

# Primary and Secondary Prevention Strategies in Healthcare

## **PRIMARY PREVENTION STRATEGIES**

Primary prevention efforts target healthy individuals and aim to prevent harmful exposures from ever occurring. These include universal efforts to change or establish structural and systemic conditions, including raising public awareness and promoting education, to prevent the exposures that lead to disease or negative outcomes, alter unhealthy or unsafe behaviors, and increase protective factors or resistance to disease or injury, should exposures occur.

Primary prevention of Adverse Childhood Experiences (ACEs) and toxic stress targets the entire population, with the goal of preventing exposure to ACEs and other risk factors for toxic stress, preventing intergenerational transmission of ACEs and toxic stress, and increasing protective or buffering factors so that should adversity be encountered, it is likely to be buffered.<sup>69</sup> Primary prevention of ACEs and toxic stress in the healthcare sector has two components: the clinical approach within the healthcare setting, and cross-sector work between the healthcare setting and other sectors.

## **CLINICAL APPROACH IN THE HEALTHCARE SETTING**

The healthcare setting offers a unique opportunity to help patients and families understand the impact of ACEs and toxic stress on health and to increase access to positive or buffering childhood experiences for the purposes of prevention, while reducing the overall dose of adversity.

A critical strategy for primary prevention of ACEs and toxic stress in the healthcare setting begins with the universal implementation of trauma-informed care (TIC), which improves care for all patients, but especially for those with a history of adversity.<sup>69</sup> While part of the purpose of the TIC framework is to recognize and respond appropriately to the symptoms and consequences of adversity and trauma to support patient needs, it also promotes an important primary prevention framework as a universal protocol that presumes a potential history

of adversity for all patients. Its principles help support a strengths-based and nonjudgmental approach to toxic stress assessment and intervention, and prevent inadvertent retraumatization of patients. Providers can also empathize, motivate, and empower patients or clients with active listening skills and motivational interviewing techniques, while safeguarding against potential retraumatization and vicarious trauma.<sup>660,661</sup> It is therefore beneficial for all patients, providers, and staff.<sup>662,663</sup>

The TIC framework, adapted by ACEs Aware from the Substance Abuse and Mental Health Services Administration (SAMHSA), with an enhanced focus on the health impacts of adversity, involves:<sup>659,664</sup>

- **Understanding** the prevalence of trauma and adversity and their impacts on health and behavior;
- **Recognizing** the effects of trauma and adversity on health and behavior;
- Training leadership, providers, and staff on **responding** to patients by incorporating best practices for trauma-informed care;
- **Integrating** knowledge about trauma and adversity into policies, procedures, practices, and treatment planning; and
- **Resisting retraumatization** by approaching patients who have experienced ACEs or other adversities with nonjudgmental support.

The following key principles of trauma-informed care serve as a guide for all healthcare providers and staff:<sup>659,664</sup>

1. Establish the physical and emotional safety of patients and staff.
2. Build trust between providers and patients.
3. Recognize and respond to the signs and symptoms of trauma exposure on physical and mental health.
4. Promote patient-centered, evidence-based care.
5. Ensure provider and patient collaboration by bringing patients into the treatment process and discussing mutually agreed-upon goals for treatment.
6. Provide care that is sensitive to the patient's racial, ethnic, and cultural background, and gender identity.

The healthcare setting also provides an opportunity to help patients and families develop skills and capacities necessary to increase positive, buffering experiences to prevent ACEs and toxic stress. Caregivers are fundamental to fostering child well-being and establishing the trajectories for children to reach their full potential. A child who has a strong and secure emotional attachment to a primary

caregiver has the foundation for safe, stable, and nurturing relationships, school and occupational functioning, and strong health throughout life.<sup>23,31,47</sup> In order for caregivers to provide the safe, stable, nurturing relationships and environments that children need for healthy development, caregivers need support to meet basic needs.<sup>23,31,47</sup> Promoting family strengths and healthy parenting is fundamental to preventing ACEs as well as to the mitigation of and healing from impacts of ACEs.<sup>23</sup>

## **Promoting family strengths and healthy parenting is fundamental to preventing ACEs as well as to the mitigation of and healing from impacts of ACEs.**

The science of child and human development demonstrates the importance of cumulative protective factors or positive childhood experiences (PCEs) to lifelong health.<sup>41,43,44,97,604,665,666</sup> The effects of PCEs are sometimes referred to as “flourishing,” which can be assessed for children in terms

of their curiosity and interest in learning, ability to pay attention and persist in completing tasks, and ability to regulate their emotions and behavior when facing daily stressors.<sup>667</sup> This self-regulation is often assessed by observing the extent to which children stay calm and engaged when facing a challenge. Such qualities are necessary for children to grow into flourishing adults who live with a sense of meaning and purpose, have positive relationships, and experience positive emotions, and a sense that they matter and can contribute meaningfully.<sup>604,667</sup> Studies on the impact of PCEs on adult health especially emphasize the significance of positive relational experiences, such as having someone to turn to, feeling cared about and heard when things are hard, and having a sense of belonging in school and in the community.<sup>41,43,44,97,604,665,666</sup>

PCEs can coexist with ACEs and can reduce the risk that ACEs will lead to toxic stress and associated negative outcomes.<sup>41,43-45,97,604,665,666</sup> Social support and PCEs have also been associated with decreased asthma symptoms and improved immune responses, including inhibiting inflammation, providing protection against infection, and promoting wound healing.<sup>668-672</sup> Research also shows the independent effects of having or not having PCEs: children who have no ACEs, but also lack PCEs, like living in a resilient family with strong parent-child connection, are at increased risk for physical, mental, and social problems.<sup>41,604</sup> They are also substantially less likely to experience positive relationships and social connection as adults.<sup>41</sup> Thus, the absence of ACEs is not enough for optimal child development or adult health; PCEs and other buffering factors are needed as well. These findings call for proactive efforts to foster family resilience, caring and supportive family relationships,

including strong parent-child communication, and strong school and community connections, each of which contribute to promoting positive health.

Child healthcare providers can help patients and families build these PCEs through the support and care they offer by counseling, educating and modeling healthy interactions during patient visits. For example, providers can educate parents and caregivers on their critical role in healthy child development, such as teaching the importance of and demonstrating serve-and-return for infants and young children.<sup>673</sup> Many science-based tools and resources are available for healthcare providers on the [Harvard Center on the Developing Child](#) website.<sup>674</sup> Other sources of specific educational messaging and tools include the American Academy of Pediatrics' (AAP's) [Connected Kids: Safe, Strong, Secure Clinical Guide](#)<sup>675</sup> and the [Healthy Outcomes from Positive Experiences](#) (HOPE) websites.<sup>676</sup>

Adult care providers also play an important role in primary prevention of ACEs and toxic stress.<sup>23</sup> Intergenerational transmission of toxic stress happens when ACEs alter parental biology or behavior in ways that affect the development and health of their children (discussed in detail in Part I's **Intergenerational Transmission of Adversity**). Therefore, secondary or tertiary prevention—or detection and treatment of toxic stress—in one generation is primary prevention of toxic stress in the next.<sup>2</sup> Obstetric, pediatric, and family practice providers, among others, have an important opportunity to promote family planning resources for wanted pregnancies, and once conception occurs, to provide counseling and intervention for ACEs and toxic stress among expectant parents during prenatal care visits.<sup>677-679</sup> Many ACE-Associated Health Conditions (AAHCs) in adults are ACE risks for the next generation (such as violence, mental illness, and substance use),<sup>2</sup> and AAHCs can enhance family stressors, including disability and financial impacts due to lost productivity.<sup>63,64,680</sup> Therefore, all adult care providers can support patients with AAHCs in regulating their stress responses to mitigate the effects of toxic stress and reduce the intergenerational transmission of toxic stress<sup>23</sup> (discussed further as part of **Secondary Prevention** below).

Ensuring access to high-quality healthcare for all is another key component of primary prevention of ACEs and toxic stress. Healthcare and medical employees are on the front lines in identifying and addressing the immediate health needs of millions of California children and families. Therefore, it is imperative to ensure all families have access to high-quality, affordable care provided in a culturally and linguistically sensitive way. Efforts aimed at preventing discrimination and social oppression are also critical in preventing toxic stress in children and families. In its policy statement, “The Impact of Racism on Child and Adolescent Health,” the AAP details actions that pediatric healthcare providers can take, such as creating a culturally safe medical home (discussed further in **Systems-Level Implementation**

**Considerations** in Part III), using evidence-based screening tools incorporating perceived and experienced racism, and offering appropriate referrals, assessing for strengths and protective factors to mitigate exposure to racism, providing youth and families with guidance on recognizing and responding to racism, and training clinic and office staff in culturally competent care.<sup>681</sup> For example, the Pediatric ACEs and Related Life-Events Screener (PEARLS), the pediatric ACE screening tool recommended by ACEs Aware, incorporates inquiries about experiences of discrimination, and other potential risk factors for toxic stress, such as community violence, food and housing insecurity, bullying, or a caregiver's physical illness or death. This tool can enable more effective referrals, guidance, and support around preventing and addressing cumulative risk for toxic stress.

Given the importance of well child services in the prevention of ACEs and toxic stress, deliberate efforts are especially needed to expand access to and use of such services in California. In 2019, the Auditor of the State of California reported that only 45.2% of children eligible for Medi-Cal actually received recommended preventive services, with wide variation across the state.<sup>682</sup>

## CROSS-SECTOR WORK

As the science illuminates the extent to which our experiences and environments shape our biology, there is increased recognition that clinical interventions are necessary, but not sufficient, to reduce the health impacts of ACEs and toxic stress. Cross-sector coordination, including from within healthcare, is necessary. In the healthcare setting, providers can emphasize the following in patient education, anticipatory guidance, and linkages or referrals to resources:<sup>23,31,619</sup>

- Optimizing social-emotional and other learning at home, such as through the Talk. Read. Sing.<sup>®683</sup> or Reach Out and Read<sup>684</sup> programs;
- Promoting healthy relationship norms;
- Parenting and family relationship skill-building;
- Connecting youth to caring adults and activities;
- High-quality, affordable home visitation, child care;
- Preschool and school enrichment with family engagement;
- Economic supports, such as links to Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) and tax credit programs; and
- Legal supports (such as through medical-legal partnerships like Developmental Understanding and Legal Collaboration for Everyone, DULCE).<sup>685</sup>

Coordination with other sectors, such as schools, child care, justice, social services,

and public health, can be done sustainably when providers leverage team-based approaches to clinical care. Models of care that integrate primary care and behavioral health in one setting help both patients and providers by blending the expertise of mental health or behavioral health clinicians and primary care clinicians. These models have been effective, especially when they incorporate feedback from patients and/or their caregivers.<sup>686-688</sup>

Clinicians on the healthcare team can refer families who are at risk for ACEs and toxic stress to home visiting programs, like the Nurse-Family Partnership program (NFP).<sup>689</sup> NFP has resulted in a 48% reduction in child abuse and neglect, improved cognitive and language development, gains in academic achievement, lower rates of substance use, fewer behavioral problems, and fewer arrests, convictions, and parole violations by age 19 for participating children.<sup>690-693</sup> It has also been shown to benefit parents, associated with better parenting practices, improved pregnancy outcomes, reduced welfare and other government assistance use, greater rates of employment, lower substance use, and reduced exposure to intimate partner violence (IPV).<sup>31,690,691,694,695</sup>

Families can also be linked to high-quality child care, which reduces parental stress and depression, both risk factors for child abuse, neglect, and other ACEs. Child care subsidies tend to enable access to higher-quality child care, which increases the potential for exposure to optimally safe, stable, nurturing relationships and environments.<sup>31</sup>

Coordinating and serving as a liaison between families and schools is an important role for social service or behavioral health clinicians on the team because ACEs are consistently associated with worse educational outcomes,<sup>696</sup> and the school environment can provide both harmful (e.g., bullying) and protective (e.g., trusted adult role models) exposures. Clinicians can encourage connection with caring adults (such as teachers, coaches, or mentors) and support engagement in protective activities like sports, arts and music programs during or after school hours. These connections can reduce absenteeism, prevent substance use, and improve parent-child and student-teacher relationships.<sup>31</sup> Younger children enrolled in preschool enrichment programs that actively involve parents have better math, language, and social skills on school entry, require less special education services, have lower grade retention, are more likely to graduate from high school and attend college, are more likely to be employed as adults, and have greater earnings.<sup>31</sup>

Importantly, social service or behavioral health clinicians on the primary care team can engage with child welfare agencies to ensure that referrals not only address child safety, but also attend to root causes of adversity through services such as stress management, parenting support, and assistance with financial,

housing, and food security,<sup>697</sup> depending on family needs. One valuable resource is [Help Me Grow](#), available in many local communities to connect service providers to each other to create an interconnected system of care to meet individual family needs.<sup>698</sup> When referrals are made to onsite or community resources, it is critical for providers to follow up with patients to ensure the referral was successful and address any barriers.

## SECONDARY PREVENTION STRATEGIES

**Secondary prevention** efforts target individuals who have experienced an exposure (ACEs) and aims to prevent the development of symptoms, disease, or other negative outcomes (toxic stress). The National Academies of Sciences, Engineering, and Medicine (NAEM), CDC, and AAP all recommend early screening for sources of toxic stress and coordination of a cross-sector response to mitigate the harmful effects of early adversity.<sup>7,23,31</sup> A complete ACE screen involves assessing for the triad of adversity (ACE score), clinical manifestations of toxic stress (ACE-Associated Health Conditions, AAHCs), and protective factors. The first two components are used in assessing clinical risk for toxic stress and all three help to guide effective responses.<sup>699</sup> Of note, though clinical manifestations of toxic stress are currently best assessed by the presence or absence of AAHCs, efforts are underway to develop reliable clinical biomarkers that may inform diagnosis, prognostic precision, and therapeutic targets in identifying and intervening on toxic stress. Secondary prevention of ACEs therefore serves as primary prevention of toxic stress, as it seeks to take advantage of the window of opportunity between exposure to ACEs and the development of negative health and social outcomes.

Clinical response to identification of ACEs and increased risk of toxic stress should include:

1. Applying principles of **trauma-informed care**, such as establishing trust, safety, and collaborative decision-making.
2. Supplementing usual care for **AAHCs** by providing **patient education** on toxic stress and offering strategies to regulate the stress response (discussed further in **Tertiary Prevention in Healthcare**) including:
  - Supportive relationships, including with caregivers (for children), other family members, and peers;
  - High-quality, sufficient sleep;
  - Balanced nutrition;
  - Regular physical activity;
  - Mindfulness and meditation;

- Access to nature; and
  - Mental healthcare, including psychotherapy or psychiatric care, and substance use disorder treatment, when indicated.
3. Validating **existing strengths** and **protective factors**.
  4. **Referrals** to patient resources or interventions, such as educational materials, social work, school agencies, care coordination or patient navigation, and community health workers.
  5. **Follow up** as necessary, using the presenting AAHCs as indicators of treatment progress.

Anticipatory guidance (proactive counseling that anticipates likely upcoming concerns) can help patients and/or caregivers understand potential health impacts of ACEs and toxic stress so they can better regulate the toxic stress response and seek to minimize these impacts. Clinicians should be familiar with the various manifestations of the toxic stress response throughout the life course, such as sleep disturbance in infants,<sup>700</sup> asthma in school-age children,<sup>701</sup> delayed menarche in teenage girls,<sup>702</sup> and cardiovascular disease in adults.<sup>207</sup>

An example of how early identification of ACEs can prevent the development of toxic stress is highlighted in a 2020 publication from the Bay Area Research Consortium on Toxic Stress and Health (BARC). In a randomized controlled trial, Thakur and colleagues reported a strong graded relationship between ACE exposure and clinically significant impairment of executive functioning. While only 5.3% of children with no reported ACEs had global executive functioning concerns, 23.4% of children with one to three reported ACEs and 50% of children with four or more ACEs met criteria for such concerns.<sup>703</sup>

While the link between ACEs and executive functioning impairment is well established, the authors uncovered a remarkable insight which highlights the importance of ACE screening as an opportunity to prevent toxic stress:

“A notable finding is the lack of statistically significant associations between childhood adversities and certain health outcomes. Particularly, the finding that 50% of children with  $\geq 4$  ACEs demonstrate clinically measurable impairment of global executive functioning but **do not demonstrate an association with ADHD**. Prior studies have demonstrated a strong association between early life adversities (i.e. ACEs before 5 years of age) and mental health outcomes, including ADHD diagnosis, in middle childhood... As the median age of our study population was 5.8 years, and ADHD is more often diagnosed later in childhood, it is not surprising that we did not observe this association in the present study. While we did not observe this association with ADHD, we did observe a strong association between high PEARLS score (regardless of screening method and subset of PEARLS score) and **poor global executive dysfunction** as measured by the BRIEF-P/2, **which may be an early indicator of children at risk of developing ADHD later in childhood** (emphases added).”



ACE screening, therefore, represents an important opportunity to identify patients at high risk of developing negative health outcomes, such as ADHD, and provides an opportunity to apply targeted interventions to prevent further exposures, strengthen resilience, and provide buffering care and resources. Intervention during the early childhood period, when there are high levels of neuroplasticity and amenability to return to baseline physiologic functioning in neuroendocrine, immune, metabolic, and potentially even genetic regulatory domains, allows providers and caregivers to optimally work with a child's biology to improve the effectiveness and efficiency of interventions.<sup>23,603,704</sup>

ACE screening may begin during prenatal care or newborn well-child care and continue through adulthood. Identifying and addressing caregivers' and parents' ACEs and toxic stress can improve their capacity to support their children and reduce intergenerational transmission of ACEs and of toxic stress. Parental ACE exposures can negatively impact child development in multiple ways (see **Intergenerational Transmission of Adversity** in Part I).<sup>705</sup> However, intergenerational transmission of ACEs can be reduced through interventions such as positive parenting skill-building and treating parental AAHCs.<sup>553</sup> Prenatal providers can screen for and support maternal mental health, including postpartum depression, which is more common in mothers who were maltreated as children and is a risk factor for child maltreatment.<sup>706</sup> Prenatal providers can also help parents space births, which may reduce the risk of child maltreatment<sup>707</sup> by preventing unintended pregnancies, which is a risk factor for abuse and neglect behaviors in both parents.<sup>708</sup> Prenatal providers are well positioned to help prevent the transmission of ACEs and toxic stress because they see parents frequently during a time when they may be more motivated to participate in interventions to optimize their children's health.<sup>679</sup>

Adult care providers play a crucial role in addressing parental health outcomes that serve as ACEs for children, such as mental illness, substance use, and interpersonal and self-directed violence.<sup>2</sup> Additionally, when adult care providers address the role of the toxic stress response in mental, behavioral, and physical health conditions, they can also improve individual and family outcomes by improving management and therefore reducing the impact of AAHCs.<sup>63,64,680</sup> Finally, providers may refer families to public assistance programs as needed because strengthening financial security is an important multigenerational strategy to reduce ACEs and toxic stress and enhance families' ability to provide buffering relationships and environments.<sup>31</sup>

A key area of relational health in adolescent and adult primary care includes supporting healthy romantic relationships and offering IPV screening and intervention. For example, Kaiser Permanente Northern California implemented a Family Violence Prevention Program which coordinated care across the

entire healthcare environment, partnered with community programs, and used ongoing quality improvement methods to increase IPV identification, increase more appropriate, effective use of healthcare services (increased mental and behavioral health services, and reduced emergency department visits), and increase connections to advocacy services.<sup>709-712</sup> The CUES (confidentiality and safety, universal education and empowerment, support for disclosures) approach recommends warm referrals to local and/or national advocacy hotlines and services (e.g., the [National Domestic Violence Hotline](#)<sup>713</sup> and [love is respect](#)<sup>714</sup>), documenting referrals in the patient's chart to facilitate follow-up, discussing harm reduction strategies, and planning close follow-up.<sup>715</sup> This approach has been shown to improve patient knowledge and decrease reproductive coercion and abuse.<sup>715,716</sup>

The [HealthySteps](#) program is another example of a healthcare-based secondary prevention program, because it targets low-income families, who are at increased risk for ACEs and for toxic stress. An expert in child development, called a HealthySteps Specialist, joins the primary care pediatric team caring for infants and toddlers and uses an evidence-based, team-based care model to promote health, well-being, and school readiness. The HealthySteps model is structured to ensure successful interventions, referrals, and follow-up to support AAP's Bright Futures recommendations.<sup>717,718</sup> HealthySteps Specialists or other mental health or social services clinicians on the integrated team can identify and connect patients and families to vital resources outside the clinic setting.

The ACEs Aware initiative applies the consensus of scientific evidence that early detection is key to improving health outcomes related to toxic stress and seeks to proactively focus on eradicating disparities, with the goal of reducing the impacts of ACEs, toxic stress, and AAHCs among all people. Using the triad approach for universal screening for clinical toxic stress in primary care—which includes assessing for an ACE score for cumulative adversity, clinical manifestations of toxic stress in the form of AAHCs, and protective factors—individuals with risk factors and/or early signs of toxic stress can be targeted for early intervention.<sup>699</sup>

As discussed above under Primary Prevention, protective factors such as PCEs, like having someone to turn to, feeling cared about and heard when things are hard, and having a sense of belonging in school and in the community, are essential for healthy human development. Additionally, helping patients and families build skills and capacities for more PCEs can be a primary or secondary prevention strategy because, among those who have experienced ACEs, PCEs are associated with decreased risk of developing the toxic stress response. When PCEs co-exist with ACEs, they mitigate negative impacts on mental, relational, and physical health. For instance, adults with ACEs who also report higher levels of PCEs were shown

to have 72% lower odds of having depression or poor mental health and an over 350% greater odds of having social and emotional support needs met.<sup>41</sup> A study of school-age children with ACEs similarly reported that those who also had families that stayed connected in difficult times and maintained hope were 4.6 times more likely to demonstrate the ability to regulate their emotions and behavior when faced with a challenge.<sup>604</sup> Many studies show that reinforcing existing buffering relationships and environments can mitigate the impacts of ACEs.<sup>41,43,45,62,97,696</sup> A study of 2,452 Welsh adults found that recalling having any resilience assets in childhood, including a trusted adult figure, was associated with attenuation of the impact of adversity (four or more ACEs) on reported childhood allergies, headaches, digestive conditions, poor childhood health, and school absenteeism.<sup>45</sup> For example, in those with four or more ACEs, the presence of all resilience factors (having a trusted adult figure, being treated fairly, supportive childhood friends, being given opportunities to use your abilities, and having someone to look up to) reduced the prevalence of total childhood poor health from 59.8% (in those without these factors) to 21.3% (with resilience factors).<sup>45</sup> Another study (N = 7,047) found that in those with high doses of adversity (four or more ACEs), recalling having an always available adult figure in childhood reduced adulthood health-harming behaviors like poor nutrition, heavy drinking, and daily smoking by 67% and poor mental well-being by 46%.<sup>44</sup> Longer-term impacts and specific effects of PCEs and other buffering factors on the toxic stress response are under study.

Analysis for this report of data from the National Survey of Children's Health (NSCH) provided California-specific cross-sectional data on prevalence of ACEs, some AAHCs, PCEs, flourishing, and access to high-quality healthcare among children (**Table 6**).<sup>32</sup> Among all California children, 28.1% have experienced at least one of the ACEs assessed in the NSCH that align with the ACEs evaluated in the original CDC study. Out of California children with public insurance, ACE prevalence goes up to 37.4%. Fewer than half (46.6%) of California's publicly insured school-age children without ACEs demonstrate the qualities of flourishing assessed in the NSCH, including being curious and interested in learning new things, working to complete tasks begun (persistence), and staying calm when facing challenges (regulating emotions and behavior). For children experiencing two or more ACEs, this fraction is reduced to 26.7%.<sup>32</sup> Clearly much opportunity exists in California for the healthcare sector to play a significant role in prevention of ACEs and promotion of PCEs and other buffering experiences.

## RATIONALE FOR SCREENING FOR ACES IN PRIMARY CARE

ACE screening is optimally performed in primary care because of providers' central role in offering guidance for healthy development, proactively detecting and addressing health risks, and referring individuals and families to necessary services. Primary care providers also develop longitudinal relationships with patients, providing multiple opportunities to screen and to build the level of trust necessary to discuss ACEs.<sup>56,722</sup> Child-serving healthcare providers (including pediatricians, family physicians, nurse practitioners, and physician assistants) play a key role because they follow children regularly during rapid periods of development when they are particularly sensitive to toxic stress,<sup>723</sup> presenting a unique opportunity to interrupt the biological impacts of early adversity. In order to reduce ACEs and toxic stress by one half in a generation, providers who care for adults must mitigate the toxic stress response that underlies and contributes to the presentation of their AAHCs, and avert the intergenerational transmission of ACEs and toxic stress.<sup>2</sup>

Wilson and Jungner's *Principles of Early Disease Detection*, originally published by the World Health Organization (WHO) in 1968, outlines 10 principles for optimal population-based screening efforts.<sup>724</sup> These principles are widely used in public health to guide decisions to implement screening for specific health conditions (see [BREAST CANCER SCREENING AS SECONDARY PREVENTION](#)) and are robustly applicable to toxic stress risk assessment and intervention.

### 1. The condition sought should be an important health problem.

ACEs are highly prevalent and are strongly associated with some of the most common, serious, and expensive health conditions in our society.<sup>2,3,5,15,16,30,613</sup> While the prevalence of toxic stress is unknown, exposure to childhood adversity is well established to be mechanistically linked to toxic stress,<sup>6,12,60,319</sup> and thus, screening for toxic stress using a combination of the ACE score, presence of AAHCs (or their molecular markers), and protective factors, is essential.

### 2. There should be an accepted treatment for patients with recognized disease.

One of the biggest barriers to implementing ACE screening is the false but widely held belief that there is no treatment for toxic stress. Confusion about the condition contributes to this misperception. It is important to clarify that the goal of ACE screening is to identify individuals who are at risk of developing toxic stress physiology. Further, there is significant evidence that the science-based strategies for toxic stress intervention (**Figure 7**) can mitigate the neuro-endocrine-immune-

## Healthcare: Primary, Secondary Prevention Strategies

Prevalence of ACEs (CDC Aligned-5 Topics*) and prevalence of child health services quality, health conditions, risks, and positive health outcomes	All Children	No ACEs	1 ACE	2+ ACEs
Prevalence of ACEs (only includes 5 ACEs items from the NSCH included in the CDC study)	n/a n/a	71.9% 62.6%	19.3% 25.0%	8.8% 12.4%
Prevalence of children receiving care in a primary care medical home (as assessed in the NSCH**)	43.5% 35.5%	47.2% 42.2%	38.6% 29.1%	27.3% 19.6%
Prevalence of children in a high-quality system of care (has a medical home, had at least yearly well-care and dental visit, has adequate insurance and no forgone care/frustration getting needed care, feels a partner in care, got help with transition to adulthood, if needed)	17.4% 14.6%	19.6% 17.8%	13.3% 10.5%	8.8% 7.4%
Child has a chronic condition requiring above routine amount or type of healthcare services	14.5% 17.3%	11.9% 13.2%	17.9% 20.0%	29.8% 34.6%
Child has a mental, emotional, behavioral or developmental problem (3-17)	17.4% 19.9%	13.5% 14.1%	21.4% 20.6%	37.5% 42.9%
Child is overweight or obese (10-17)	31.5% 46.4%	28.0% 44.0%	34.6% 52.3%	43.2% 47.1%
Child is bullied, picked on, or excluded by other children (6-17)*	18.3% 20.3%	14.6% 16.9%	18.0% 13.3% <sup>y</sup>	37.2% 38.6% <sup>y</sup>
Child's mother is in very good/excellent health	65.2% 59.9%	69.1% 63.7%	59.0% 60.9%	38.0% 28.1%
Child engages in school (6-17)*	73.7% 73.1%	77.9% 77.0%	67.3% 71.1%	56.3% 59.2%
Child meets flourishing & resilience criteria (6-17)*	45.0% 43.3%	49.0% 46.6%	36.9% 41.2%	35.7% 26.7%
Child's family stays hopeful when facing problems	60.2% 66.1%	62.8% 68.9%	59.3% 66.2%	42.7% 53.0%
Child lives in a neighborhood that is safe, supportive, and where they have not witnessed or experienced violence	42.0% 38.9%	43.0% 40.9%	44.4% 42.0%	27.9% 29.8%

*% All California children<sup>s</sup>*

*% California children with public insurance*

Prevalence of ACEs (CDC Aligned-5 Topics*) and prevalence of child health services quality, health conditions, risks, and positive health outcomes	All Children	No ACEs	1 ACE	2+ ACEs
Child lives with a family that experiences food insecurity	5.5% 10.5%	3.5% 6.8% <sup>‡</sup>	5.9% <sup>‡</sup> 7.9% <sup>‡</sup>	20.9% 35.3%
Child lives with a family that experiences serious economic hardship to meet basic needs	17.9% 29.5%	12.2% 21.8%	23.8% 33.6%	49.4% 61.0%

<sup>§</sup> % All California children<sup>§</sup>

<sup>¶</sup> % California children with public insurance

**Table 6.** Population-wide prevalence of California’s children with ACEs, as assessed in the National Survey of Children’s Health (NSCH), prevalence of child health services quality, and health risks and outcomes by CDC-aligned ACEs.<sup>39</sup>

<sup>§</sup>All variations in child health services quality, health conditions, risks or positive health outcomes are significant at the 0.05 level of significance, unless otherwise indicated.

\*NSCH CDC-Aligned-5 Topic ACEs are: child lived in a household where he/she was exposed to mental illness, substance abuse, domestic violence and/or had a parent who was incarcerated or parents were separated, divorced, or a parent died. All data are based on the 2016-2018 combined NSCH, with the exception of “bullied,” “school engagement,” and “flourishing”, which use the 2016-2017 NSCH only.

\*\*NSCH Medical Home indicator measures: child has a usual source for sick and well care, a personal doctor or nurse that knows the child well, family-centered care, effective care coordination, and ease of getting referrals.

<sup>‡</sup>This prevalence rate has a relative standard error that is greater than 30%, and estimates are less stable.

metabolic dysregulation that characterizes toxic stress physiology and that they may even reduce or reverse genetic regulatory changes (discussed further in the next section, **Tertiary Prevention Strategies for Healthcare**).<sup>6,23,603,725,726</sup> These interventions can supplement usual care in patients who are at risk for toxic stress (as discussed further in **The ACEs Aware Initiative** in Part III).

### 3. Facilities for diagnosis and treatment should be available.

ACE screening and response can be integrated into existing healthcare facilities, with the purpose of targeting the toxic stress response in prevention and treatment of AAHCs. There are many examples of successful integration of ACE screening in various clinical settings, including pediatric primary care,<sup>56,722,727-733</sup> adult primary care,<sup>734,735</sup> family medicine,<sup>736</sup> and prenatal care.<sup>678,679</sup> While some patients may require referrals for additional resources for interventions not available within the primary

care home, the core components of the clinical response to ACEs and toxic stress outlined in **Principle 2** can be incorporated into usual primary care.<sup>737</sup>

#### 4. There should be a recognizable latent or early symptomatic stage.

Cumulative ACE exposure causes toxic stress and, consequently, a multitude of adverse clinical and social outcomes.<sup>6,60</sup> The physiological stress response is characterized as either positive, tolerable, or toxic.<sup>6,7</sup> With positive and tolerable stress responses, there is a return to homeostasis with adequate buffering. The tolerable stress response is an early period which can serve as a window of opportunity for identification and intervention. Fortunately, the negative consequences of ACEs can be averted by preventing additional exposures in children and providing buffering interventions for both children and adults as soon as exposure to ACEs and risk for toxic stress is identified, but ideally, before the development of significant toxic stress physiology or clinically apparent disease. However, it is important to screen for ACEs and provide buffering care as early

#### BREAST CANCER SCREENING AS SECONDARY PREVENTION

Breast cancer screening is an example of a successful secondary prevention in healthcare, which focuses on widespread screening for early detection of risk factors and/or disease to enable earlier, more effective intervention. In the 1980s, mammography units became more widely available and more frequently used to screen for early breast cancer in women with no symptoms.<sup>719</sup> Breast cancer registry data from 1970–2010 show that mammography increased all breast cancer diagnoses by 23.1%, increasing early-stage disease detection specifically (by 14.7% for invasive breast cancer, and 54.5% for ductal carcinoma in situ), and decreasing the incidence of late-stage breast cancer by 29.0% during that time period.<sup>720</sup> Death from breast cancer has declined by 40% since the

rise in mammography usage for breast cancer screening, with 375,900 deaths averted between 1989 and 2017.<sup>630</sup> The 5-year survival rate for breast cancers diagnosed between 2009 and 2015 was 98% for stage I, 92% for stage II, 75% for stage III, and 27% for stage IV.<sup>630</sup> These data illustrate highly successful secondary prevention, with widespread breast cancer screening enabling earlier detection, resulting in more successful treatment and lower rates of more serious disease and death. Unfortunately, despite reductions in breast cancer mortality among all racial groups, the rates are still unequal: from 2006 to 2015, non-Hispanic Black women had 39% higher breast cancer death rates than non-Hispanic White women, due in large part to inequitable access to screening and care.<sup>721</sup>



*Figure 7. Employing the evidence-based strategies for toxic stress regulation can help patients reduce stress and build resilience. Reproduced with permission from ACEs Aware.<sup>26</sup>*

as possible because adversity can become biologically embedded as early as the prenatal period,<sup>421</sup> and the signs of toxic stress can manifest as early as infancy.<sup>700</sup>

## 5. There should be a suitable test or examination.

ACE screening involves assessing for the triad of adversity (ACE score), clinical manifestations of toxic stress (AAHCs), and protective factors. The first two components are used in assessing clinical risk for toxic stress and all three help to guide effective responses.<sup>699</sup> The Bay Area Research Consortium on Toxic Stress and Health (BARC) developed and established face validity of the Pediatric ACEs and Related Life-Events Screener (PEARLS), which includes age-appropriate ACE questions and seven to nine questions on other potential risk factors for toxic stress, such as poverty and discrimination.<sup>56</sup> A randomized controlled trial validating the PEARLS tool against biomarkers of toxic stress is currently underway. The California Surgeon General's Clinical Advisory Subcommittee (comprised of medical, behavioral health, and public health experts) updated the original 10 ACE questions and developed both [identified and de-identified formats for adults](#), which are available at [AcesAware.org](https://acesaware.org).<sup>738</sup>

## 6. The test should be acceptable to the population.

ACE screening has been shown to be acceptable to patients, parents, providers,



and staff across clinical settings (pediatrics, adult medicine, family medicine, and maternity care), provider types (physicians, nurse practitioners, and trainees), practice types (community, safety net, and academic), locations (urban, suburban, and rural), and patient populations (with varying race/ethnicity, language, income, and insurance).<sup>56,678,727-730,734-736</sup> Studies show that patients and parents want to discuss ACEs and receive guidance and resources so they can address the toxic stress response, avert the intergenerational impact of ACEs, and address co-occurring social determinants of health.<sup>678,697,728,729,739,740</sup> Studies also suggest that screening does not significantly extend visit times (<5 minutes),<sup>736</sup> and may even reduce them.<sup>730,731</sup> Screening for the total number of ACEs (instead of specific exposures) may further enhance acceptability to patients.

### **7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.**

While further investigation into the precise mechanisms is still needed, decades of scientific advancements in animal models and human studies have built an expansive body of evidence demonstrating the mechanisms through which ACEs harm health by activating the toxic stress response.<sup>6,12,60,319</sup> The toxic stress response is defined as “prolonged activation of the stress response systems that can disrupt the development of brain architecture and other organ systems, and increase the risk for stress-related disease and cognitive impairment, well into the adult years.”<sup>23</sup> When adversity and toxic stress are not buffered by safe, stable, nurturing relationships and environments and other protective factors, long-term risk for poorer health and well-being increases significantly.<sup>6,7,23</sup> This physiologic cascade can lead to many adverse clinical and social outcomes, which can be transmitted from generation to generation (as discussed in **The Biology of Toxic Stress and Intergenerational Transmission of Adversity** in Part I).

### **8. There should be an agreed-upon policy on whom to treat.**

The California Department of Health Care Services and the Office of the California Surgeon General recommend integrating ACE screening and response into the clinical care of all pediatric and adult patients (with reimbursement available for Medi-Cal patients up to age 65 years).<sup>86</sup> An expert advisory group convened by the California Surgeon General developed evidence-based guidance on whom to treat. These recommendations/guidelines on whom to treat are captured in the [clinical algorithms](#),<sup>86</sup> discussed further in **The ACEs Aware Initiative**.<sup>86</sup> The [National Pediatric Practice Community on ACEs \(NPPC\)](#) has put forward similar algorithms for assessment and response.<sup>741</sup> The focus on early intervention aligns with NASEM, CDC, and AAP recommendations on the importance of proactively identifying and mitigating adverse outcomes in individuals exposed to sources of toxic stress.<sup>7,23,31</sup>

## 9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.

While the true cost of diagnosing and treating ACEs and toxic stress is unknown at this time, the cost of their associated health and social impacts is substantial. A meta-analysis of 23 studies in adults found that the annual costs of the ACE-attributable portion of 10 common AAHCs were US \$1.3 trillion (3.55% of US gross domestic product (GDP) and 2.67% of Europe's GDP), with cardiovascular disease being a major contributor.<sup>64</sup> More than 75% of the costs were attributed to individuals with two or more ACEs.<sup>64</sup> The study suggested that reducing ACE prevalence by just 10% could save \$105 billion annually, considering just the 10 AAHCs included in the study.<sup>64</sup> As referenced in **Principle 1**, the cost of AAHCs in California is similarly enormous.<sup>63</sup> While further studies are needed, current evidence suggests that screening and intervention for toxic stress may be associated with improved healthcare utilization.<sup>697,739,740</sup>

## 10. Case-finding should be a continuing process and not a “once and for all” project.

Children should be screened on an ongoing basis, because ACEs tend to accumulate over time in childhood. Identifying cumulative exposure is crucial, because the risk of almost all adverse outcomes increases with each additional ACE.<sup>3,5,13,30</sup> The original ACE Study found that those with one ACE had a 65-93% chance of having one other type and a 40-74% chance of having two other types.<sup>3</sup> Not only do ACEs co-occur, but they accumulate through childhood, underscoring the need for routine periodic screening. In a large, multi-site study, Thompson and colleagues found that by age six, children had an average ACE score of 1.94. Between the ages of six and 12, they accumulated another 1.53 ACEs on average, and between the ages of 12 and 16, another 1.15 ACEs.<sup>742</sup> Children should be rescreened periodically to monitor for additional ACEs.<sup>743</sup> Adults should be screened at least once for cumulative ACE exposure; although ACE exposure in adults will not change, ACE reporting may evolve as patients develop more trust in their provider and with normalization of screening practice.

## SETTING UP HEALTHCARE PRACTICES FOR SUCCESSFUL IMPLEMENTATION OF ACE SCREENING

Successful ACE screening initiatives in diverse healthcare settings provide key evidence-based insights for implementing screening,<sup>56,678,722,728-731,734,735,739</sup> synthesized as

follows:

1. **Changing systems.** Clinic leaders must be engaged early to orchestrate and support a systems-level commitment to trauma-informed care. Creating standardized workflows for screening and response, integrating ACE scores into the electronic medical record (EMR), and conducting Plan-Do-Study-Act (PDSA) cycles can streamline the process.<sup>422</sup>
2. **Engaging providers and staff.** All providers and clinic staff should receive training on the long-term effects of ACEs and toxic stress and the principles of trauma-informed care. Training should also include information about vicarious trauma (negative impacts of hearing about trauma) and resources for providers and staff. Providing ongoing training (especially for new staff) and regularly soliciting and addressing staff feedback are key to successful implementation.
3. **Engaging patients and families.** ACE screening should be presented to patients and families in a sensitive, empathic, and nonjudgmental way that highlights the value of screening, normalizes the prevalence of ACEs, reinforces existing resilience factors, and respects autonomy in responding, discussing results, and receiving services and interventions. Screening for the total number of ACEs rather than specific exposures, sometimes referred to as de-identified screening, can help protect patient privacy, and encourages greater disclosure, which allows for earlier intervention (discussed in more detail in **The ACEs Aware Initiative** in Part III).
4. **Responding to ACEs and toxic stress.** Positive ACE screens should prompt a response, starting with a statement of compassion and appreciation for sharing the information. The ACEs screening process offers an opportunity to demystify links to patients' AAHCs and reduce any shame and stigma. Response should also include supplementing usual care for AAHCs with interventions targeted at regulating an overactive stress response. Strong linkages to social and behavioral health services are helpful, whether they are co-located in an integrated care model or provided in partnership with community organizations. It is also important to proactively address barriers to service utilization through resources such as bilingual and/or culturally congruent wellness navigators and care coordinators.

Additional examples of how early adopters have implemented ACE screening and response in diverse healthcare settings are explored in-depth in **Implementation Clinical Case Studies** and **Systems-Level Implementation Considerations** in Part III.

It is crucial to ensure that universal screening leads to improved health for all patient populations, particularly given the disproportionate burden of ACEs among marginalized communities (discussed further in **Defining ACEs and Toxic Stress** in Part I). Monitoring for disparities in screening, referral patterns, and treatment outcomes<sup>678</sup> can help promote equity in ACE screening and response. Proactively addressing barriers to the utilization of resources and services that help promote safe, stable, and nurturing relationships and environments<sup>729</sup> can also help promote equitable outcomes.

### IMPLICATIONS OF COVID-19

During the coronavirus disease 2019 (COVID-19) pandemic, it is imperative for the primary care providers to assess for and respond to risk factors for toxic stress. Infectious disease outbreaks, natural disasters, economic downturns, and other acute stressors are associated with short- and long-term negative health outcomes, including heart attacks and strokes,<sup>376</sup> hypertension,<sup>212</sup> chronic obstructive pulmonary disease exacerbations,<sup>372</sup> and poor birth outcomes.<sup>394</sup> For example, the 1995 Hanshin-Awaji earthquake in Japan was associated with a three-fold increase in heart attacks and a two-fold increase in strokes. These increases in morbidity were reported to be, at least in part,

triggered by overactivation of the sympathetic nervous system and an increase in acute risk factors.<sup>212,376</sup> Acute stressors are also associated with increased incidence of ACEs, such as child abuse<sup>362</sup> and intimate partner violence,<sup>396</sup> and with new or recurrent health conditions that in parents may serve as ACEs, including substance use disorders<sup>385</sup> and mental health exacerbations.<sup>360,362,383,744,745</sup> Individuals with ACEs, other risk factors for toxic stress, and/or fewer buffering supports are particularly vulnerable to acute stressors. For example, mothers with a history of childhood trauma or intimate partner strain had worse psychological outcomes related to Hurricane Katrina,<sup>403</sup> and

## IMPLICATIONS OF COVID-19

children without social supports were at greater risk of persistent post-traumatic stress symptoms related to disasters.<sup>364</sup>

The COVID-19 pandemic has led to a prolonged period of stress, physical distancing, financial insecurity, and decreased healthcare access, heightening the risk of stress-related morbidity and mortality. With school closures, vulnerable children who face potentially dangerous home environments have reduced access to external support. Given that social connection is one of the evidence-based strategies for buffering stress and toxic stress, the implications of physical distancing has included substantial increases in mental distress and disorders across the population. More than ever, the primary care medical home plays a crucial role in screening for sources of toxic stress and monitoring for AAHCs<sup>86</sup> that may arise or worsen during and after the pandemic. Supplementing usual care with the evidence-based strategies for toxic stress management, as outlined in the "[California Surgeon General's Playbook: Stress Relief during COVID-19](#),"<sup>746</sup> can help reduce stress-related health impacts.

Additionally, pediatric providers can offer anticipatory guidance on how children manifest stress at different ages and supply developmentally appropriate ways to help them process current events.<sup>361,383</sup> With physical distancing, many families are

spending much more time together; while this may be dangerous for children experiencing abuse at home, it also provides an opportunity for increased buffering supports against external stressors in safe and stable households. Providers can help connect patients to critical resources, such as existing and expanded public assistance programs and enhanced resources for stress management and mental healthcare (such as the CalHOPE program) compiled by the California state government in response to the pandemic.<sup>747</sup> Finally, healthcare systems must provide access to regular care as much as possible and increase their capacity to provide or refer to behavioral health services, for example, by expanding telehealth, to optimize health and support patients during and after the pandemic.<sup>748</sup>