, Boynton-Jarrett R. Modifiable resilience factors to childhood adversity for clinical pediatric practice. *Pediatrics* 2017;139:e20162569.
108. American Academy of Pediatrics. Helping foster and adoptive families cope with trauma: a guide for pediatricians. Itasca (IL): American Academy Of Pediatrics; 2016.
109. American Academy of Pediatrics. Helping foster and adoptive families cope with trauma. Itasca (IL): American Academy Of Pediatrics; 2013.