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Roadmap for Resilience

The California Surgeon General's Report on Adverse Childhood Experiences, Toxic Stress, and Health

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OFFICE OF THE GOVERNOR

December 2, 2020

In one of my first acts as Governor, I established the role of California Surgeon General. Among all the myriad challenges facing our administration on the first day, addressing persistent challenges to the health and welfare of the people of our state—especially that of the youngest Californians—was an essential priority. We led with the overwhelming scientific consensus that upstream factors, including toxic stress and the social determinants of health, are the root causes of many of the most harmful and persistent health challenges, from heart disease to homelessness.

An issue so critical to the health of 40 million Californians deserved nothing less than a world-renowned expert and advocate. Appointed in 2019 to be the first-ever California Surgeon General, Dr. Nadine Burke Harris brought groundbreaking research and expertise in childhood trauma and adversity to the State's efforts. In this new role, Dr. Burke Harris set three key priorities – early childhood, health equity and Adverse Childhood Experiences (ACEs) and toxic stress – and is working across my administration to give voice to the science and evidence-based practices that are foundational to the success of our work as a state.

The Office of the California Surgeon General has already established strong programs, including the first-in-the-nation ACEs Aware initiative, in partnership with the Department of Health Care Services (DHCS), taking a systematic and science-based approach by training healthcare providers to screen for ACEs and toxic stress in children and adults. We have also matched our resolve with funding. Through the California Initiative to Advance Precision Medicine, we have invested $9 million for research demonstration projects that address health impacts of ACEs using precision medicine approaches.

California is leading the way on addressing ACEs and toxic stress as a public health crisis because it is one. This work is a key preventive measure to improve health and societal outcomes for our state's residents for generations to come.

GOVERNOR GAVIN NEWSOM • SACRAMENTO, CA 95814 • (916) 445-2841

As we collectively face an unprecedented confluence of challenges—the COVID-19 pandemic, the ensuing economic recession, our ongoing national reckoning on racial injustice, devastating wildfires exacerbated by climate change—our state and communities are grateful for Dr. Burke Harris' leadership to respond to the waves of trauma and adversity that are upon us.

It is our responsibility to meet the moment. This report provides a roadmap for a systemic and equitable way forward, based on science and strong cross-sector partnerships. We must listen and be advised by the evidence that clearly tells us that cumulative adversity, particularly when experienced early in life, is a root cause of some of the most detrimental, longest lasting and costly health challenges facing our state and nation.

This report highlights how ACEs and toxic stress, if unaddressed, will cost California over a trillion dollars in the next 10 years due to the costs of direct health care and years of life lost from poor health, disability or early death. It is clear to me that implementing the type of evidence-based, cross-sector responses necessary to decrease the burden of ACEs are not only an ethical and moral imperative, but critical to our economic vitality.

This first California Surgeon General's Report offers not only critical insights for policymakers, scientists, healthcare providers, educators, and advocates, but also advances evidence-based solutions and approaches to better the health and safety of the Golden State's residents now and in the future. Furthermore, this exceptional blueprint can truly set the stage for better health, well-being and equity for countless communities here and elsewhere in the nation and world.

Sincerely,

Gavin Newsom
Governor of California

GAVIN NEWSOM
GOVERNOR

DR. NADINE BURKE HARRIS
SURGEON GENERAL

In establishing the Office of the California Surgeon General, it was important to me to begin by visiting communities and listening. I wanted to more fully understand the complexities of our most pressing challenges, as well as the bright spots of innovation and the creative problem-solving that exist all over our great state.

In the past year and a half, I have had the privilege to visit the places where Californians live, learn, work, play, and pray, as well as the opportunity to see up close what residents throughout our state are experiencing. Each community shared their unique challenges—such as homelessness, substance dependence, mental illness, and difficulty accessing healthcare—and successful approaches or proposed solutions.

Over and over, I heard that communities identified trauma as a root cause of many of the challenges they are facing. Californians clearly recognize what the science has been revealing over the past several decades: that adversity, especially in the early years of life, can dramatically curtail health and life opportunities.

In California, more than six out of 10 of us have experienced at least one Adverse Childhood Experience (ACE), such as having a caregiver with mental illness or witnessing domestic violence, and one in six of us have experienced four or more ACEs. The consequences for individuals and communities across our state are significant. An individual with four or more ACEs has a 70% higher risk of kidney disease, more than double the risk of heart disease, and triple the risk of chronic lung disease as someone without ACEs. He or she is also 4.7 times as likely to experience depression and 10.2 times as likely to become dependent on substances; experiencing any ACEs increases the risk of homelessness by two to four times. We now have the science to understand that the toxic stress response is a key biological mechanism by which ACEs lead to these downstream consequences.

ACEs and toxic stress represent a public health crisis in California and across our nation.

The good news is that ACEs are not destiny! Every day, we are learning more about how to effectively interrupt the progression from early adversity to disease and early death. These lessons are being applied to policy and practice in our clinics and hospitals, schools, workplaces, childcare centers, courtrooms, and elsewhere throughout our communities.

What has surprised me most, and what fuels my optimism, is the broad range of steps already being taken by passionate healthcare providers, community leaders, government officials, advocates, educators, and others to advance innovative solutions. We have an army of people who have rolled up their sleeves and are willing and ready, or already hard at work on these issues. In my role as California Surgeon General, I am committed to empowering these medical and social innovations, and marshalling the energy and insights of our healthcare and community leaders to catalyze breakthrough solutions.

This work could not be more timely. Today, in the midst of a global pandemic, record-setting wildfires, and historic civil unrest, many communities across California are experiencing greater adversities than ever before. The extraordinary disruptions and hardships brought on by these circumstances have impacted everyone, but particularly our most vulnerable neighbors. There has never been a more urgent time for trauma-informed care *everywhere*.

This report is intended to act as a blueprint for **primary, secondary,** and **tertiary prevention**—that is, prevention, early detection, and cross-sector coordinated interventions to address ACEs and toxic stress in a systematic way. None of these strategies is sufficient alone, and each extends the reach of the others.

As California Surgeon General, I have set a bold goal to **cut ACEs and toxic stress in half in one generation.** I believe that we can get there with shared vision, shared understanding, and clear roles and responsibilities to help align cross-sector efforts. This report is grounded in the most up-to-date science, and highlights evidence-based and promising practices that can be applied at the federal, state, county, and community levels within and across sectors. Together, we can break the intergenerational cycle of adversity.

Most importantly, as we move forward in this work, I urge everyone to start by putting their own "oxygen masks" on. This is long and difficult work, and we need you in this fight. Self-care is not selfish—it is an essential first step in an individual, family, or community's journey to healing.

Please join me in enacting the solutions laid out in these pages to realize a more just and equitable reality where we can truly prevent and heal from childhood adversity.

With gratitude,

Nadine Burke Harris, MD, MPH
California Surgeon General

CALIFORNIA HEALTH AND HUMAN SERVICES AGENCY

Office of the Secretary

Adverse Childhood Experiences (ACEs) and toxic stress comprise preventable root causes of some of the most intractable health and social challenges facing our state. Over the past few decades, a powerful body of evidence has emerged which demonstrates the extent to which our environments shape our health. While this science is important, it is most useful when put into practice in the service of improving the health and the lives of our communities.

The California Surgeon General's report that follows lays out a first-in-the-nation roadmap to address ACEs and toxic stress through an evidence-based, cross-sector approach, and is a vital component of our overarching efforts to create a healthier California for All. This work has been a collaborative effort, driven by data and the rigorous application of science, while always keeping the person and family at the heart of decision-making.

I'm proud that California is leading the way in improving the lives of our most vulnerable residents by investing in a cross-sector framework for preventing, screening for, and treating ACEs and toxic stress. Preventing and addressing ACEs and toxic stress are key components of our overarching efforts to advance equity, improve health and well-being, reduce homelessness and other adversities, and move towardsperson-centered, value-based care.

In the last year, Californians have faced historic adversities in the form of the COVID-19 pandemic, the sudden and dramatic economic recession, record-breaking wildfires, and threats to equity and racial justice. Now, more than ever, it is critical that we meet the unique challenges of this moment while we further our commitment to make our government more effective, efficient, and person-centered.

With the recent, historic challenges, this work is especially crucial. Everyone is experiencing increased stress. We know, however, that people who have experienced ACEs and other adversities are at greater risk for developing adverse health outcomes as a result of this acute stress. There has never been a more important time for California to have a trauma-informed workforce and evidence-based strategies to address toxic stress than in this moment.

Sincerely,

Mark Ghaly

Mark A. Ghaly, MD, MPH
Secretary

WILL LIGHTBOURNE
DIRECTOR

State of California—Health and Human Services Agency

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GAVIN NEWSOM
GOVERNOR

In early December 2019, most Californians hadn't yet heard of coronavirus disease 2019 (COVID-19). That was when the California Department of Health Care Services (DHCS) and the Office of the California Surgeon General launched ACEs Aware, a groundbreaking effort to address the health impacts of Adverse Childhood Experiences (ACEs).

Ten months later, COVID-19 is known by all, and is a major factor in the increased stress felt by California's children and adults alike, particularly as the pandemic disrupts their access to healthcare. The unacceptable disparities in COVID-19 infection and death rates in our communities of color reflect the structural inequities created by generations of racist policies and practices, but they also are a direct result of the day-to-day differences in lived experience that increase the risk of toxic stress in persons of color.

Since its launch, the first-in-the-nation ACEs Aware initiative has pivoted to meet the demands of the COVID-19 emergency, providing patients and providers with the tools and resources they need to navigate this stressful time, even as it lays the groundwork for a new trauma-informed and more equitable approach to healthcare.

The health impacts of COVID-19 go far beyond positive cases. The stress caused by the pandemic, the physical distancing needed to slow the spread of the virus, and the resulting distress from lost wages, unemployment, and school closures are taking a huge toll on our mental and physical health. These secondary impacts will affect the health and well-being of Californians in the weeks, months, and even years ahead.

ACEs Aware has been an integral part of the Medi-Cal program's response to COVID-19, giving providers the tools to identify, prevent, and treat these secondary health effects.

ACEs are potentially traumatic events that occur in childhood (0–18 years), but can have lasting effects through adulthood. ACEs and toxic stress lead to some of the most harmful and expensive care challenges facing our state and nation.

I am pleased to report that California is leading the way by training and paying Medi-Cal providers to conduct ACE screenings and respond with trauma-informed care to improve the health and well-being of Californians. In a short time, DHCS has made remarkable progress in developing:

- provider tools;

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- patient resources; and
- an online core training for qualified providers to help them learn about ACEs and to screen, treat, and heal children and adults (up to age 65).

These materials are available for providers to download and use today at ACEsAware.org.

The core training and available payment for Medi-Cal providers is at the forefront of the ACEs Aware initiative, but Medi-Cal is also supporting providers in other ways:

- Through the ACEs Aware Grants program, DHCS has awarded 150 grants to 100 organizations across the state in three categories—Provider Training, Provider Engagement, and Communications—to expand the reach and impact of the ACEs Aware initiative.
- DHCS has implemented provider awareness and engagement activities, including monthly educational webinars to promote shared learning and quality improvement among providers.
- DHCS has developed tools and materials to support ACE screening implementation, including the ACEs Aware Provider Toolkit, ACE Clinical Assessment & Treatment Planning, and the ACE Resources Library, all available at ACEsAware.org.
- DHCS is working with Medi-Cal managed care plans to ensure they have the tools they need to support ACE screening implementation.

We have also developed an ACEs Aware provider directory that will connect patients and organizations with Medi-Cal providers who have completed the ACEs Aware training, and we are working to expand the tools and resources available to support providers and trauma-informed primary care organizations.

Our partnership with Dr. Nadine Burke Harris and the Office of the California Surgeon General will allow us to continue our work of building trauma-informed networks and supporting Medi-Cal providers and beneficiaries to treat the impacts of ACEs and toxic stress in our communities.

ACEs Aware has made significant progress, but we still have work to do. Together, we can respond to the current public health crisis, improve health equity, advance our healthcare system, and lead a national movement to ensure everyone is ACEs Aware.

Sincerely,

Will Lightbourne
Director

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Roadmap for Resilience: The California Surgeon General's Report on Adverse Childhood Experiences, Toxic Stress, and Health

Preface

Part I: The Science, Scope, and Impacts of Adverse Childhood Experiences and Toxic Stress

Part II: The Public Health Approach for Cutting Adverse Childhood Experiences and Toxic Stress in Half Within a Generation

Part III: California's Response to Adverse Childhood Experiences and Toxic Stress

Part IV: What Lies Ahead

References and Appendices

A NOTE TO THE READER

This report, *Roadmap for Resilience: The California Surgeon General's Report on Adverse Childhood Experiences, Toxic Stress, and Health*, is intended for a wide range of audiences. These include individuals, families, community members and leaders, policymakers, cross-sector practitioners in fields like public health, justice, early childhood, education, and social services, healthcare professionals, community organizations, scientists and researchers, funders, and advocates. Thus, the report distills cutting-edge learnings from a variety of scientific disciplines in a way that seeks to be accessible to a broad array of readers.

The scientific standards used to develop the report include systematic and targeted searches using electronic research and grey literature databases of English-language articles, with preference given to systematic literature reviews, meta-analyses, and replicable findings in multiple, large-scale, and/or well-designed studies from reputable sources. Where possible, such well-supported evidence is presented and related methodologies are described. Where not available, supportive or promising evidence, emerging from fewer studies and/or studies with smaller or otherwise less representative samples, are presented instead. These instances are flagged as such, and are presented only when better quality evidence does not yet exist and because they still represent findings of emerging interest and relevance to the field.

ABBREVIATIONS

AAHC(s)	ACE-Associated Health Condition(s)
AAP	American Academy of Pediatrics
ABC	Attachment and Biobehavioral Catch-up
ACA	Affordable Care Act
ACE(s)	Adverse Childhood Experience(s)
ACERT	Adverse Childhood Experiences Response Team
ACTH	Adrenocorticotropic hormone
ACTS	Advancing California's Trauma-Informed Systems
Add Health	National Longitudinal Study of Adolescent Health
ADHD	Attention-deficit/hyperactivity disorder
AIDS	Acquired immunodeficiency syndrome
aOR	Adjusted odds ratio
ARV	Antiretroviral
AZT	Zidovudine (antiretroviral drug for HIV)
BARC	Bay Area Research Consortium on Toxic Stress and Health
BARHII	Bay Area Regional Health Inequities Initiative
BDNF	Brain-derived neurotrophic factor
BLL	Blood lead level
BMI	Body mass index
BRFSS	Behavioral Risk Factor Surveillance System
CALQIC	California ACEs Learning and Quality Improvement Collaborative
CalYOUTH	California Youth Transitions to Adulthood Study
CAM	Complementary and alternative medicine
CA-OSG	Office of the California Surgeon General
CARE Act	Ryan White Comprehensive AIDS Resources Emergency Act
CAS	Clinical Advisory Subcommittee

CBT	Cognitive-behavioral therapy
CCORE	Capitol Collaborative on Race and Equity
CDC	Centers for Disease Control and Prevention
CDE	California Department of Education
CDPH	California Department of Public Health
CDSS	California Department of Social Services
CEBC	California Evidence-Based Clearinghouse for Child Welfare
CHVP	California Home Visiting Program
CI	Confidence interval
CLEAR	Collaborative Learning for Educational Achievement and Resilience
CLPPB	Childhood Lead Poisoning Prevention Branch
CME	Continuing Medical Education
CMS	Centers for Medicare and Medicaid Services
CMQCC	California Maternal Quality Care Collaborative
COPD	Chronic obstructive pulmonary disease
COPE	Creating Opportunities for Personal Empowerment
COVID-19	Coronavirus disease 2019
CPM	California Poverty Measure
CPP	Child-Parent Psychotherapy
CPS	Child Protective Services
CPQCC	California Perinatal Quality Care Collaborative
CRH	Corticotropin-releasing hormone
CRP	C-reactive protein
CTC	Child Tax Credit
DACA	Deferred Action for Childhood Arrivals
DALY(s)	Disability-adjusted life year(s)
DBP	Developmental and behavioral pediatrics
DHCS	California Department of Health Care Services
DSM-V	Diagnostic and Statistical Manual of Mental Health Disorders, fifth edition
DULCE	Developmental Understanding and Legal Collaboration for Everyone
ECE	Early childhood education

EfC	Essentials for Childhood
EITC	Earned Income Tax Credit
EMDR	Eye movement desensitization and reprocessing
EMR	Electronic medical record
FDA	Food and Drug Administration
fMRI	Functional magnetic resonance imaging
FQHC(s)	Federally qualified health center(s)
HB	House bill
GAINS	Gather, Assess, Integrate, Network, and Stimulate
GARE	Government Alliance for Race and Equity
GDP	Gross domestic product
GnRH	Gonadotropin-releasing hormone
HAART	Highly active antiretroviral therapy
HEARTS	Healthy Environments and Response to Trauma in Schools
HFA	Healthy Families America
HHS	US Department of Health and Human Services
HiAP	Health in All Policies
HIV	Human immunodeficiency virus
HMO	Health maintenance organization
HOPE	Healthy Outcomes from Positive Experiences
HPA	Hypothalamic-pituitary-adrenal (axis)
ICD	International Classification of Diseases
IEP	Individualized education program
IGF-1	Insulin-like growth factor-1
IHI	Institute for Healthcare Improvement
IL-6	Interleukin-6
IPV	Intimate partner violence
K-12	Kindergarten through grade 12
KPNC	Kaiser Permanente Northern California
LAC-DHS	Los Angeles County Department of Health Services
MBSR	Mindfulness-based stress reduction

MCP	Managed care plan
MIECHV	Maternal, Infant, and Early Childhood Home Visiting Program
MIHA	Maternal Infant Health Assessment
MOC	Maintenance of Certification
MTSS	Multi-Tiered System of Supports
NAEPP	National Asthma Education and Prevention Program
NASEM	National Academies of Sciences, Engineering, and Medicine
NCTSN	National Child Traumatic Stress Network
NIH	National Institutes of Health
NFP	Nurse-Family Partnership
NPPC	National Pediatric Practice Community on Adverse Childhood Experiences
NPY	Neuropeptide-Y
NSCH	National Survey of Children's Health
OCAP	Office of Child Abuse Prevention
OR	Odds ratio
PBIS	Positive Behavioral Interventions and Supports
PBRN	Practice-Based Research Network
PCE(s)	Positive Childhood Experience(s)
PCIT	Parent-Child Interaction Therapy
PCMH	Patient-Centered Medical Home
PDSA	Plan-Do-Study-Act
PEARLS	Pediatric ACEs and Related Life-Events Screener
PEPFAR	President's Emergency Plan for AIDS Relief
PI	Prevention Institute
PNS	Parasympathetic nervous system
PrEP	Pre-exposure prophylaxis
PTSD	Post-traumatic stress disorder
QI	Quality improvement
RCT	Randomized controlled trial
RSA	Respiratory sinus arrhythmia

RTI2	Response to Intervention and Instruction
SAAF	Strong African American Families
SAM	Sympatho-adreno-medullary (axis)
SAMHSA	Substance Abuse and Mental Health Services Administration
SCPMG	Southern California Permanente Medical Group
SDOH	Social determinant(s) of health
SHARK	Strong, Healthy, and Resilient Kids
SNAP	Supplemental Nutrition Assistance Program
SNS	Sympathetic nervous system
SRCH	Santa Rosa Community Health
SSRI(s)	Selective serotonin reuptake inhibitor(s)
suPAR	Soluble urokinase plasminogen activator receptor
TASD	Trauma-associated sleep disorder
TF-CBT	Trauma-focused cognitive-behavioral therapy
TIC	Trauma-informed care
TIPC	Trauma-Informed Primary Care Implementation Advisory Committee
TM	Transcendental meditation
TNF-α	Tumor necrosis factor-alpha
TRAP	Traffic-related air pollution
UCSF	University of California, San Francisco
UNAIDS	Joint United Nations Programme on HIV/AIDS
US	United States
USPSTF	United States Preventive Services Task Force
VTA	Ventral tegmental area
WHO	World Health Organization
WIC	Special Supplemental Nutrition Program for Women, Infants, and Children

GLOSSARY

ACE-attributable fraction: the excess risk of a specific disease or condition that is determined to be due to exposure to Adverse Childhood Experiences (ACEs).[64]

Adverse Childhood Experiences (ACEs): when capitalized, this term refers to 10 specific categories of adversity in three domains experienced by age 18 years, studied in the 1998 Centers for Disease Control/Kaiser Permanente study of the same name. These include physical, emotional, or sexual abuse; physical or emotional neglect; and growing up in a household with incarceration, mental illness, substance use, parental separation or divorce, or intimate partner violence (collectively assessed under the domain household challenges).[3-5]

Allostasis: "literally meaning 'maintaining stability, or homeostasis, through change,' allostasis refers to the process of adaptation to acute stress, involving the output of stress hormones which act to restore homeostasis in the fact of a challenge."[68]

Allostatic load: the collective biological effects of cumulative stress, manifested through changes in biological set points that govern neuroendocrine, immune, metabolic, and genetic regulatory functioning. Examples of allostatic load include changes in levels of stress hormones, reproductive hormones, inflammatory mediators, blood pressure, or other physiologic parameters in attempt to achieve allostasis.[12,68,1607]

Biomarker: "a defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or biological responses to an exposure or intervention, including therapeutic interventions. Molecular, histologic, radiographic, or physiologic characteristics are types of biomarkers."[335]

Critical period: a "window of heightened brain plasticity for encoding specific environmental inputs through experience-expectant mechanisms that results in irreversible changes in brain function with permanent effects on behavior."[1608] While the concept of critical periods arose from the neurobiological literature, it is increasingly recognized that immune functions and other developmental processes may also exhibit critical periods when exposures result in programming of a life-long functional trajectory.[1609]

Cultural competence: a framework that promotes nuanced handling of complex relational issues, often in the healthcare setting, based on patients' and providers' culture, gender, class, national origin, and race/ethnicity, among other factors.[1032]

Cultural humility: a framework that recognizes that one may never fully understand another's culture and offers a road for personal accountability, ongoing learning, and challenging of the specific barriers that impact marginalized communities.[1033]

Disability-adjusted life years: the sum of years of life lost due to premature death and to disability for people living with a health condition or its consequences.[64]

Epigenetic changes: the process by which particular environmental influences can move a particular genetic switch to an "on" or "off" position; these changes may be transmitted to the next generation, and mechanisms can include DNA methylation, histone post-translational modifications, and small noncoding RNAs.[302,303]

Health inequities: the unjust and avoidable differences in health status seen within and between population groups.[1099]

Positive stress response: a brief, time-limited activation of the biological stress response (including transient elevations in stress hormones, heart rate, and blood pressure) in response to a routine stressor.[6]

Primary prevention: efforts that target healthy individuals and aim to prevent harmful exposures from ever occurring. These include efforts to change or establish structural and systemic conditions to prevent 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.[24,25]

Protective factors: intrinsic or extrinsic conditions or attributes that mitigate risk for toxic stress, such as curiosity and interest in learning, ability to pay attention and persist in completing tasks, ability to regulate emotions and behavior, feeling cared about and heard when things are hard, and having a sense of belonging in school and in the community, in addition to biological factors like differences in telomere length and the serotonin transporter gene.[36,41-46,87-95,97,604,665-667]

Resilience: the ability to withstand or recover from stressors, resulting from a combination of intrinsic factors (such as self-regulation or telomere length), extrinsic factors (like safe, stable, and nurturing relationships with family members and others), and predisposing biological susceptibility.[41-46,96-100] Of note, while the term resilience is often considered in the mental health and behavioral domains, scientific advances in understanding of the impact of stress on neuro-endocrine-immune-metabolic and genetic regulatory health compel advancement of the definition of resilience to also include these domains as well. At the molecular level, resilience arises from a combination of neural, hormonal, immune, metabolic, epigenetic, and genetic factors that interact with environmental influences and foster an individual's ability to adapt in a healthy manner.

Risk factor: a circumstance or condition that increases susceptibility to or the probability of an adverse outcome.

Risk factor for toxic stress: a circumstance, exposure, or condition with documented associations with increased likelihood or susceptibility of development of the toxic stress response. In addition to ACEs, other risk factors for toxic stress include poverty, exposure to discrimination, and exposure to the atrocities of war.[103]

Secondary prevention: "screening to identify diseases in the earliest stages, before the onset of signs and symptoms, through measures such as mammography and regular blood pressure testing."[24]

Sensitive period: "a time in development in which the developing organism is especially likely to undergo change (either positive or negative) in response to some experience or environmental change (e.g., an environmental toxicant, intervention training, or certain nutrients). Sensitive periods for certain functions can extend into adulthood."[23]

Social determinants of health: "the conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life."[1097]

Telomeres: protective sequences of non-coding DNA capping the ends of chromosomes that shorten over time. Chronic stress exposure leads to accelerated telomere length shortening, which has been linked to increased susceptibility to and faster progression of aging-related diseases.[12,310-314] A growing body of research is finding that interventions such as supportive parenting, aerobic exercise, and nutrition may reduce stress and protect or even lengthen telomeres.[488-492]

Tertiary prevention: efforts that target individuals who have already developed a disease or social outcome, and that aim to lessen the severity, progression, or complications associated with that outcome.[24,25]

Tolerable stress response: involves an activation of the stress response that results from moderately "severe, longer-lasting difficulties, such as the loss of a loved one, a natural disaster, or a frightening injury. If the activation is time-limited and buffered by relationships with adults who help the child adapt, the brain and other organs recover from what might otherwise be damaging effects."[79]

Toxic stress response: "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... For children, the result is the disruption of the development of brain architecture and other organ systems and an increase in lifelong risk for physical and mental health disorders."[23] The term toxic stress is often mistakenly used to refer to the drivers of stress or the stressors. In fact, toxic stress refers to the dysregulated biological stress response and the concomitant long-term changes in physiology.[6-12,23,79,80,103]

Trauma-informed care: care that includes awareness of the prevalence of trauma and adversity (including early adversity) and understanding of the impacts of trauma on physical, emotional, and mental health. Its principles help support a strengths-based and nonjudgmental approach to toxic stress risk assessment and intervention, and to prevent inadvertent retraumatization of patients and vicarious traumatization of service providers.[659-664]

EXECUTIVE SUMMARY

Adverse Childhood Experiences (ACEs) and toxic stress represent an urgent public health crisis with wide-reaching health and societal impacts, from heart disease to homelessness.[1-13] According to recent data, **62.3%** of California adults have experienced at least one ACE, and **16.3%** have experienced four or more ACEs (2011–2017 data).[27]

ACEs are 10 categories of adversities in three domains experienced by age 18 years: child abuse (physical, emotional, or sexual); neglect (physical or emotional); and household challenges (growing up with household incarceration, mental illness, substance dependence, parental separation or divorce, or intimate partner violence).[3-5]

The high prevalence of ACEs in California, along with the intergenerational accumulation of impacts for individuals, families, and communities, have resulted in a public health crisis, with the greatest impacts on already disadvantaged individuals and communities. The time to act on this crisis is now.

ACEs are strongly associated, in a dose–response fashion, with some of the most common and serious health and social conditions facing our society, including nine of the 10 leading causes of death in the United States (US, **Table 1**), and with earlier mortality.[2,16,17,28-30]

In addition, ACEs are associated with our most pressing social problems, including learning, developmental, and behavior problems, high school noncompletion, unemployment, poverty, homelessness, and felony charges—many of which can serve as additional vectors for the intergenerational transmission of adversity.[2,16,17,34-40]

When their root causes are inadequately addressed, the health and other effects of ACEs are also very costly.[13,16,63,64,555,611-616] For example, a recent estimate based on 2013 expenditures revealed that **ACEs cost California $112.5 billion overall annually** ($10.5 billion in personal healthcare spending and $102 billion in years of productive life lost), and may cost over $1.2 trillion in the next 10 years in California. This estimate only considers impacts from eight common ACE-Associated Health Conditions (AAHCs): asthma, arthritis, chronic obstructive pulmonary disorder (COPD), depression, cardiovascular disease, smoking, heavy drinking, and obesity.[13,63] The real cost impacts are likely to be much greater.

Table 1. Association of ACEs with leading causes of death in the US

Leading causes of death in the US, 2017	Odds ratios for ≥ 4 ACEs (relative to no ACEs)
1. Heart disease	2.1
2. Cancer	2.3
3. Accidents (unintentional injuries)	2.6
4. Chronic lower respiratory disease	3.1
5. Stroke	2.0
6. Alzheimer's disease or dementia	11.2
7. Diabetes	1.4
8. Influenza and pneumonia	unknown
9. Kidney disease	1.7
10. Suicide (attempts)	37.5

In 2020, multiple simultaneous public health emergencies have laid bare the substantial structural and systemic forces that imperil health and well-being. These include the coronavirus disease 2019 (COVID-19) pandemic; the devastating impacts of climate change, including wildfires; and the deep-rooted systemic racism in our society, which has been brought into sharper focus. It is clear that vulnerable and systematically overlooked communities bear the brunt of each new crisis, and that these communities deserve a much more effective set of buffering systems and supports.

ACEs impact all communities; however, some populations are affected disproportionately. The original ACE Study was conducted among a population that was largely White, middle class, college-educated, and privately insured.[3,4] Subsequent studies have found a higher prevalence of ACEs in individuals who are racially marginalized (Black, Latinx, Native American, or multi-racial), high school nongraduates, unemployed or unable to work, in lower income brackets, uninsured or underinsured, involved in the justice system, women, and/or identify as lesbian, gay, or bisexual.[10,13-22]

To truly transform the negative outcomes associated with ACEs, California, as well as other states and nations, must act intentionally and inclusively to address the structural factors that result in disparities in health, social, and economic outcomes and opportunities.

Toxic stress response

We now understand that a key mechanism by which ACEs lead to increased health risks is through a health condition called the **toxic stress response**.[6-12] When significant adversity is experienced during critical and sensitive periods of early life development, without adequate buffering protections of safe, stable, and nurturing relationships and environments, it can lead to prolonged activation of the biological stress response, and to long-term disruption of neuro-endocrine-immune-metabolic and genetic regulatory mechanisms. These biological changes can also be transmitted to the next generation.[414,433]

More research is needed to precisely identify clinically useful biomarkers to diagnose and follow risk of toxic stress longitudinally, as well as more specific therapeutic targets.

Links to coronavirus disease 2019 (COVID-19)

ACEs (acting through the toxic stress response) increase the burden of AAHCs such as heart disease, diabetes, kidney disease and obesity, which, in turn, predispose to a more severe COVID-19 disease and increased risk of death. Further, those with a history of ACEs may also be more susceptible to the health effects of acute or chronic stress. Thus, the biological condition of being stress-sensitized also increases the risk of stress-related chronic disease exacerbations associated with living through the pandemic.

Exposure to ACEs can also set up transmission of health risks across generations by altering gene expression (epigenetics) in parents to be, which can affect the development and health of their children, and future generations to come.[32,33] Intergenerational transmission of toxic stress physiology can also perpetuate and exacerbate socially rooted inequities in health, achievement, socioeconomic mobility, and mortality.[16,29,35,36,60,62]

Risk factors for toxic stress

In addition to the original 10 ACEs, other adversities, including racism and poverty, are also risk factors for developing a toxic stress response.[2,6,10,23,31,53-61,178,510,1100,1101,1116-1118] Further research is currently underway to assess the extent to which these and other important social determinants of health, such as food and housing insecurity, may act directly through the toxic stress pathway or may mediate or modulate the toxic stress response.

Primary, secondary, and tertiary prevention of ACEs and toxic stress

This first California Surgeon General's report serves a blueprint for how to transform outcomes by engaging a cross-sector approach to cutting the burden of ACEs and toxic stress in half in a generation, using California's nation-leading efforts as an exemplar.

A public health approach to preventing ACEs and healing toxic stress involves prevention at three levels—**primary, secondary, and tertiary**—or prevention, early detection, and early intervention, to reverse or prevent further harms.[24,25] **None of these strategies is sufficient alone, and each extends the reach of the others.** The synergistic effect of primary, secondary and tertiary prevention is illustrated by the US response to the human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) epidemic. Coordinated efforts for public awareness and prevention, testing for early detection, and effective treatment were all necessary for achieving a reduction in the AIDS mortality rate of more than 87% in one generation (from 50,628 deaths in 1995 to 6,465 deaths in 2015).[620]

This report specifies a sector-specific and cross-sector blueprint for achieving these goals at the state level, in the service of prioritizing prevention, upstream strategies, equity in outcomes, and enhancing coordination across the following sectors:

- Healthcare
- Public health
- Social services
- Early childhood
- Education
- Justice

Primary prevention

These efforts target healthy individuals and aim to prevent harmful exposures from ever occurring. In the example of HIV, primary prevention includes promoting public education, condom use, and needle exchange practices to prevent acquisition of HIV during sex or other high-risk activities.[622]

For ACEs and toxic stress, primary prevention strategies are designed to prevent and reduce the likelihood of ACEs and other risk factors for toxic stress from ever occurring. Investments in cross-sector policies and programs that promote stable, safe, and nurturing relationships and environments, and optimizing the systems and structural conditions that "set the odds" for health and well-being. These include:[23,31,564]

- Mechanisms to address poverty and food insecurity, including **economic supports** and family-friendly work policies like **paid family leave**;
- Models to enhance parenting efficacy, resilience, attachment, and family bonds, including **high-quality child care** and early childhood **home visitation**;
- **Public education campaigns** to raise awareness of ACEs and toxic stress, and to arm the public with science-based solutions for reducing the impact of ACEs on children and adults, paired with policy strategies to support safe, stable, and nurturing relationships and environments;
- Access to **high-quality mental and physical healthcare**, including family-centered treatments;
- Enabling opportunities for stress-buffering activities such as **access to nature**, **mindfulness** activities, **physical activity**, and sufficient and high-quality **sleep**;
- Providing high-quality **early and ongoing learning opportunities**, including for social-emotional learning, executive function skills, healthy relationship skills, and responding to challenges;
- Cross-sector and sector-specific **training** in **trauma-informed tools**, approaches, and strategies for all providers engaging with children and families; and
- **Public health surveillance** and policy-oriented applications of population-level indicators of exposure to ACEs and impacts of toxic stress.

Secondary prevention

These efforts involve "screening to identify diseases in the earliest stages, before the onset of signs and symptoms, through measures such as mammography and regular blood pressure testing."[24] In the example of HIV prevention, this includes HIV testing to determine who is HIV+ and might benefit from treatment to prevent opportunistic infections.[631-634]

In the case of ACEs and toxic stress, ACE screening can identify individuals at increased risk of having a toxic stress response and target interventions early, when they are likely to be more effective and less expensive. There is a consensus of scientific evidence that early detection and early intervention improves outcomes related to toxic stress.[6-9,23,31,603,704] California's nation-leading **ACEs Aware Initiative** has trained over 15,000 healthcare providers to date to screen for ACEs, to recognize and respond to clinical evidence of toxic stress in primary care, and to address the role of toxic stress as a root cause for many chronic diseases. The ACEs Aware program,[1133] which reimburses Medi-Cal providers for conducting screening and response, is the most comprehensive approach in the nation for enacting large-scale screening and intervention for toxic stress in the healthcare sector (**Figure 1**).

Early detection of ACEs and other risk factors for toxic stress provides an opportunity to strengthen existing protective factors, initiate early buffering interventions, and ultimately prevent toxic stress physiology and downstream consequences, such as earlier-onset, more severe AAHCs or toxic stress-related social consequences.[6-12] The report outlines how each sector can coordinate to enhance early detection, including training of cross-sector personnel such as educators, law enforcement, and courts, to recognize the signs of toxic stress and refer affected individuals for appropriate care.

__Figure 1.__ The spectrum of implementation strategies needed to achieve prevention, practice transformation, and research and innovation in addressing toxic stress. Reproduced with permission from the Center for Youth Wellness.[1532]

Tertiary prevention

These efforts target individuals who have already developed a disease or social outcome, and aim to lessen the severity, progression, or complications associated with that outcome. In the example of HIV, tertiary prevention evolved from treatment of opportunistic infections in the 1980s to the modern era of more than 25 sophisticated antiretrovirals developed through the proliferation of basic, clinical, and translational research on HIV biology. As a result, AIDS-related deaths in the United States have declined by more than 87% from their peak in 1995.[620]

For ACEs and toxic stress, tertiary prevention targets individuals who have experienced ACEs and have developed consequences of the toxic stress response, such as earlier-onset or more severe AAHCs. The goal is to regulate the stress response system and counter-act the disruptions in neuro-endocrine-immune-metabolic and genetic regulatory function that characterize the toxic stress response.

Robust evidence demonstrates that enhancing supportive relationships, regular exercise, access to nature, sufficient and high-quality sleep, balanced nutrition, mindfulness practices, and mental and behavioral healthcare, can mitigate the neurologic, endocrine, immune, metabolic, and genetic regulatory derangements of the toxic stress response.[603,704,725] Tertiary prevention of toxic stress in one generation can equate to primary prevention in the next—treating toxic stress in parents can prevent the passing down of health risks to the next generation.

Tertiary prevention involves interventions beyond the clinical setting. This report outlines how each sector—healthcare, public health, social services, early childhood, education, and justice— can contribute to healing the harmful effects of ACEs and toxic stress. To truly achieve practice and population health transformation, coordinating a cross-sector network of highly effective and transformative referral and service options is imperative.

Conclusion

This report highlights the exciting work happening across California to recognize and respond to ACEs and toxic stress as a public health crisis. It also serves as a roadmap for other states or nations to replicate and innovate from California's experiences.

Examples of key policy tools for supporting California's public health approach to addressing ACEs and toxic stress are highlighted, including investments in:

- **Leadership**, such as Executive Order N-02-19,[1530] creating the Office of the California Surgeon General;
- **Legislation** to support early identification and early and effective intervention for ACEs and toxic stress;
- **Funding** for the ACEs Aware initiative and cross-sector supports for primary, secondary and tertiary prevention of toxic stress; and
- Biomedical research, such as funding for the **California Initiative to Advance Precision Medicine**[65] to advance novel precision medicine approaches to assessing for and treating toxic stress, to take healthcare innovation to the next level.

While much work lies ahead, this **California Surgeon General's report on ACEs and toxic stress** provides a framework for shared understanding, shared language, and a shared vision with which state and local leaders can align cross-sector efforts for prevention, early detection, and effective intervention.

PART I

The Science, Scope, and Impacts of Adverse Childhood Experiences and Toxic Stress

Framing the Public Health Crisis of ACEs and Toxic Stress

Adverse Childhood Experiences (ACEs) and toxic stress represent an urgent public health crisis with wide-reaching health and societal impacts. ACEs affect millions of Californians and the resulting toxic stress is a root cause of many chronic health and societal challenges – from heart disease to homelessness.[1,2] The high prevalence of ACE exposure in adults and children in California, along with the intergenerational accumulation of impacts for individuals, families, and communities, have resulted in a public health crisis, with the greatest impacts on already disadvantaged individuals and communities. We now readily understand how ACEs can drive biologic risks for health, social, and relational challenges.

The purpose of this report is to bring together the latest science and insights from leading experts, share the most promising community innovations, and advance best practices, systems, approaches, and tools to address ACEs and toxic stress. The development of this report has been guided by the foundational principles of prevention, equity, and rigor. Addressing ACEs and toxic stress is a fundamental prevention strategy to head off major public health and societal morbidity for future generations.

Though there are multiple potential adverse experiences in childhood that matter for health, in this report, when capitalized, the term Adverse Childhood Experiences (ACEs) specifically refers to the 10 categories of adversities in three domains experienced by age 18 years that were studied by in the landmark ACE Study published in 1998. The categories are: child abuse (physical, emotional, or sexual); neglect (physical or emotional); or household challenges (as reframed by the Centers for Disease Control and Prevention in 2015 from "household dysfunction"—growing up in a household with incarceration, mental illness, substance use, parental separation or divorce, or intimate partner violence).[3-5] High doses of adversity, occurring early in life, without adequate buffering protections of trusted caregivers and safe, stable environments, may lead to prolonged activation of the biological stress response and changes in brain structure and function, how genes are read and transcribed, functioning of the immune, metabolic, and endocrine systems, and growth and development. These changes comprise what is now known as the toxic stress response.[6-12]

With great optimism and intention at the forefront, this first California Surgeon General's report lays out a roadmap for advancing systematic reforms that recognize and respond to the effects of ACEs and toxic stress. The science is clear: ACEs affect all communities and are common in all regions and populations. At the same time, inequities exist in the prevalence of ACEs along axes of race, ethnicity, class, gender, sexuality, and educational attainment.[10,13-22] We know that historically rooted inequities translate into significant day-to-day differences in lived experiences that get embedded in our brains and bodies. Neighborhood, community, systemic, and structural factors also strongly shape and can "set the odds" for negative or positive health and developmental trajectories and outcomes, and these upstream factors must be targeted as part of a cross-sector approach to addressing ACEs and toxic stress.[23] To truly transform the negative outcomes associated with ACEs, we must act intentionally and inclusively to address the structural factors that result in disparities in health, social, and economic outcomes and opportunities.

In 2020, multiple simultaneous public health emergencies—the Coronavirus disease 2019 (COVID-19) pandemic; the devastating impacts of climate change, including wildfires; and the sharper focus on the deep-rooted systemic racism in our society—have laid bare the substantial structural and systemic forces that imperil health and well-being. It is clear that vulnerable and systematically overlooked communities bear the brunt of each new crisis, and that these communities deserve a much more effective set of buffering systems and supports.

The approaches outlined in this report recognize and respond to the ways in which experiences of trauma and adversity directly increase risk for acute and chronic disease as well as early death. Seeking to fundamentally upend and intervene on the root causes of these outcomes is guided by the values of prevention, equity, and rigor. These values have been and continue to be critical touchstones of this work.

California is leading the way in addressing ACEs and toxic stress as a public health crisis with key priorities, engagements, and investments in communities and sectors across the state. Several principles are emphasized in this report. The first is cross-sector collaboration. Since the root causes of ACEs and toxic stress are complex and deeply interconnected, effectively addressing them requires a coordinated approach across sectors that attends to the multi-layered systemic and structural determinants of health, starting from upstream factors.[2]

Second, an effective response to ACEs and toxic stress requires prevention at all three levels—primary, secondary, and tertiary—or prevention, early recognition, and early, evidence-based intervention.[24,25] To break the intergenerational cycle of ACEs and toxic stress and improve outcomes at scale, both the upstream or systems-level factors, and individual-level treatment must be attended to.

Third, this report shares and seeks to build from the current, on-the-ground efforts of advocates, medical professionals, public health experts, public servants, cross-sector leaders, communities, and others to systematically prevent and address ACEs and toxic stress. These models, best practices, and protocols can be replicated, tailored, or built upon in other contexts. The solutions highlighted in this report offer a guide and shared language for other communities', states', and nations' responses to ACEs and toxic stress. With this broader application in mind, the authors of this report set forth approaches, guidance, and recommendations to foster cross-sector collaboration, workforce training, continuous learning and quality improvement, dissemination of best practices and avoidance of unintended harms, data gathering and utilization, and rigorous research and evaluation.

Many of the recommendations set forth here do not require further investments. Rather, they highlight the opportunity to leverage and improve upon existing approaches by acting on the evidence that through preventing ACEs and healing toxic stress, we can more efficiently and effectively address some of the most deeply rooted health and societal issues that plague our communities today. When we have the courage, creativity, compassion, and commitment to address the root causes of these pervasive health and social inequities, we take an essential step closer to realizing a world in which everyone is afforded opportunities to reach their full potential and thrive.

Defining ACEs and Toxic Stress

ADVERSE CHILDHOOD EXPERIENCES

The term adverse childhood experiences is often colloquially used to refer to a variety of adversities in childhood but, when capitalized, Adverse Childhood Experiences (ACEs) specifically reference the 10 categories of adversities investigated in the landmark research study of the same name. The ACE Study was conducted by the Centers for Disease Control and Prevention (CDC) and Kaiser Permanente among a clinical population of 17,337 middle-class adults and investigated a set of 10 categories of common, though under-recognized, experiences occurring in the first 18 years of life. The findings, first published in 1998, revealed that ACEs are highly prevalent and demonstrate a strong dose-response relationship with a multitude of negative health and social consequences in adulthood.[3-5] **Figure 1** displays the 10 ACE categories, organized in three domains.

ADVERSE CHILDHOOD EXPERIENCES

Abuse

1. Physical,
2. Emotional, or
3. Sexual

Neglect

4. Physical or
5. Emotional

Household challenges (originally phrased as "household dysfunction"; reframed by the CDC in 2015), caused by having a household member who:

6. Experienced mental illness
7. Used substance(s)
8. Experienced intimate partner violence (initially queried as violence towards the mother or stepmother)
9. Was absent because of divorce or separation, or
10. Was incarcerated

Figure 1. The 10 ACE categories investigated in the landmark study by the CDC and Kaiser Permanente. Image reproduced with permission from ACEs Aware,[26] which adapted this with permission from the Robert Wood Johnson Foundation.

Three key findings from the substantial body of ACEs research published over the last two decades are summarized below.

1. ACEs are highly prevalent.

Nearly two-thirds of respondents in the CDC/Kaiser study reported at least one ACE and one in eight reported four or more ACEs.[3-5] In subsequent and more generally representative studies, ACEs have been found to be even more common—approximately one in six individuals have reported four or more ACEs.[15,16] For example, in a recent report on results from the 2011-2014 Behavioral Risk Factor Surveillance System (BRFSS) survey of 214,157 adults from 23 states, 61.6% reported at least one ACE and 15.8% reported four or more.[15] These findings represent the largest US sample queried to date on ACEs. Of note, the BRFSS utilizes questions about eight of the original 10 ACE criteria (those on abuse and household challenges, but neither type of neglect).

In California, ACEs are just as prevalent as they are nationally: **62.3%** of California adults have experienced at least one ACE, and **16.3%** have experienced four or more ACEs (2011-2017 BRFSS aggregated data).[27] The most commonly reported ACEs in California are verbal or emotional abuse (30.4%) and household substance use (28.2%). While ACEs are common in all populations, adults enrolled in California's Medicaid program (Medi-Cal) are 1.3 times as likely to report having experienced four or more ACEs, compared to those with employer-based or private insurance. Among Medi-Cal enrollees, 68.7% have experienced at least one ACE, and 22.8% have experienced four or more ACEs.[27]

2. ACEs are strongly associated, in a dose–response fashion, with some of the most common, costly, and serious health conditions, including nine of the 10 leading causes of death in the United States (US, Figure 2, Table 1), as well as earlier death.[2,16,17,28–30]

While data on adults is better known, in recent California population-based data on five of the original 10 ACEs (household mental illness, substance abuse, domestic violence, parental incarceration, and parental death,* separation, or divorce), publicly insured children in California exposed to two or more ACEs were 2.6 times as likely to have a chronic health condition as those with no ACEs (34.6% with two or more ACEs; 13.2% without ACEs, National Survey of Children's Health, 2016-2018).[32] (*Parental death was not included in the original ACE study, but here is combined with parental absence due to separation or divorce.) See **Appendix A** for more information on the three population-based surveys used to gather information on ACEs in California.

High doses of cumulative adversity experienced during critical and sensitive periods of early development, without adequate buffering protections of safe, stable, and nurturing relationships and environments, can become "biologically embedded." The subsequent biological changes are known as the "toxic stress response," which refers to "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."[23] While the term "toxic stress" was originally coined by the National Scientific Council on the Developing Child[33] to describe the developmental changes associated with prolonged adversity in a policy context, it is now recognized that the accumulated changes to the physiologic stress response system, as well as brain and other organ system development, represent a health condition with clinical implications.[6-12] These changes include disruptions in brain development and function of the neuro-endocrine-immune-metabolic axes, acting through epigenetic (or genetic regulatory) mechanisms that can be transmitted to the next generation (for further details, see the next two sections, **The Biology of Toxic Stress** and **Intergenerational Transmission of Adversity**).[6-12]

Cumulative adversity is also associated with poorer educational and social outcomes, including learning, developmental, and behavior problems, high school noncompletion, unemployment, poverty, and felony charges—many of which can serve as additional vectors for the intergenerational transmission of

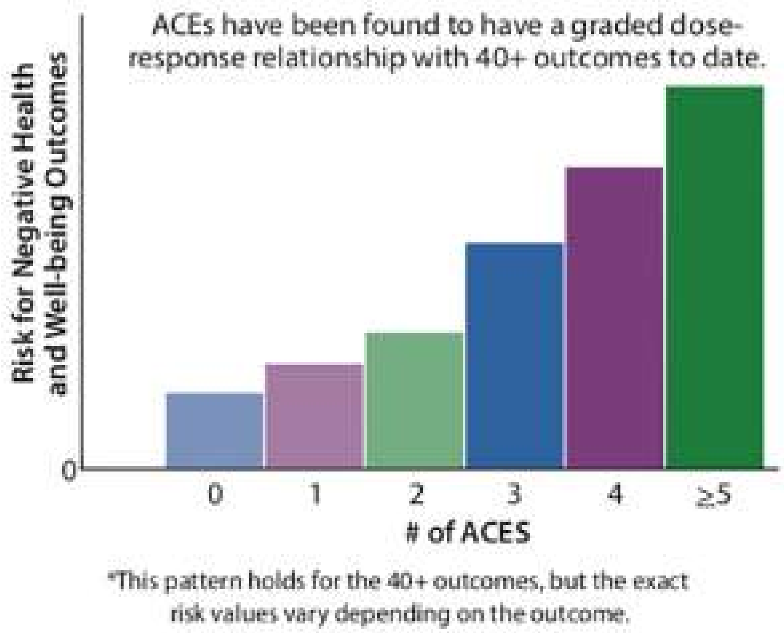


Figure 2. *There is a dose-response relationship between the number of ACE categories experienced and successively increasing risk of numerous negative health and social outcomes. Image reproduced from the CDC.*[31]

adversity.[2,16,17,34-40] Fortunately, exposure to ACEs does not always lead to toxic stress. The presence of protective factors, like buffering relationships, environments, and interventions, timing of risk and protective factors, and individual differences in biological susceptibility, can alter the risk of toxic stress and related health and social sequelae.[41-47]

3. While ACEs affect all communities, some populations are affected disproportionately.

The original ACE Study was conducted in a population that was largely White, college-educated, middle class, and privately insured.[3,4] Subsequent studies have found a higher prevalence of ACEs among groups who are racially marginalized (Black, Latinx, Native American, or multiracial), non-high school graduates, unemployed or unable to work, in lower income brackets, uninsured or underinsured, involved in the justice system, women, and/or identify as lesbian, gay, or bisexual.[10,13-22]

Social and structural inequities disproportionately concentrate ACEs, toxic stress, their precursors, and their consequences in racially, socially, and economically marginalized communities. Such contexts can exacerbate the impacts of ACEs and toxic stress and reduce access to buffering resources. Given California's diverse

Leading causes of death in the US, 2017	Odds ratios for ≥4 ACEs (relative to no ACEs)
1. Heart disease	2.1
2. Cancer	2.3
3. Accidents (unintentional injuries)	2.6
4. Chronic lower respiratory disease	3.1
5. Stroke	2.0
6. Alzheimer's disease or dementia	11.2
7. Diabetes	1.4
8. Influenza and pneumonia	unknown
9. Kidney disease	1.7
10. Suicide (attempts)	37.5

Table 1. *Association of ACEs with leading causes of death in the US.*
Source of causes of death: CDC (2017)[28]
Sources of odds ratios: Hughes et al. (2017)[2] *for 1, 2, 4, 7, 10; Petrucelli et al. (2019)*[30] *for 3 (injuries with fracture), 5; Center for Youth Wellness (2014)*[17] *for 6; Center for Youth Wellness (2014)*[17] *and Merrick et al. (2019)*[16] *for 9*

demographic profile, these social and structural factors are critically important to recognize and address in deploying a statewide strategy for toxic stress mitigation. The majority (63.2%) of Californians identify as non-White.[48] Over a third of Californians (35.2%) are considered poor or near poor, earning 150% or less than California's living wage, by the California Poverty Measure (CPM, 2018), which accounts for the state's cost of living and family needs.[49] In California, poverty is most prevalent among Black, Latinx, and Native American families, and families with children—18.8% of families with children (compared to 17.6% of Californians in general) lacked sufficient resources to meet basic needs, earning less than $34,200 for a family of four.[49]

Families living in poverty are more likely to experience ACEs and other adversities and are less likely to have access to the individual and community resources necessary to prevent ACEs from leading to toxic stress.

Many Californians are also recent immigrants, with 26.9% being foreign-born (compared with 13.5% nationally) and 44.1% speaking a language other than English at home (compared with 21.5% nationally).[48,49] While diversity is a rich strength of California, it presents unique challenges. Immigrant communities face a higher rate of poverty, concomitant stressors like harrowing migration experiences,

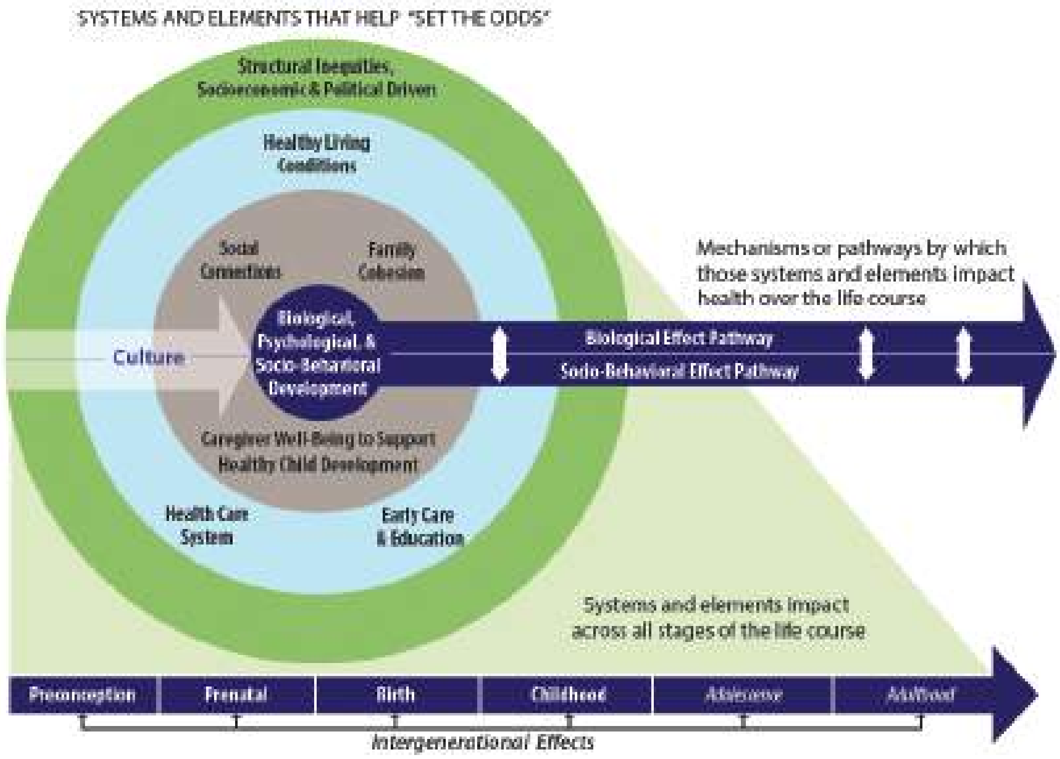


Figure 3. Multi-layered structural and contextual factors that influence life course health. Reproduced with permission from the National Academies of Sciences, Engineering, and Medicine (NASEM, 2019), courtesy of the National Academies Press, Washington, D.C.[23]

and reduced access to buffering supports, such as familiar medico-legal systems and family or community support networks left behind in the country of origin. Additionally, immigrants may have less familiarity with and access to specific local resources needed to buffer ACEs and toxic stress, including healthcare, cross-sector linkages, and social supports.[50-52]

We also know that the original 10 categories of ACEs are not the only sources of early or recurrent stress and adversity that are relevant for setting the odds for life course health and well-being (see **Figure 3**). They were simply the most common in the CDC/Kaiser Permanente population under study. Some of the other adversities that may be additional risk factors for toxic stress include: exposure to racism, sexism, poverty, food and housing insecurity, interpersonal and community violence, bullying, death of a family member, and justice system involvement.[2,53-61] Recognizing these additional risks is important since they often co-occur with ACEs, contribute to their prevalence, and can exacerbate their impacts. It is also crucial to understand and address the ways in which these factors may compound the cumulative dose of adversity and reduce caregivers' ability to provide safe, stable, and nurturing relationships and environments, particularly given the disproportionate burden of ACEs in marginalized communities.

The literature exploring these potential risk factors for toxic stress and their long-term sequelae is less standardized than that for the 10 original ACEs, and it is important to note that the odds ratios for risk of acute and chronic health conditions cannot simply be extrapolated to communicate the health impacts of these additional factors. However, these factors are important for health and well-being — and are correlated with poorer health outcomes. The evidence on whether and to what extent they act via the toxic stress pathway versus other biological pathways is still being built (see **The Biology of Toxic Stress**). Thus, for mechanistic clarity, we will term these factors "additional risk factors for toxic stress," rather than ACEs, and discuss them under this label, where appropriate.

In sum, severe, frequent, and/or chronic adversity in childhood, in the absence of sufficient buffering factors, is a root cause of the most prevalent, debilitating, and costly health conditions in California. Acting through the toxic stress pathway, these childhood adversities also perpetuate and exacerbate socially rooted inequities in health, achievement, socioeconomic mobility, and mortality for generations to come.[16,29,35,36,60,62] ACEs and toxic stress are very common, highly consequential for health and well-being, and costly to society. They represent an acute and under-addressed public health crisis of our era.[2,13,63,64] The time to act on this crisis is now.

The Biology of Toxic Stress

Scientific progress over the past several decades has allowed researchers to characterize, with greater precision than ever before, the extent to which our experiences and environments shape our biology. Advances in functional neuroimaging, developmental neurobiology, genomics, epigenomics, transcriptomics, proteomics, and metabolomics have begun to decode the complex mechanisms by which early adversity can become biologically embedded and influence life-course health and even the health of the next generation.

The growing body of evidence linking environmental factors, including social and economic conditions, to immediate and long-term health outcomes allows healthcare providers and public health systems to better serve patients and communities. Demystifying the root causes of illness and behavior can lead to more targeted clinical and policy interventions as well as greater compassion, patience, and the opportunity for relational healing through caring relationships. Across the healthcare landscape, modern **precision medicine** approaches and technologies are facilitating targeted prevention, pinpoint diagnostics, and individually tailored therapies.[65] At the cutting edge, the research community continues to deliver strong evidence that individuals with Adverse Childhood Experiences (ACEs) and likely toxic stress are at much higher risk for health and social challenges for decades to come, and that increased risk may be passed down to subsequent generations. What follows is an overview of scientific studies describing the biological mechanisms by which early adversity, through the toxic stress response, affects health.

Stress is defined as a "real or interpreted threat to the physiological or psychological integrity of an individual which results in physiological and/or behavioral responses."[66] Stressors include experiences as diverse as navigating a new environment, running a marathon, witnessing violence, or enduring a physical injury. The body reacts to stress via a complex process of physiological and behavioral adaptation known as **homeostasis**, which allows biology to remain within physiologic parameters necessary for life.[67] An example of homeostasis is the activation of perspiration and thirst as body temperatures rises on a hot day. These responses serve to cool the body and maintain temperatures within a preset normal range.

More recently, the term **allostasis**[66] was developed by McEwen and colleagues in recognition that certain circumstances result in physiological adaptations that result in new biological set points that may be temporary or permanent. An example of allostasis is the many hormonal and physiologic changes associated with lactation when an infant is born. In response to the birth of the child, the mother's body establishes and maintains new biological set points necessary to support milk production and infant feeding. The energy required to achieve allostasis is known as **allostatic load**.[67]

In response to a stressor, the body releases stress hormones, including adrenaline (also known as epinephrine) and cortisol, that activate a range of biological responses: heart rate and blood pressure increase, brain structures associated with threat and vigilance become more active, aspects of learning and memory are altered, and the parts of the brain that facilitate impulse control, judgment, and executive function become less active.[68-72] Blood is more efficiently channeled to the parts of the brain, organs, and muscles involved in the fight-or-flight response.[73] Elsewhere in the body, respiration and immune activity increase, digestion slows, and the reproductive system nearly shuts down completely.[74] These responses are essentially identical in mammals, birds, fish, and reptiles, and are central to surviving the types of stressors typically experienced by organisms, namely short-term, physical emergencies. Humans, in contrast, activate the same physiological responses during acute or chronic, non-physical, psychosocial stress.

As the crucial concept in the field, when the stress response is activated too frequently, intensely, or chronically, allostasis may occur, resulting in new biological set points being "wired" as an adaptation to respond to stressful environments. The stress response, which is life-saving when activated in the short term, as in most organisms, becomes health-damaging when activated chronically, producing a state of pathologically heavy allostatic load.[75-77] For example, in the short term, stress hormones increase blood pressure, which can bring greater blood flow to muscles to save an animal sprinting for its life, but when activated chronically, can lead to increased wear and tear on blood vessels and damage to the cardiovascular system.

WHAT IS "TOXIC STRESS"?

The biological stress response has been characterized as falling into three types: positive, tolerable, and toxic (see **Figure 4**).[78] Not all stress is bad. Some stress is a necessary and even essential part of growth and development; it can help us transiently mobilize energy and increase focus to perform better at the task at hand, such as an upcoming test, the big game, or a presentation at work. The **positive stress response** is characterized by brief elevations in stress hormones, heart rate, and blood pressure in response to a routine stressor. The **tolerable stress response** "activates the body's alert systems to a greater degree as a result of more severe, longer-lasting difficulties, such as the loss of a loved one, a natural disaster, or a frightening injury. If the activation is time-limited and buffered by relationships with adults who help the child adapt, the brain and other organs recover from what might otherwise be damaging effects."[79]

The **toxic stress response** is defined by the National Academies of Science, Engineering, and Medicine's (NASEM) 2019 consensus report 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... For children, the result is the disruption of the development of brain architecture and other organ systems and an increase in lifelong risk for physical and mental health disorders."[23]

Adversity experienced during the prenatal or early life periods, without adequate buffering protections of safe, stable, and nurturing relationships and environments, can alter the biological stress response, disrupt the development of neuro-endocrine-immune-metabolic and genetic regulatory mechanisms, and lead to toxic stress, thus increasing risk for poor health.

The term toxic stress is often mistakenly used to refer to the drivers of stress or the stressors. In fact, toxic stress refers to the dysregulated biological stress response and the concomitant long-term changes in physiology (**Figure 5a,b**).[6-12,23] Frequent, chronic, or intense stress in a child's environment may tip the balance

TOXIC STRESS RESPONSE

The toxic stress response is defined by the National Academies of Science, Engineering, and Medicine's (NASEM) 2019 consensus report 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... For children, the result is the disruption of the development of brain architecture and other organ systems and an increase in lifelong risk for physical and mental health disorders."[23]

CRITICAL PERIOD

A time in development when the presence or absence of an experience results in irreversible change.[83,84]

SENSITIVE PERIOD

A time when the brain is particularly responsive to a stimulus in the environment.[84]

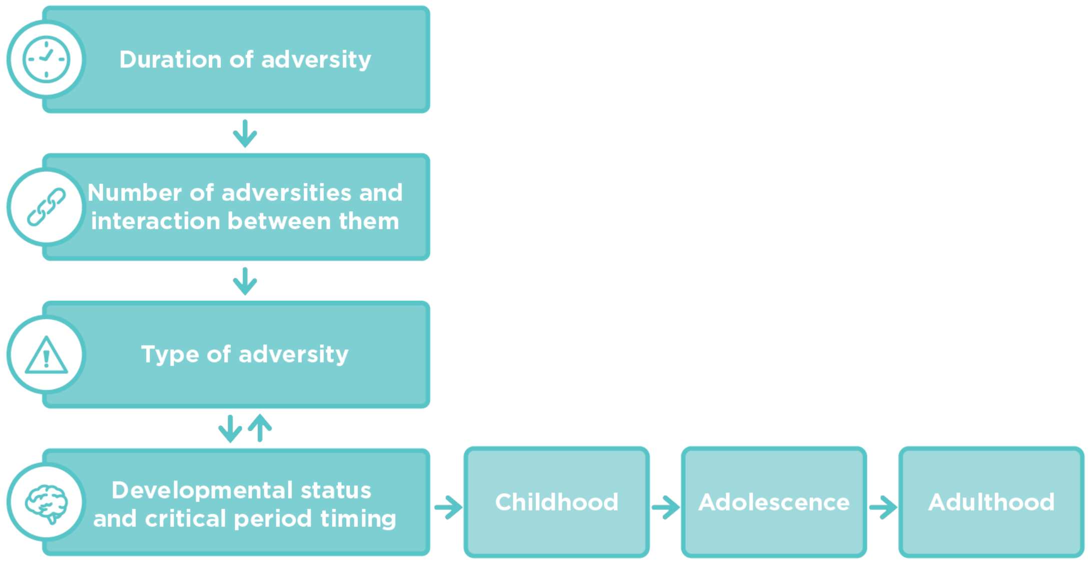
STRESS RESPONSE

POSITIVE	TOLERABLE	TOXIC
Physiological response to mild or moderate stressor	**Adaptive response to time-limited stressor**	**Maladaptive response to intense and sustained stressor**
Brief activation of stress response elevates heart rate, blood pressure, and hormonal levels	Time-limited activation of stress response results in short-term systemic changes	Prolonged activation of stress response in children disrupts brain architecture and increases risk of health disorders
Homeostasis recovers quickly through body's natural coping mechanisms	Homeostasis recovers through buffering effect of caring adult or other interventions	Prolonged allostasis establishes a chronic stress response
Tough test at school, playoff game	***Immigration, natural disaster***	***Abuse, neglect, household dysfunction***

Figure 4. *Stressors such as homework and training in team sports are normative, even positive experiences, and help build adaptive capacities that result in resilience. Tolerable stressors may occur due to early experiences such as moving, routine family hardship, and in some cases, natural disasters. These are time-limited and, with enough positive support, are able to be overcome. Toxic stress may arise due to ACEs or significant stressors such as exposure to discrimination or poverty that are not sufficiently buffered by a positive supportive environment and other interventions. Figure reproduced with permission from Elsevier.*[6]

from the positive or tolerable stress response to a toxic stress response, leading to stress-related disease and cognitive impairment.[3,6] While the term "toxic stress" was originally coined by the National Scientific Council on the Developing Child[33] as a means to describe the developmental changes associated with prolonged adversity in a policy context, it is now recognized that the accumulated changes to the physiologic stress response system, as well as brain and other organ system development, represent a health condition with clinical implications.[6-12,80]

Children are especially susceptible to effects of adversity because their brains and bodies are developing, that is, laying a foundational architecture for a lifetime of health and experiences. Critical and sensitive periods of development mark distinct and time-limited periods when children's growth and maturation is, respectively, dependent on or heavily influenced by interactions with the environment and people around them.[81,82] A **critical period** is a time in development when the presence or absence of an experience results in irreversible change.[83,84,1608,1609] Binocular vision (the ability of the brain to consolidate input from the two eyes into a single,



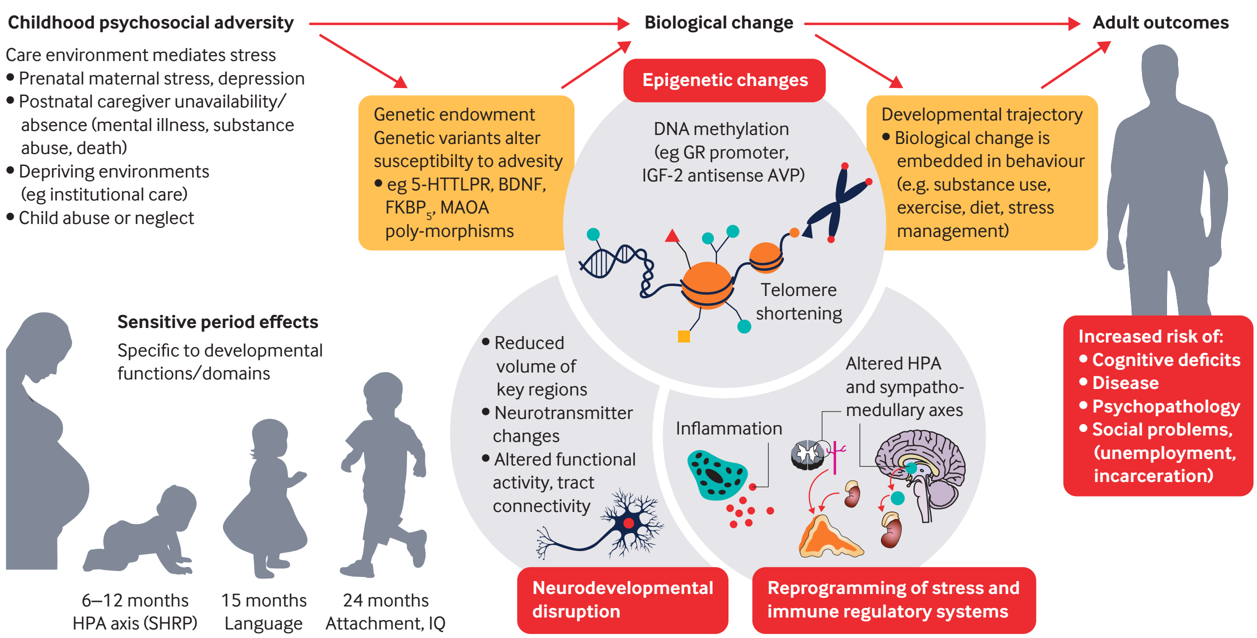


Figure 5a,b. *A depiction of how childhood adversity (important variables include: duration, number, interactions, and types) interacts with an individual's genetic endowment and developmental trajectory to lead to a variety of biological changes called the toxic stress response, including neuro-endocrine-immune-metabolic and genetic regulatory disruptions, to increase risk for lifelong health and social problems. Reproduced under a creative commons open access license from The BMJ.*[103]

integrated, three-dimensional picture) is an example of a developmental process that has a critical period. If a child has misalignment of one or both eyes that is not corrected within a specific window of time (typically by age eight), then the ability of the brain to form a 3-D image from ocular inputs is lost, even if the eye alignment is subsequently corrected. Similarly, a **sensitive period** is a time when the brain is particularly responsive to a stimulus in the environment.[23,84] Unlike critical periods, the window doesn't entirely close at the end of the sensitive period, but the brain's responsiveness diminishes significantly. Language acquisition is an example of a developmental process that has a sensitive period. Learning a new language happens more quickly and with less effort in early childhood due to high levels of neuroplasticity in the brain centers governing language, but the ability to acquire new languages does continue throughout life, albeit at a reduced level. Experiencing adversity during critical and sensitive periods is therefore more likely to lead to long-term changes in epigenetics, neurophysiology, endocrine systems, immune function, metabolism, and other biological systems.

The more ACE categories to which a person is exposed, the more likely it is that they will develop a toxic stress response and that health conditions also known as ACE-Associated Health Conditions (AAHCs) will develop earlier on and more severely than if the individual had not been exposed. These conditions include cardiovascular disease, chronic obstructive pulmonary disease (COPD), liver disease, cancer, diabetes, obesity, cognitive impairments, risky sexual behaviors, early and high-risk substance use, depression, suicidality, poor self-rated health, and premature mortality.[2-5,13,16,29,30,63,64,85] The list of currently understood AAHCs for adult and pediatric patients in presented in **Tables 2** and **3**.

Cumulative adversity is also associated with poorer educational and social outcomes, including learning, developmental, and behavior problems, high school noncompletion, unemployment, low life satisfaction, poverty, and felony charges—many of which can serve as additional vectors for the intergenerational transmission of adversity.[2,16,17,34-40]

It is important to note that ACE exposure alone does not determine or foretell an individual's future health or life outcomes. Rather, the risks associated with ACE exposure are modulated by multiple factors, such as biological susceptibility, which includes genetic material inherited from one's parents, and protective factors, such as supportive relationships, environments, and community resources.[36,41-46,87] One example of biological susceptibility is the presence of several versions of the serotonin transporter gene, which control the concentration of the neurochemical serotonin, which is important for mood, reward, and learning. Those with one form of the gene are more likely to develop psychopathology, such as depression, after stressful situations than those with a different version of the gene.[88-95]

ACE-Associated Health Conditions: Pediatrics

Symptom or Health Condition	For ≥ X ACEs (compared to 0)	Odds Ratio
Asthma	4	1.7 - 2.8
Allergies	4	2.5
Dermatitis and eczema	3*	2.0
Urticaria	3*	2.2
Increased incidence of chronic disease, impaired management	3	2.3
Any unexplained somatic symptoms (eg, nausea/vomiting, dizziness, constipation, headaches)	3	9.3
Headaches	4	3.0
Enuresis; encopresis	–	–
Overweight and obesity	4	2.0
Failure to thrive; poor growth; psychosocial dwarfism	–	–
Poor dental health	4	2.8
Increased infections (viral, URIs, LRTIs and pneumonia, AOM, UTIs, conjunctivitis, intestinal)	3*	1.4 - 2.4
Later menarche (≥ 14 years)	2*	2.3
Sleep disturbances	5**	PR 3.1
Developmental delay	3	1.9
Learning and/or behavior problems	4	32.6
Repeating a grade	4	2.9
Not completing homework	4	4.0
High school absenteeism	4	7.2
Graduating from high school	4	0.4
Aggression; physical fighting	For each additional ACE	1.9
Depression	4	3.9
ADHD	4	5.0
Any of: ADHD, depression, anxiety, conduct/behavior disorder	3	4.5
Suicidal ideation		1.9
Suicide attempts	For each additional ACE	1.9 - 2.1
Self-harm		1.8
First use of alcohol at < 14 years	4	6.2
First use of illicit drugs at < 14 years	5	9.1
Early sexual debut (<15-17 y)	4	3.7
Teenage pregnancy	4	4.2

Table 2. *ACEs are associated in a dose-response fashion with many leading causes of poor health in children; the odds ratios represent data on health risks in those with four or more ACEs, relative to those with none. Reproduced with permission from ACEs Aware.*[86]

Accumulating positive experiences during childhood can buffer the developing brain and body from the harmful effects of stress—in other words, they build resilience.[42,96,97] **Resilience** is the ability to withstand or recover from stressors, and results from a combination of intrinsic factors, extrinsic factors (like safe, stable, and nurturing relationships with family members and others), and predisposing biological susceptibility.[42,98,99] Of note, while the term resilience is often considered in the mental health and behavioral domains, scientific advances in understanding of the impact of stress on neuro-endocrine-immune-metabolic and genetic regulatory

ACE-Associated Health Conditions: Adults

Symptom or Health Condition	Odds Ratio (excluding outliers)
Cardiovascular disease (CAD, MI, ischemic heart disease)	2.1
Tachycardia	≥ 1 ACE: 1.4
Stroke	2.0
Chronic obstructive pulmonary disease (emphysema, bronchitis)	3.1
Asthma	2.2
Diabetes	1.4
Obesity	2.1
Hepatitis or jaundice	2.4
Cancer, any	2.3
Arthritis (self-reported)	3 ACEs, HR: 1.5 ≥ 1 ACE: 1.3
Memory impairment (all causes, including dementias)	4.9
Kidney disease	1.7
Headaches	≥ 5 ACEs: 2.1
Chronic pain, any (using trauma z-score)	1.2
Chronic back pain (using trauma z-score)	1.3
Fibromyalgia	≥ 1 ACE: 1.8
Unexplained somatic symptoms, including somatic pain, headaches	2.0 - 2.7
Skeletal fracture	1.6 - 2.6
Physical disability requiring assistive equipment	1.8
Depression	4.7
Suicide attempts	37.5
Suicidal ideation	10.5
Sleep disturbance	1.6
Anxiety	3.7
Panic and anxiety	
Post-traumatic stress disorder	4.5
Illicit drug use (any)	5.2
Injected drug, crack cocaine, or heroin use	10.2
Alcohol use	6.9
Cigarettes or e-cigarettes use	6.1
Cannabis use	11.0
Teen pregnancy	4.2
Sexually transmitted infections, lifetime	5.9
Violence victimization (intimate partner violence, sexual assault)	7.5
Violence perpetration	8.1

Table 3. *ACEs are associated in a dose-response fashion with many leading causes of poor health in adults; the odds ratios represent data on health risks in those with four or more ACEs, relative to those with none. Reproduced with permission from ACEs Aware.*[86]

health compel advancement of the definition of resilience to also include these domains as well.

A nurturing parent or caregiver is a critically important resilience factor for children, turning potentially toxic stress into tolerable stress.[41,43,44,46,100] Other factors that reduce the likelihood of developing a toxic stress response include freedom from discrimination, supportive friend networks, safe neighborhoods, and community resources, like access to high-quality healthcare, nutrition, and child care.[45,101] At the molecular level, resilience arises from a combination of neural, hormonal, immune, metabolic, epigenetic, and genetic factors that interact with environmental influences and foster an individual's ability to adapt in a healthy manner. In order to determine why some individuals are less sensitive to stress than others, researchers have sought methods to peer more deeply into biological mechanisms and observe the inner workings of the cell and other biological systems to, in the metaphor often used, "get underneath the skin" in understanding how ACEs lead to AAHCs.[102] These mechanisms by which toxic stress is embedded in the functioning of different organ systems, and how those processes affect health and behavior, are discussed below (**Figure 5**, **Table 4**).

TOXIC STRESS: NEUROLOGIC, NEUROENDOCRINE, AND NEUROPSYCHIATRIC EFFECTS

HPA and SAM axes

We react to perceived threats with the fight-flight-or-freeze response—preparing our bodies to be able to take action to oppose danger by running away, or remaining in place to challenge the threat. Most of the biological reactions that facilitate these normal responses are driven by two main systems: the sympatho-adreno-medullary (SAM) axis, which makes the stress hormone adrenaline and hypothalamic-pituitary-adrenal (HPA) axis, which makes the stress hormone cortisol. These circuits originate in the brain and are essential for adaptive biological responses. Both the HPA and SAM systems are normally active at baseline levels, but in response to stress, activity intensifies. When activated too frequently or for too long, these systems can become dysregulated.

When the SAM axis is activated, the sympathetic nervous system (SNS), which connects to nearly all the organs in our body, directly releases the neurochemical noradrenaline (also known as norepinephrine), causing the adrenal glands to release adrenaline (also known as epinephrine). These chemicals typically act within seconds to minutes. The release of adrenaline rapidly and systemically prepares multiple organ systems to fight or to flee a threat by enhancing alertness, increasing heart rate, blood pressure, and respiration, funneling oxygenated blood and cellular fuel to the brain and skeletal muscles in the arms and legs, increasing immune activation, and temporarily pausing non-essential functions, including suppressing appetite and reproductive drive.[74,104-106] Briefly, the HPA axis is activated when multiple brain regions identify a threat. The hypothalamus responds by releasing corticotropin-releasing hormone (CRH), which triggers the pituitary gland to release adrenocorticotropic hormone (ACTH), which, in turn, stimulates the adrenal glands to release cortisol, which works over hours to days. During stressful episodes, cortisol triggers the liver, fat cells, muscles, and

System	Mechanism(s)	Health Impact
Neurologic; neuroendocrine	Dysregulation of the sympatho-adren-medullary (SAM) and hypothalamic-pituitary-adrenal (HPA) axes, with long-term changes in regulation of key hormones, including cortisol and adrenaline; autonomic imbalance	Difficulty modulating, sustaining, or dampening the stress response; heightened or blunted stress sensitivity
	Altered reactivity and size of the amygdala	Increased fear responsiveness, impulsivity, and aggression
	Inhibition of the prefrontal cortex	Impaired executive function, with poorer planning, decision-making, impulse control, and emotion regulation
	Hippocampal neurotoxicity	Difficulty with learning and memory
	Ventral tegmental area (VTA) and reward processing dysregulation	Increased risky behaviors and risk of addiction
Immunologic; inflammatory	Increased inflammatory mediators and markers, especially of the Th2 response; inhibition of anti-inflammatory pathways; gut microbiome dysbiosis	Increased risk of infection, auto-immune disorders, cancers, chronic inflammation; cardiometabolic disorders
	Changes in growth hormone, thyroid hormone, and pubertal hormonal axes	Changes in growth, development, basal metabolism, and pubertal events
Endocrine; metabolic	Changes to leptin, ghrelin, lipid and glucose metabolism, and other metabolic pathways	Increased risk of overweight, obesity, cardiometabolic disorders, and insulin resistance
	Sustained changes to the way DNA is read and transcribed	Mediates all aspects of the toxic stress response
Epigenetic; genetic	Sustained changes to the way DNA is read and transcribed	Mediates all aspects of the toxic stress response
	Telomere erosion, altered cell replication, and premature cell death	Increased risk for disease, cancer, and early mortality

Table 4. *Biological systems disrupted by toxic stress.*

the pancreas to increase blood sugar levels available to the brain and skeletal muscles, which boosts energy levels and readies the body to respond to a threat. Cortisol also increases blood pressure and cardiac output, while suppressing sleep, immune, reproductive, and growth functions.[74] The fact that most human cells are sensitive to cortisol helps explain the wide-ranging impacts of the hormone on the body during normal times, including on metabolism, immune and inflammatory mechanisms, reproductive function, cognition, mood, sleep and wakefulness, and motivation.

When fight or flight is not possible, the freeze response may be employed. The freeze response can consist of either "playing dead," which involves dissociating and/or fainting, conserving energy and releasing endogenous opioids, or a "frozen stiff" state, which involves heightened awareness with an inability to move.[107,108]

Normal regulation of the stress response works much like a thermostat, in which increasing levels of adrenaline and cortisol trigger the brain to turn off the stress response in a process called feedback inhibition, just as a thermostat turns off the heat when the desired temperature is reached. Thus, homeostasis is restored.

However, chronic stress not only activates the stress response repeatedly, but gradually impairs feedback inhibition, compromising an organism's capacity to recover back to baseline after a stressor.[75-77] For example, exposure to ACEs and other adversities may be associated with reduced responsiveness of the brain to the hormones cortisol (glucocorticoid resistance) and adrenaline. This occurs when prolonged exposure to these hormones causes brain cells to reduce the number and effectiveness of the receptors where these hormones bind: the glucocorticoid receptors that bind cortisol and the β-2 adrenergic receptors that bind adrenaline and noradrenaline. Glucocorticoid resistance makes cells less responsive to cortisol, which impairs negative feedback. Glucocorticoid resistance is involved in many of the diseases associated with toxic stress, such as obesity,

IMMEDIATE RESULTS OF THE STRESS RESPONSE

- Central nervous system: Vigilance, changes in cognition and decision-making
- Cardiopulmonary: Increased respiration, heart rate, blood pressure, oxygenation, and blood flow to brain and skeletal muscles
- Metabolism: Mobilization of stored energy, increased blood sugar, insulin resistance, and shutdown of processes like digestion, growth, and reproduction
- Immune: In early stages (autonomic nervous system), increased inflammation to fight pathogen(s); in later stages, decreased inflammation to rebalance the system

type 2 diabetes, and heart disease.[109,110] Persistently abnormal levels of cortisol and adrenaline alter cell and tissue functions in ways that increase cellular aging and heighten health risks.[10,111-114]

Toxic stress is associated with increased risk for numerous neuropsychiatric disorders, including post-traumatic stress disorder (PTSD), depression, anxiety, substance abuse, attention-deficit/hyperactivity disorder (ADHD), Alzheimer's disease and other dementias, and chronic pain.[39,115-120] While the causes of neuropsychiatric disorders are numerous and complex, changes to the brain's threat response, impulse control, motivation and reward pathways, and pain perception mechanisms are associated with toxic stress and are believed to contribute to these risks. It is important to highlight that although neuropsychiatric disorders are among the most widely recognized manifestations of toxic stress, there is wide variation in which health conditions specific individuals may experience as a result of toxic stress. For example, some experience only immune, metabolic, or endocrine consequences of toxic stress, without any diagnosable neuropsychiatric conditions. Clinical outcomes depend on a complex interplay of predisposing biological factors, genetic and epigenetic makeup, timing and duration of exposures, and buffering factors. These effects can also interact synergistically with those of other toxic exposures (see **LEAD TOXICITY**).

Toxic stress is also associated with structural and functional changes in brain architecture, including many brain regions, such as the amygdala (which governs fear and emotion), hippocampus (memory), prefrontal cortex (executive function), and mesolimbic dopamine system (reward and motivation).[77,121-123] The amygdala, with its role in threat detection, fear, and anxiety, has been measured to be larger and more active in people who exhibit anxiety due to experiencing early childhood adversity. By contrast, the hippocampus and prefrontal cortex have been documented in functional neuroimaging studies to be smaller and less active in individuals with a history of ACEs, and these changes are associated with difficulty with learning, memory, attention, impulse control, and executive functioning.[122,124-135] Further, in toxic stress, the reward system, including the nucleus accumbens, the ventral tegmental area, and the neurochemical receptors for dopamine and noradrenaline (from the SAM system), can change in complex ways.[136-141] One such change is a reduction in dopamine signaling, leading to less intrinsic motivation to perform routine activities, which also become less rewarding, with a predisposition toward mood disorders like depression.[142-152] These changes in reward circuitry may also increase the likelihood of engaging in risky behaviors such as substance use.[142,143,153-157] Because the experiences of reward and motivation can be blunted with early life adversity, it may take more intrinsically motivating factors (such as substance use) to produce a rewarding response. Following childhood adversity, the pain and emotional control circuitry of the brain may be sensitized to respond more intensely to threatening stimuli, including perceived pain.[158-160] The combination of greater awareness of pain due to changes in specific circuits and hypersensitivity in its perception due to changes in other circuits results in consequences such as increased susceptibility to acute and chronic pain disorders.[161-168]

TOXIC STRESS: IMMUNE AND INFLAMMATORY EFFECTS

Toxic stress is associated with immune dysregulation, which can involve either under-activation or over-activation of components of the immune system. These changes can affect both innate (nonspecific) and acquired (specific) immunity.[175-179]

LEAD TOXICITY

Lead is an example of a specific environmental exposure that interacts with the toxic stress response, in that the effects of lead exposure are more powerful in children who are experiencing toxic stress, and vice versa. Lead exposure disrupts a child's ability to recover from early life stress. Both animal and human studies have identified toxic stress and lead as affecting shared neurobiological systems, including the hypothalamic-pituitary-adrenal (HPA) axis, as well as the frontal cortex and hippocampus (parts of the mesocorticolimbic system). Exposure to lead in early life can result in potentially lifelong alterations in the HPA axis and accentuate physiologic responses to stress.[169]

Exposures to both lead and toxic stressors (like ACEs) together result in enhanced neurotoxicity.[170] Exposure to lead also acts synergistically with stress during pregnancy and early childhood, and is associated with decreased IQ, increased incidence of attention-deficit/hyperactivity disorder (ADHD), antisocial behavior, preterm birth, lower birth weight, and juvenile justice involvement. Higher levels of maternal self-esteem are associated with decreased levels of ADHD and increased cognitive abilities in children, but higher blood lead levels in children reduce that benefit of high maternal self-esteem.[171-174] After pregnant rats were exposed to both lead and stress, their great-grandchildren were found to have residual changes to their stress-related gene expression and biomarkers.[170] In other words, the third generation, which was never exposed to early adversity or lead, exhibited chemical changes to specific genes that are involved in the stress response. This has implications for intergenerational transmission of adversity without the child having experienced direct adversity. (See the next section, **Intergenerational Impacts of Adversity**, for more details.)

A dysregulated immune system is less efficient at fending off pathogens. Most importantly, stress in and of itself often leads to greater vulnerability to infection and autoimmunity (a condition in which the immune system attacks itself, causing disease).[180,181] Toxic stress affects immune cell function, maturation, and reactivity. Chronic stress alters the response to adrenaline and cortisol signaling in the bone marrow, where immune cells are made, resulting in newly born immune monocytes that are proinflammatory and resistant to cortisol's anti-inflammatory signaling.[182-185] Further upstream, stress can also impact the early establishment of gut bacteria, known as the microbiome, which in turn influences the generation of certain immune cells in bone marrow for essential inflammatory responses.[186,187] An individual may also exhibit oversensitivity to the anti-inflammatory properties of cortisol.[188] As a result, dysregulated immune system activity can cause increased likelihood of inflammatory and autoimmune diseases among people with high ACEs and toxic stress, such as arthritis, asthma, food and seasonal allergies, and eczema, as well as increased vulnerability to infectious pathogens.[45,111,189-191]

Altered immune and inflammatory system function is marked by an increase in biomarkers of chronic inflammation, including C-reactive protein (CRP), interleukin-6 (IL-6), and NF-κB.[176,177,192-194] It is also possible to detect elevated levels of virus antibodies, such as to the Epstein-Barr virus, during episodes of high stress. While viruses can exist in the body in a latent, neutral form that does not lead to symptoms because they are maintained in that state by the immune system, stress can suppress the immune system and reactivate these latent viruses, leading to higher levels of active virus, which also triggers the production of antibodies against the virus.[195,196]

Optimal function of the innate and adaptive immune systems is critical for the body to mount a robust defense to new infections like coronavirus disease 2019 (COVID-19).[197] ***Toxic stress physiology may increase risk of contracting or dying from COVID-19***, either through dysregulation of the immune response and/or through increased burden of AAHCs, which may predispose to a more severe COVID-19 disease course (see COVID-19 AND TOXIC STRESS). For example, stress is a known trigger of inflammation in the lungs, an organ highly impacted by the the novel coronavirus, SARS-CoV-2.[198-201] Stress-induced lung inflammation can impair respiratory function, similar to that seen in patients with asthma, potentially placing individuals with toxic stress at risk of worse outcomes from COVID-19.[202,203] Beyond the direct influence on lung function, stress can specifically exacerbate the progression of viral pulmonary diseases by impairing innate lung tissue defenses against viral infection.[204-206]

Further, those with toxic stress may also be more susceptible to the health effects of acute or chronic stress. Thus, the biological condition of being stress-sensitized also increases the risk of stress-related chronic disease exacerbations related to the numerous stressors (e.g., psychosocial, financial, and grief-related) associated with living through the pandemic. For example, acute stress is associated with changes in endothelial cell function, increased arterial stiffness, vessel wall damage, increased blood viscosity, and/or a hypercoagulable state, all of which promote increased risk of blood clots. These changes can result in increased risk for heart attacks and/or strokes, which have been documented to rise significantly in the months following natural disasters such as earthquakes and hurricanes.[207-216]

One study found that people with the highest rates of stress were nearly six times as likely to become infected by cold viruses and over two and a half times as likely to develop clinical symptoms than people with low levels of stress.[197] Children living in stressful situations are approximately one and a half times more prone to fevers than those in low-stress households.[217,218] People who grew up in families of low socioeconomic status, which is also a risk factor for toxic stress, are also more susceptible to viruses that cause respiratory infections.[219,220] People experiencing high levels of stress also receive less protection from influenza vaccines.[221] One recent national study found that, compared to low-stress controls, people with the highest levels of stress are more likely to die from infections overall (67% increased risk), and are especially likely to die from viral infections (114% increased risk), develop pneumonia (83% increased risk), or have bacterial infections (23% increased risk).[222]

Chronic respiratory diseases like emphysema, bronchitis, and asthma all involve inflammation in the lungs, which can be caused by a combination of factors, including stress, cigarette smoking, genetic susceptibility, and environmental exposures.[223,224] The toxic stress response triggers a pro-inflammatory state and also increases the risk of smoking in a dose–response manner, posing cumulative hazards to respiratory health. For adults with an ACE score of five or higher, the likelihood of ever smoking is more than triple the rate for adults with zero ACEs.[225] Due to additional risk factors for poor lung conditions, including environmental exposures, individuals with ACEs are subject to chronic lung diseases more often, demonstrating synergistic interactions between the inflammatory and neurologic consequences of toxic stress.[186] Even when controlling for smoking behavior, adults with five or more ACEs are more than twice as likely to develop chronic obstructive pulmonary disease (COPD), one of the leading causes of death in the US.[226-228]

Children with four or more ACEs face a 1.7-fold increased risk of asthma, with Latinx children exhibiting 4.5-fold increased risk, compared to those with zero ACEs.[229] Asthma arises from a diverse interplay of factors, involving the gut microbiome, immune and inflammatory system alterations, environmental exposures (see **EARLY ADVERSITY AND EXPOSURE TO POLLUTION**), acute stressors, and changes to the stress response system, including to key receptors.[202,230,231] At the molecular level, early adversity is associated with lower concentrations of the β-2 adrenergic receptor, which is the molecular target of a first-line medication for asthma exacerbations called albuterol, and lower concentrations of the glucocorticoid receptor, targeted by steroid treatments like prednisone. Due to the receptors' downregulation, these standard asthma treatments may be less effective in individuals with ACEs (see **Primary and Secondary Prevention Strategies in Healthcare** and **Tertiary Prevention Strategies in Healthcare**, in Part II, for more information).[230]

Chronic inflammation may heighten the risk of cancer through multiple mechanisms, including increasing the DNA mutation rate and increasing new blood vessel growth (angiogenesis), which funnels nutrients to tumors. Once a cancer has developed, chronic inflammation can promote its transformation and spread by interfering with normal anti-tumor mechanisms, increasing cytokine production, and creating cancer-protective micro-environments.[237-240] Chronic inflammation

EARLY ADVERSITY AND EXPOSURE TO POLLUTION

During the earliest years of life, the lungs are most sensitive to environmental pollutants. Prolonged or extreme exposure to air pollutants can affect pulmonary development, impacting health outcomes throughout childhood and beyond. As the tissues develop, the lungs are especially vulnerable to exposure to particulate matter, such as from smoke, traffic-related air pollution (TRAP), or high concentrations of dust. Exposure to ACEs and the associated dysregulation of the immune system involved in toxic stress can combine with breathing polluted air to exacerbate negative asthma-related outcomes. For example, one study demonstrated that children who lived among high levels of TRAP were at 1.5 times greater risk of developing asthma, but only if their parents reported a high degree of stress, suggesting a concomitant immunological vulnerability from early adversity.[232,233] In childhood, air pollutants and stress interactions are associated with changes in specific inflammatory mediators that can be related to worsened asthma outcomes, including interleukin-5, IgE (the allergic-type antibodies), and eosinophil counts (allergic-type immune cells).[234]

As another example, in utero exposure to both stress and air pollution can increase oxidative stress, which may affect the development of the fetal lungs, including increasing airway inflammation and adverse simplification of the normally complex structure.[235,236] In fact, an increased risk of asthma was found in children co-exposed in utero to fine particulate matter ($PM_{2.5}$) and maternal stress (OR 1.15; 95% CI, 1.03-1.26) during the phase of lung development when many of the peripheral airways important in asthma develop (canalicular phase).

and increased generation of oxygen radicals (also known as oxidative stress), in combination with failure of genetic regulatory mechanisms, can also interfere with the success of some cancer treatments.[237-240] Many cancers are caused by underlying inflammatory changes. For example, studies estimate that 18% of cancers are linked to chronic infection, 30% to smoking, and 35% to dietary factors (14% to 20% specifically to obesity).[241-244] Particulates and carcinogens from cigarette smoke, and other environmental hazards such as asbestos and pollution, lead to chronic inflammation in the lungs and other places in the body.[245] There is growing evidence, as well, that exposure to nicotine during pregnancy or infancy leads to accelerated cellular aging, through epigenetic changes.[246]

TOXIC STRESS: ENDOCRINE AND METABOLIC EFFECTS

The endocrine system consists of a finely tuned internal communications network driven by hormone production, transportation, and negative feedback loops via a network of glands and blood vessels throughout the body. Collectively, hormones coordinate and drive the most essential functions, including metabolism, growth and development, reproduction, and responses to stress, injury, and environmental factors. Stress, infections, disruptions to metabolic activity, and many other circumstances can trigger and exacerbate endocrine disorders, potentially leading to abnormal growth patterns, weight gain or loss, early or delayed puberty, loss of bone mass, reproductive problems, and dysregulation of metabolic processes like energy storage and use, among others.

Metabolic syndrome describes a clustering of health conditions, including high blood pressure, high fasting blood sugar, insulin resistance, excess abdominal fat, abnormal cholesterol, or abnormal triglyceride levels, and it is more likely to occur in people who have experienced adversity during childhood.[247,248] Metabolic syndrome is, in turn, related to increased risk for cardiovascular disease, including heart attacks and ischemic heart disease; cerebrovascular disease, including stroke; type 2 diabetes; and obesity.[249-251] Notably, of all the health costs associated with AAHCs studied to date, cardiovascular disease comprises the greatest share.[63,64] Toxic-stress-related inflammation is one cause for increased risk of metabolic syndrome after adversity. Elevation of one marker of inflammation, IL-6, is correlated with risk of heart attack (myocardial infarction). One study found that people in the highest 25% of IL-6 expression have a 2.3-fold increased rate of heart attack, compared with the lowest 25%.[252] In other studies, people with the highest levels of the inflammatory marker CRP are at 4.4-fold increased risk for heart failure, heart disease, and death, while tumor necrosis factor-alpha (TNF-α) levels are associated with increased risk for heart failure, heart attacks, and small-vessel disease.[250,251,253-255] Cardiometabolic risk is also increased by smoking, lower physical activity, increased body mass index, and increased blood pressure. The first three of these factors are independently associated with a history of ACEs in a dose–response fashion, further increasing cardiometabolic risk for those with toxic stress.[2,3,13,256,257]

Toxic stress also increases risk for obesity and for being overweight.[3] Changes in brain reward signaling pathways, as well as metabolic hormones which govern feeding and hunger cues, may predispose to overconsumption of high-fat, high-sugar foods.[113,258,259] Leptin is a hormone that helps signal satiety or fullness.[260] During the fight-flight-or-freeze stress response, leptin is released acutely. However, following chronic stress, leptin resistance occurs, and the body may not appropriately signal fullness (satiety) after a meal, and this may contribute to overeating.[259,261,262] The production of other appetite- and metabolism-regulating hormones, including neuropeptide Y and ghrelin, has also been measured to be altered following adversity in ways that promote cardiometabolic risk.[263-268]

Type 2 diabetes is caused by dysregulated insulin production by the pancreas and reduced sensitivity (insulin resistance) exhibited by cells throughout the body and brain. Toxic stress can increase risk for these outcomes. Prenatal exposure to major stressors may result in impaired regulation of glucose metabolism.[269-273] Early adversity can reduce the production of insulin, a key hormone needed to regulate glucose levels, resulting in abnormalities in insulin and glucose metabolism.[113,274-278] Moreover, prolonged exposure to glucocorticoids can result in whole-body insulin resistance.[279-283] Stress may even change patterns of insulin secretion intergenerationally, leading subsequent generations to be more susceptible to diabetes.[113,117,269,271] Insulin resistance has been identified as a potential unifying factor for certain mental and physical health problems in individuals who experienced early life adversity. Lipid metabolism can also be disrupted by toxic stress, further increasing metabolic risk—and these changes can be transmitted to future generations.[284,285]

Kidney disease is also a major source of mortality in the US, affecting more than one in seven (37 million) people. People with four or more ACEs are at 1.7-fold increased risk of developing kidney disease (relative to those with zero ACEs).[16,286] Converging risk factors include heart disease, obesity, diabetes, and high blood pressure.[286-289] Several studies have suggested a convergent mechanism for cardiovascular and kidney disease through dysregulation of endothelin-1, which plays a role in blood pressure and arterial stiffness and is activated in response to stress.[290-298]

TOXIC STRESS: EPIGENETIC AND GENETIC EFFECTS

Adversity in early life is associated with changes in how DNA is read and maintained, broadly called the epigenetic landscape, and it is capable of altering the regulation of gene expression that governs multiple biological processes.[299-301] A diverse set of factors attached to DNA, called epigenetic markers, can alter the

BIOMARKERS ASSOCIATED WITH TOXIC STRESS

While there currently exist no widely agreed-upon clinical diagnostic criteria for toxic stress, a number of biomarkers associated with neuro-endocrine-immune-metabolic disruption are under investigation.[332-334] Although the definition continues to be refined, in broad terms, a **biomarker** is "a defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or biological responses to an exposure or intervention, including therapeutic interventions. Molecular, histologic, radiographic, or physiologic characteristics are types of biomarkers."[335] Though this research is still nascent, the biomarkers below have been associated with toxic stress and/or ACEs and may become clues or targets to identify patients at risk for toxic stress and associated poor health outcomes. These biomarkers and the clinical pathways they inform may also offer insight into potential therapeutic targets and precision medicine treatments to ameliorate the impact of toxic stress on health and well-being.[336,337]

Markers of inflammation

- Soluble urokinase plasminogen activator receptor (suPAR); interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α); C-reactive protein (CRP)[194,338-342]

Markers of stress, stress reactivity

- Cortisol: both higher and lower levels of cortisol have been reported in toxic stress[343-346]

Markers of altered metabolism

- Leptin[259,261,341,347]; ghrelin[263,264]; neuropeptide-Y (NPY)[265-268]
- Mitochondrial DNA accumulation[348,349]

Marker of cellular aging

- Telomere length[299,350]

Markers of epigenetic regulation

- Various, including methylation of the serotonin promoter and FκBP-5[313,316,351-353]

While many potential biomarkers for toxic stress have been proposed, few have been fully validated. Fewer have been translated into successful models for use in diagnosis, risk stratification, or assessing treatment efficacy modalities in treating toxic stress or its health complications or subtypes (i.e., metabolic, immune, neuropsychiatric, or endocrine).

way in which genes are transcribed in response to lived experiences; they include DNA methylation, histone post-translational modifications, and small noncoding RNAs.[302,303] Epigenetic markers can arise from environmental influences or may be passed from parent to child via the sperm and egg (paternal and maternal germ lines). Studies using animal models on the effects of early life stress on maternal separation, maternal care quality, and exposure to stressors demonstrate how epigenetic changes may affect offspring behavior and health throughout life.[304-307]

For people with toxic stress, aging faster is not a metaphor; those with six or more ACEs live, on average, almost 20 years less than those with none.

Recent studies suggest that childhood adversity is associated with premature cellular aging, which is measured by proxies such as shortened telomeres and an advanced epigenetic clock (a combination of epigenetic markers that indicate the biological age of cells). Telomeres are regions at the ends of DNA strands that protect them from degradation, and because telomeres are shortened over time, they act as a countdown clock to cellular senescence and death.[301,308] As cells age, their functioning declines.[309] Stress, especially in early and middle childhood, leads to shortened telomeres and premature cellular aging.[12,310-316] Accelerated cellular aging as a component of toxic stress physiology may lead to higher rates of cancer, diabetes, rheumatoid arthritis, lupus, and Alzheimer's disease and other dementias.[317-323] Toxic stress is associated with cognitive decline and other markers of aging.[10,249] For people with toxic stress, aging faster is not a metaphor; those with six or more ACEs live, on average, almost 20 years less than those with none.[29]

It is also known that, in addition to the 10 ACEs, there are other risk factors for toxic stress, such as poverty and racism, that exacerbate these impacts. For example, the top 1% of earners live an average of 14.6 years longer than the bottom 1%; further, White Americans live approximately five years longer than Black Americans, and about 80% of this difference can be attributed to socioeconomic factors.[29,324-328]

Epigenetic changes are driven by life experiences, both positive and negative. While initially thought to be permanent, recent studies provide examples that building resilience and targeted treatments can reverse or prevent negative epigenetic changes resulting from childhood adversity, as well as subsequent biological risks.[329-331] This unique capacity for reversibility of some epigenetic changes offers some hope for epigenetic processes as targets for toxic-stress-specific buffering interventions.

While many potential biomarkers for toxic stress have been proposed, few have been fully validated. Fewer have been translated into successful models for use in diagnosis, risk stratification, or assessing treatment efficacy modalities in treating toxic stress or its health complications or subtypes (i.e., metabolic, immune, neuropsychiatric, or endocrine).

The current status of biological impacts of interventions to regulate toxic stress physiology is presented in **Tertiary Prevention Strategies in Healthcare** (in Part II), but much work remains to be done in these domains.

COVID-19 AND TOXIC STRESS

Public anxiety about the risk and consequences of the novel coronavirus disease 2019 (COVID-19), compounded by economic distress due to lost wages, employment, and financial assets, fear and grief, coupled with mass school closures and wide-scale physical distancing measures, represent a "perfect storm" for stress-related morbidity and mortality.

Widespread infectious disease outbreaks, natural disasters, economic downturns, and other crises have in common a number of well-documented short- and long-term health impacts, including increased cardiovascular, metabolic, immunologic, and neuropsychiatric risk. These risks accrue through a variety of mechanisms, including:

- Disruption of access to healthcare, including medications;
- Disruption of access to resources needed for health maintenance, such as nutritious foods and safe places to exercise;
- The direct effect of the inciting event driving an overactivity of the biological stress response, leading to neurologic, endocrine, immunologic, and genetic regulatory disruptions, with
  - increased incidence of ACEs and other risk factors for toxic stress, and
  - decreased sources of buffering care.

The conditions imposed by the COVID-19 pandemic have placed families at greater risk for ACEs and other risk factors for toxic stress; decreased access to buffering sources of support such as schools and community-based organizations; and downstream health impacts.[354-356]

At a population level, the impacts of crises also tends to worsen social inequities and health disparities. These health and social impacts particularly affect those with higher baseline vulnerability, including individuals with a history of adversity, those with lower incomes and education, those more vulnerable to job loss, housing insecurity, food insecurity, and poverty, as well as those with underlying chronic health conditions, disabilities, and older age.[212,214,216,357-403] Fear-related thoughts and behaviors can both worsen pandemic spread, as well as increase the short- and long-term health risks, because fear interferes with cognitive processing and executive functioning. For example, in West Africa, during the Ebola crisis (2013–2016), fear-related behaviors were implicated in speeding up the spread of Ebola; preventing treatment; enhancing the spread of malaria, tuberculosis, and HIV; disrupting care and leading to maternal and neonatal mortality; magnifying stigma; and accelerating negative economic effects.[386-388]

The health impacts of prior infectious disease outbreaks, natural disasters, and economic downturns include:

- **Increased heart attack and stroke.** After the Hanshin-Awaji

COVID-19 AND TOXIC STRESS

earthquake, there was a threefold increase in myocardial infarctions and a doubling of the incidence of stroke in those living close to the epicenter.[214,376]

- More than two years after Hurricane Katrina, survivors were found to have a threefold increase in myocardial infarction rates, relative to pre-Katrina rates.[216] Heart disease was also increased (15% greater) at one year post-Katrina.[397]
- Mechanistically, "acute stress can trigger cardiovascular events predominantly through sympathetic nervous activation and potentiation of acute risk factors (blood pressure increase, endothelial cell dysfunction, increased blood viscosity, and platelet and hemostatic activation)."[376]
- **Blood pressure increases.** Major disasters can produce systolic blood pressure increases of 5-25 mmHg for 1–6 months thereafter, particularly for those with risk factors (older age, chronic kidney disease, obesity, metabolic syndrome, diabetes), and only resolve "when the disrupted behavioral and biological circadian rhythm is restored."[212]
- **COPD and asthma exacerbations.** In the wake of the 2008 financial crisis, 11.5% more COPD exacerbations and 14.1% more hospitalizations resulted.[372] Acute and chronic stress are well known to lead to increased rates of asthma exacerbation. "Stress-induced asthma may be explained by epigenetic, immunological and neuro-mediator mechanisms. Stress has a neuro-immune modulating effect, leading to bronchoconstriction. One study reports half of new-onset asthma in war is due to stress, especially PTSD."[378] PTSD can lead to long-lasting alteration of the immune system, including dysfunction of regulatory T cells and switching to an IgE antibody profile, making asthma more likely.[378]
- **Poorer diabetes outcomes.** Hemoglobin A1c levels rose from 7.7% to 8.3% in diabetes patients in a safety net system, many without insurance, who did not receive continuous diabetes care for about a year, when measured 6–16 months after Hurricane Katrina.[379] Seniors with diabetes who lived in a county highly impacted by Hurricanes Katrina and Rita (N = 170,138), compared to those who did not (N = 170,138), had a nearly 40% higher all-cause mortality risk in the one month following the disasters, which diminished over the subsequent nine years, but was maintained at 5.6% at nine years.[397]
- Nephritis-related death was 27% greater at one year post-Katrina in survivors.[397]
- **Immune system dysregulation can result**, leading to increased secondary viral and other infectious disease susceptibility and poorer oral health.[212,366,377,380,381]
- **New-onset or recurrent mental and behavioral health conditions**,

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especially in those with longer duration of isolation, inadequate information, and/or inadequate supplies:[216,357-375,382,383]

- Depression, suicidality, completed suicides, by as much as 35 to 57%[369]
- Anxiety
- PTSD—about one-third of young children (5 to 8 years) who lived through the Great East Japan Earthquake had symptoms of PTSD two years later[360]
- Acute grief
- Obsessive-compulsive disorder
- Specific phobias
- Substance use—increased alcohol dependence were reported three years after quarantine for SARS.[384,385]

> **Poorer birth outcomes**, such as preterm birth, intrauterine growth restriction, low birth weight, and other intergenerational health and social risks:

- Women who were pregnant during or just after the 1998 Quebec ice storm had activation of their stress response and genetic regulatory systems in ways that were transmitted to their offspring. For instance, their children were found to have one-third of a standard deviation lower birth lengths,[389] and altered gene expression mechanisms into adolescence in ways that altered their immune and inflammatory profiles.[390,391] In adolescence, these children had altered energy and protein metabolism patterns that promoted lifelong risk for diabetes and obesity.[392] Cognitive and IQ-related deficits were also seen.[393]
- After the 2008 earthquake in Wenchuan, China, in births a year after the earthquake, the preterm birth rate went up by 130%, the low birth weight rate went up by 135%, and the rate of birth defects went up by 114%, as compared to the year prior.[394]
- Following the 1918 flu pandemic, children of infected mothers were up to 15% less likely to graduate from high school. Wages were 5-9% lower. Socioeconomic status was substantially reduced, and the likelihood of being poor rose as much as 15% compared with other cohorts.[395]

> **Risk for increased household violence.**[396]

The burden of these kinds of acute increases in ACEs, toxic stress, and AAHCs has been even more pronounced during the COVID-19 pandemic. In the first six months of the pandemic, hospitalization rates skewed higher among people with preexisting conditions. For example, individuals with diabetes, hypertension, or moderate obesity were three times more likely to be hospitalized than people without these respective diagnoses.[404] According to one study by the CDC, the mortality rate for people with underlying health conditions, including many AAHCs, was 12 times higher than for people without underlying health conditions.[405]

Intergenerational Transmission of Adversity

Parental Adverse Childhood Experiences (ACEs) and toxic stress can affect the health of subsequent generations—with effects transmitted from parent to child and even to grandchild. Both protective factors and risks for poor health can accrue over generations through innate and experiential factors. To successfully mitigate the impact of ACEs and toxic stress on health and well-being, we must understand the mechanisms by which adversity and its harmful consequences can be transmitted across generations. While the previous sections of this report detail how toxic stress may lead to poor health outcomes, this section reviews the literature linking parental and caregiver ACEs and toxic stress with the health and well-being of their children.

DEFINITION OF INTERGENERATIONAL TRANSMISSION

Intergenerational transmission of toxic stress occurs when adverse experiences alter parental biology or behavior in ways that affect the development and health of their children. This includes changes to parental and child neuro-endocrine-immune-metabolic and genetic/genetic regulatory function, in ways that matter for pre-conception health, and also influence pregnancy, birth, infant, and child health outcomes. Parenting behaviors, positive experiences, societal factors, and historical traumas also influence the way that health risks are passed on from parent to child.

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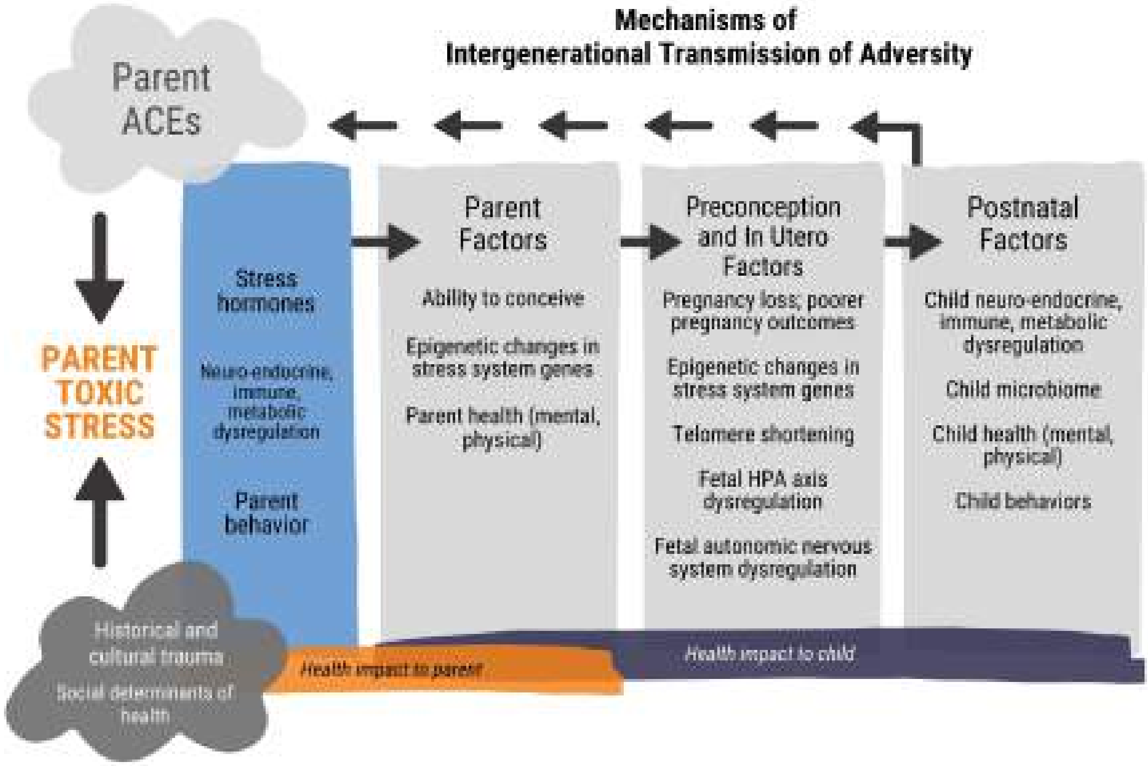

Figure 6. *Parental ACEs and toxic stress lead to multiple biological changes that may impact the health of their children.*

Children born to parents with high ACE scores are more likely to have neuropsychiatric, behavioral, and physical health problems, including sleep disturbances, anxiety, depression, attention-deficit/hyperactivity disorder (ADHD), asthma, autism, schizophrenia, and post-traumatic stress disorder (PTSD), among others.[302,303,406-427] Over the past several decades, researchers have begun to elucidate the mechanisms by which childhood adversity leads to poorer health and life outcomes.[20,275,413,422,424,428-432] Science points to the toxic stress response, or prolonged activation of the biological stress response and associated disruption of neuro-endocrine-immune-metabolic, and genetic regulatory functioning, as key mechanisms by which early adversity leads to increased risk of disease and early death across the life course and for future generations. Parental ACEs are associated with neuropsychiatric, endocrine, immune, and metabolic dysregulation in their offspring (**Figure 6**).[414,433] Unfortunately, these pathways have been largely under-recognized and under-addressed in clinical practice and policy.

Parental ACEs and other life stressors can affect their offspring both directly, via disruptions in caregiver stress hormones, neuro-endocrine-immune-metabolic function, and epigenetics, and indirectly, via caregiver behavior, societal factors, and historical and cultural trauma. These topics and their consequences for parental health are discussed in more depth in the previous section, T**he Biology of Toxic Stress**, and will be addressed here specifically in the context of the intergenerational transmission of toxic stress. Understanding the mechanisms by which this transmission occurs will allow clinicians, educators, researchers, and policymakers to develop and use specific strategies to address these issues.[413-416]

While this review focuses on the potential risks of ACEs across generations, it is important to recognize that (1) some stressful experiences are healthy, and the studies presented here are focusing on repeated, prolonged, or severe stress;[6] (2) many of these pathways may represent flexible adaptations to help prepare the next generation for the harsh world experienced by the caregiver;[434] (3) resilience can also be passed to the next generation through potentially many of the same pathways;[434,435] and (4) many, if not all, of these pathways can be mitigated or healed with supportive caregiving and other interventions (see later sections of this report, including **Tertiary Prevention Strategies in Healthcare** in Part II).

DIRECT IMPACTS OF PARENTAL TOXIC STRESS PHYSIOLOGY: STRESS HORMONES

In their summary of evidence on the developmental origins of disease, Keenan and colleagues discussed the relationship of preconception stress exposure to health disparities in obstetrics and offspring outcomes.[436] They posited that pregnancy health depends on maternal health prior to conception. They cited strong evidence across species for negative effects of maternal prenatal stress on the developing fetus and on subsequent development throughout childhood. Furthermore, while it is still debated by the field, the authors noted that the association between prenatal stress and offspring neurodevelopment may be due largely to preconception stress exposures.

Ability to conceive

ACEs and toxic stress affect the very first steps of childbearing by altering pubertal timing, age of menarche, menstrual regularity, egg and sperm quality, and ultimately, the ability to become pregnant.[6,437-440] High stress levels are associated with reduced odds of conception.[436,437,441] This has been tied directly to increased activity of the hypothalamic–pituitary–adrenal (HPA) axis, which regulates stress reactivity, suppressing the normal function of reproductive pathways.[442] Higher levels of corticotropin-releasing hormone (CRH) and glucocorticoids associated with stress (such as the hormone cortisol) suppress the normal function of the gonadotropin-releasing hormone (GnRH), resulting in lack of ovulation or egg production in women (anovulation). For women, but not men, higher perceived pre-conception stress is associated with slight reductions in peak fertility (fecundability).[441]

Pregnancy loss

Significant stress in the pre-conception and early pregnancy periods has been associated with an increased risk for pregnancy loss.[430,443-446] In the original Kaiser Permanente/Centers for Disease Control and Prevention (CDC) ACE Study, maternal ACE scores of five or more were associated with an 80% increased risk of fetal demise for pregnant adolescents.[447] A study of 2,795 adult women found that an ACE score of three or more was associated with twice the risk of miscarriage (RR 95% CI 1.25-3.22).[448] Physical abuse and sexual abuse were each individually also associated with increased risk. One meta-analysis of studies found that a history of psychological stress was associated with a 1.4-fold risk of miscarriage.[445] Frazier and colleagues detailed ways in which cortisol, other aspects of the HPA axis, and immune factors related to stress may increase risk for miscarriage.[444]

Preterm birth and low birth weight

ACEs, childhood adversity, cumulative stress exposure, and allostatic load (whole-body adaptation to stress through changes in neuroendocrine, immune, metabolic, and cardiovascular functioning)[449] during pregnancy are associated with increased risk for low birth weight and preterm birth, which are also risk factors for various adulthood diseases.[429,446,450-454] Women with an ACE score of two or more have a 2.1-fold increased risk of preterm birth compared to those with no ACEs.[429] Pregnant mothers who had experienced childhood sexual abuse were found to have increased hospitalizations during pregnancy, premature contractions, cervical insufficiency, and premature birth.[431] Exposure to intimate partner violence (IPV) has also been associated with vaginal bleeding, preterm birth, and perinatal death.[455,456]

Elevated maternal cortisol concentrations in the bloodstream give rise to elevated cortisol levels in the placenta and amniotic sac, which, in turn, may impair the development of the baby, leading to increased risk of preterm birth and lower birth weight.[457,458] In addition, lower birth weight was found in one study to be correlated with increased infant fear and distress responses.[457]

Higher levels of the stress hormone norepinephrine (also known as noradrenaline) in maternal urine, representing overactivation of the fight-flight-or-freeze system, were associated with increased risk for spontaneous preterm delivery.[459] Another study found associations between maternal childhood hardship, immune system dysregulation, high blood pressure, obesity, and preterm delivery.[460]

Preterm birth is more common in Black women and contributes to an infant mortality rate twice as high among Black women as among White women.[461] Known risk factors, including socioeconomic status, genetics, and health behaviors, do not fully account for this racial disparity.[461] Psychological stress, including the stress of experiencing racial discrimination, may contribute to this increased risk for preterm birth and higher mortality rates.[461]

Infant HPA axis

Perinatal adversity and parental stress before and during pregnancy may have significant effects on the subsequent functioning of the child's HPA axis, which, in part, controls stress reactivity.[266,462,463] The placenta plays an important role in regulating the transmission of cortisol, a major stress hormone, between the mother and fetus, and may protect the fetus from normal variations in maternal cortisol levels.[427] However, high levels of maternal cortisol may alter these regulatory mechanisms of the placenta, leading to negative impacts on fetal development.[427] Cortisol levels in tissues that surround the growing fetus, like the placenta and amnion, have been found to predict the stress response of the child after birth. For example, higher levels of cortisol in-utero predicted higher pre-stress cortisol values and a dysregulated response to stress exposure in infants.[464,465] In a study by Moog and colleagues, maternal childhood trauma (that is, trauma experienced by the mother when she was a child) was associated with increased placental production of the stress hormone, CRH.[466] Dysregulated infant cortisol responses to a stressor have been associated with maternal stress and high maternal cortisol levels.[464,467-469] These effects produce what can be conceptualized as a maladaptive HPA axis, with elevated cortisol levels both prior to stress and after it abates, coupled with blunted levels during stress.

Timing

The consequences of fetal stress exposure depend on its timing and duration. For example, stress exposure early in pregnancy is associated with increased likelihood of pregnancy loss, while stress exposure later in pregnancy has been associated with increased risk of low birth weight.[413] These effects appear to be species- and sex-specific. There may be critical windows of neurological, endocrine, and immune development affected by stress.

Buffering factors and timing

A meta-analysis of 39 studies evaluating the effects of psychosocial interventions to reduce the effects of stress on fertility rates among couples experiencing infertility found a robust effect for both psychological outcomes (including depression, anxiety and marital function) and fertility rates.[470]

Social support during pregnancy and after birth may play an important role in mitigating the impact of stress hormones on offspring. A study of 243 mother-infant dyads found that maternal ACEs were associated with maternal HPA function during pregnancy and infant HPA reactivity. However, many of their findings were observed when levels of social support were low.[454] This study also identified different trimester effects, where social support in early pregnancy moderated the impact on the pattern of maternal cortisol secretion, while support in later pregnancy impacted the amount of cortisol.[454]

DIRECT IMPACTS OF PARENTAL TOXIC STRESS PHYSIOLOGY: EPIGENETICS

Each cell in our body contains our genetic code, which consists of approximately 30,000 genes and act as a map for cell functioning. Genes, however, do not decide when they are read. Instead, they are controlled by chemical "on-off" switches: upstream elements that regulate gene expression. Epigenetics is the process by which particular environmental influences can move a particular switch to an "on" or "off" position. Through this mechanism of epigenetics, our experiences—good and bad—can change how genes are read and transcribed into proteins without altering the gene sequence. Epigenetic changes may be transmitted to the next generation, and include DNA methylation, histone post-translational modifications, and small noncoding RNAs.[302] Intergenerational transmission of epigenetic changes may occur through preconception changes to the egg or sperm (germ lines) that are passed on to the offspring or as in-utero changes directly to the fetal DNA.[433] (Of note, germ lines are formed at different times. Whereas females begin producing eggs from their time as a four-week-old embryo, still in their mother's womb, males begin producing sperm after puberty. Hence, the impact of the environment on the germ lines may be different by sex.)

Large-scale tragedies such as the Dutch Hunger Winter and the Holocaust altered epigenetics for survivors and their offspring in ways that are detectable decades and generations later.[471] In both animal and human studies, these methylation changes have been associated with lower birth weight, altered metabolic activity, and changes in cortisol levels and glucocorticoid (cortisol) receptor sensitivity, as well as increased health risks throughout life, including psychiatric and neurodevelopmental disorders.[302,414,433,472-476] Paternal and maternal adversity and stress have been associated with epigenetic changes in their offspring, including changes to genes encoding proteins that control glucocorticoid receptor function, factors that control glucose and lipid homeostasis, and the regulation of telomere length.[303,351,413,414,468,476-481] (Telomeres are parts of chromosomes that protect them from degradation. Shorter telomere length has been associated with premature cellular aging.) Given the complexities of conducting controlled adversity-related studies in humans, the most compelling research on epigenetic transmission involves animals. However, research on epigenetic patterns in humans is advancing quickly, including prospective, multi-generational studies.[475]

Paternal impact

Much of the animal epigenetics research deals specifically with male sperm and male offspring. This focus helps pinpoint effects to epigenetics, since it eliminates the profound contributions of fetal experiences, including from environmental factors and maternal behaviors, when females were studied. This research has found that epigenetics is a critical pathway by which paternal ACEs and stress can affect offspring. In mice, paternal stress (via fear conditioning and separation from their mother) has been associated with changes to DNA methylation of stress regulatory genes in sperm.[302] Male offspring born to stressed adult male rats (by forced swimming) had increased anxiety behavior, increased stress hormone levels, and epigenetic changes in a glucocorticoid-receptor gene, when compared to offspring born to non-stressed male rats.[472] Animal models have also found early traumatic stress may alter microRNA expression in sperm, influencing offspring HPA axis, neurodevelopment, and subsequent metabolic and behavioral outcomes.[302,414,433,473,482]

Placenta

Emerging evidence suggests that the placenta is highly susceptible to maternal distress prior to and during pregnancy.[483] The placenta can act as a "filter" to decrease the amount of cortisol that passes from mother to fetus. This may occur through epigenetic changes to the placental enzymes that convert cortisol into either an active or an inactive form. Methylation patterns of these genes have been found to have a significant effect on the baby's birth weight.[484] Epigenetic changes associated with pre-conception trauma in parents may also affect the DNA in eggs and sperm, altering the shared genomes of the fetus and placenta, and potentially impacting their development and interactions.[475] Changes in the genetic and epigenetic code of eggs and sperm alter the DNA blueprint for a child during development, influencing health throughout life.

Gene methylation

Fetal exposure to inflammatory proteins and cortisol has been associated with epigenetic changes (miRNA expression and DNA methylation) in the fetal brain, including alterations in neurotransmitter levels, cell survival, growth of new brain cells, connections between brain cells, and myelination (a process by which a fatty sheath surrounds axons of neurons and speeds up signaling).[433] (See the prior section, **The Biology of Toxic Stress**, for a discussion of how excessive inflammation, such as exposure to inflammatory messenger proteins during fetal life, has adverse effects on adult health.) The methylation patterns of several genes, including genes for a glucocorticoid receptor, a serotonin transporter, T cell immune function, brain-derived neurotrophic factor (BDNF), insulin-like growth factor 1 (IGF-1), and a catecholamine regulator, have all been connected to stress and health outcomes in offspring.[303,351,413,414,477-479] For example, a recent study found maternal depression was associated with methylation of a fetal cortisol receptor gene and infant cortisol responses, suggesting a mechanism for offspring HPA axis programming.[468]

Grandparents

One of the more provocative studies in the field of stress physiology involved male mice conditioned to fear certain smells by pairing these scents with a shock. Dias and colleagues found that offspring of the odor-fear-conditioned male mice were extremely sensitive to the odor, despite never having met their fathers and never having been odor-fear-conditioned themselves. Strikingly, the grandchildren of the fear-conditioned mice also experienced extreme odor sensitivity. In other words, fear conditioning was passed from grandfather to father to grandson. The researchers found this intergenerational transmission to be associated with epigenetic changes of a gene linked to the sense of smell.[485]

Telomere length

Epigenetic modifications of DNA continue to affect health and development after birth. Telomeres are non-coding sequences of DNA found at the end of each chromosome that protect the chromosome from degradation. Shorter telomere length has been associated with premature cellular aging, and has been correlated with high chronic stress, though with some mixed results. Some studies have suggested that maternal stress may impact fetal telomere length, suggesting another pathway for intergenerational transmission of toxic stress. Higher maternal prenatal stress has been associated with significantly shorter telomeres in those mothers' newborns, compared to newborns born to mothers with low prenatal stress.[480,481] Likewise, pre-pregnancy health risks like smoking, elevated body mass index (BMI), and low family support are associated with shorter telomeres in newborns.[486] A recent study by Esteves and colleagues found high maternal ACEs to be associated with shorter telomere length in their infants, as well as with increased externalizing behavioral problems at age 18 months. These findings were not explained by maternal postpartum depression or by prenatal stress.[487]

A growing body of research is finding that interventions such as supportive parenting, aerobic exercise, and nutrition may reduce stress and protect or even lengthen telomeres.[488-491] For example, Child-Parent Psychotherapy (CPP) has been shown to protect against telomere shortening associated with trauma, suggesting the intervention slowed, stopped, and for some children reversed the cellular "wear and tear" of early adversity.[492]

OFFSPRING NEURO-ENDOCRINE-IMMUNE-METABOLIC DYSREGULATION

ACEs and toxic stress are risk factors for a number of health conditions, as detailed in previous sections. Health issues in parents are known risk factors for similar health issues in their offspring. This section will focus on how caregiver stress can lead to offspring neurological-endocrine-immune-metabolic dysregulation, leading to increased risk for offspring poor health.

Neurologic and psychiatric health

Maternal stress and associated endocrine and immune system dysfunction may alter fetal brain structures involved in the stress response, including the hippocampus and amygdala, preprogramming the child for greater stress reactivity.[462,493] ACEs are a risk factor for maternal anxiety and depression, which, in turn, increase the risk of a child having mental health conditions like antisocial conduct disorder or depression.[417,494-498] Haynes and colleagues found that having a caregiver with four or more ACEs was a greater risk factor for a child's developing depression or anxiety (aOR 3.0) than having a caregiver with depression or anxiety without ACEs (aOR 2.2).[499]

Autonomic nervous system

ACEs and the associated fight-flight-or-freeze response can lead to prolonged activation of the autonomic nervous system. Markers for activation of the sympathetic nervous system (SNS) include elevated heart rate, salivary alpha amylase, and norepinephrine and epinephrine levels. The parasympathetic nervous system (PNS) counteracts the fight-flight-or-freeze response and is associated with recovery from stress. Measuring the activity of the PNS is more difficult than that of the SNS; however, markers such as respiratory sinus arrhythmia (RSA) and heart rate variability are often used, with or without association with breathing.

One study found that infants born to mothers with fearful temperaments and anxiety had higher tonic heart rates at age four months, which predicted a more fearful temperament at two and a half years.500 Higher infant heart rate reactivity and less heart rate recovery after a stressful experience at age four months also predicted a more fearful temperament during infancy and toddlerhood. This finding suggests that autonomic hyperarousal can be passed from mother to child early in infancy before learned behavior can occur. Gray and colleagues found that high maternal ACEs were associated with lower infant RSA (suggesting lower parasympathetic activity and/or increased stress activation in the infant), while prenatal stress was associated with an infant's failure to recover following a stressor.[501] Sex differences were observed, with higher RSA in boys and lower RSA in girls. Lower RSA has been linked to increased risk for stress-related disorders, including cardiovascular disease, depression, anxiety, and PTSD.[502]

Endocrine/metabolic health

Health impacts of parental stress and poor health extend beyond perinatal effects into adulthood. For example, children of parents exposed in utero to the Dutch Hunger Winter of 1944 had higher BMIs and poorer heath than those born to unexposed parents.[272,503] One recent study found that each maternal ACE successively increased the likelihood of child health problems, with children of mothers with four or more ACEs at greatly increased risk of poor health status, obesity, and asthma (3.0-, 3.9-, 3.2-fold increased risk, respectively, relative to those with zero ACEs).[420,504] The intergenerational transmission of ACE-Associated Health Conditions (AAHCs) such as obesity and diabetes can also occur when parental ACEs lead to increased health risk in the parent, and then this health risk is passed directly to their offspring. For example, children with obese parents were 2.2-fold more likely to be obese themselves.[505] Likewise, maternal gestational diabetes (2.5-fold) or parental diabetes outside of pregnancy (5.8-fold and 2.7-fold increased risk for mother and father, respectively) both increased risk for the child having diabetes.[506,507]

Immune system dysregulation

Chronic stress and adverse experiences are associated with inflammation.[508,509] Inflammation is a mechanism through which chronic stress is biologically embedded and may be passed on to the next generation.[12,510] Prenatal stress exposure has been linked to increased markers of inflammation, including NF-κB, AP-1, IL-6, IL-8, and CRP.[511,512] Using asthma as an example, three systematic reviews have found a link between maternal stress during pregnancy and an increased risk for asthma in their offspring.[513-515]

Similarly, the immune status of the mother may impact the ability of the placenta to regulate the amount of cortisol that is transferred between mother and fetus. For example, inflammatory markers have been shown to alter enzymes in the placenta that regulate fetal cortisol exposure.[452] Thus, stress-mediated maternal immune status may impact fetal cortisol exposure, and thus alter fetal brain development and fetal HPA axis function throughout life.[452]

Microbiome

Within our intestines live trillions of bacteria that help us break down our food, support our immune system, and may impact our nervous system as well.[516] In a study of 48 healthy pregnant women, a high ACE score was associated with an altered maternal gut microbiome.[517] The composition of a mother's vaginal, breastmilk, and skin microbiome during pregnancy, birth, and rearing may alter the baby's prenatal and postnatal growth, as well as brain and immune system development.[518,519]

CAREGIVER BEHAVIOR

ACEs are associated with increased risky behaviors, including smoking, alcohol dependence, substance dependence, interpersonal violence, and self-directed violence.[2,21,34,35,520-524] While these behaviors may be coping strategies adaptive to the stressful environment, they can also involve biological survival pathways, such as unconscious habits and cravings associated with changes to the mesocorticolimbic system, or reward circuit of the brain—in particular, the ventral tegmental area and nucleus accumbens.[525-527] These behaviors can themselves be ACEs for the children of those who exhibit them. ACE-related behaviors can also increase the risk for ACEs in the next generation through social learning (in which children model the behavior of their caregivers), attachment disruption, and associated parenting styles.

Risky caregiver behaviors may be ACEs for their children. ACEs are associated with increased risk of mental, behavioral health, and social conditions, such as depression, substance dependence, suicidality, intimate partner violence, and incarceration. Maternal ACEs have been associated with increased risks in the perinatal period, such as for maternal depression,[428,528-530] smoking and illicit drug use,[531] self-harm ideation,[532] teen pregnancy,[447] post-partum psychiatric episodes or illness,[533] PTSD,[529,534] and increased weight,[504] all of which can lead to ACEs for their children. Similarly, in a study of fathers, paternal ACEs were associated with paternal anxiety and depression.[535] These conditions among parents can then become ACE exposures for their children.[2,422] In addition, there is evidence that parents' behaviors are risk factors for the same behaviors in their offspring. Anda and colleagues found that children growing up with alcoholic parents were more likely to have additional ACEs, and that increasing ACE scores were associated with increased depression and alcohol dependence in adulthood, regardless of parental alcohol abuse history.[536] Unfortunately, this study was not able to clarify the role of genetic versus environmental transmission of risk.

Further, a meta-analysis of the intergenerational transmission of child maltreatment that included 84 studies found that offspring of parents who experienced maltreatment are at an almost three-fold increased risk for perpetrating child maltreatment themselves (versus having parents who did not experience child maltreatment).[537] However, the authors point out that study quality varied and the effect was smallest for physical abuse. There is a common perception that "hurt people hurt people," but it may be more appropriate to say that "people who hurt are more likely to have been hurt themselves." According to Dr. James Garbarino, a psychologist and advocate for juvenile offenders, "Approximately only 0.01% of Americans (1 in 1000) report an ACEs score of 8, 9, or 10. The scores reported by the last 10 killers I interviewed had an average score of 8."[538] The distinction is important because ACEs are much more common than the perpetration of child maltreatment. Thus, while an ACE score is not a valid predictor of violence perpetration, early detection of ACEs and treatment of toxic stress may represent a meaningful violence prevention strategy.

Additionally, not all perpetrators have a reported history of abuse, suggesting that ACEs are one pathway to increased risk for violence, but not the only one.[539] Thus, it is important not to use an ACE score to stigmatize or prematurely punish survivors as perpetration involves a complex set of factors.

Social learning

While social learning has been found in some studies to be a possible mechanism linking parental behavior and future behavior of their offspring, the data are limited and mixed. A number of studies have found IPV to be associated with social learning as a mechanism for transmission from one generation to the next.[540] However, studies suggest other mechanisms listed below are equally if not more relevant.

Parenting style

Traumatic childhood experiences may affect parental behavior and parenting, leading to an increased risk of offspring exposure to ACEs.[417,499] An inept, coercive parenting style has been associated with antisocial behavior in children, and this, in turn, has been associated with future risk for IPV.[540] Similarly, parenting without clear rules, monitoring, or positive involvement was associated with future adolescent substance use.[541]

Attachment disruption

ACEs may alter parenting behavior and attachment, leading to a higher likelihood of detached parenting, neglect, or other negative parenting traits that are risk factors for a child's future mental health.[409,542,543] Numerous studies have shown the importance of caregivers and secure attachment for children's development.[102,306,544-550] For example, research by Bowlby showed that infant monkeys needed affection to mature into healthy, well-adjusted adults.[549] Meaney found that infant rats who were raised by highly nurturant caregivers (biological or foster) had improved stress biology.[306,551] Diamond identified the importance of an enriched environment, including the impact of relational health on brain growth.[544,545] Lieberman and colleagues described how caregivers can be angels in the nursery, highlighting a strengths-based approach to interventions, including Child-Parent Psychotherapy.[550,552] Insecure or fearful attachment may lead to decreased trust, increased fear of abandonment, and affective instability.[540]

Importantly, social support appears to be a main pathway in mitigating the risk for transmission of behavior. Safe, stable, and nurturing relationships can break the intergenerational cycle of abuse.[544] Positive parent–child interactions have been shown to improve resilience later in life.[553] Parent engagement mitigated risk for adolescent smoking even when the parent themselves smoked.[554] Positive childhood experiences (PCEs), such as being able to talk to family about feelings, participating in community traditions, and feeling supported by friends, have been associated with decreased depression, better mental health, and improved social and emotional support in adulthood.[41] This is further evidence that PCEs and the promotion of safe, stable, and nurturing relationships can break the intergenerational cycle of adversity.[41,544]

SOCIETAL INFLUENCES

Increased ACEs are associated with an increased risk for challenging social determinants of health (SDOH) conditions.[38] Structural inequities, including lack of community investment, educational resources, economic opportunities, and transportation availability, all affect development, health, and quality of care.[555] Both interpersonal and structural racism also promote toxic stress.[556,557] Such factors significantly contribute to the perpetuation of ACEs and toxic stress across generations. For example, there is a dose–response relationship between ACEs and housing insecurity and homelessness, which, in turn, are considered risk factors for toxic stress themselves.[558,559]

The association of worse maternal health outcomes in Black and Native American women than in other demographic groups is thought to be due, in part, to pre-pregnancy stress, trauma, discrimination, and other challenging SDOH.[436,560,561] Poverty and discrimination as a result of historic and structural racism have been demonstrated to adversely affect both the diurnal rhythms and feedback loops of the stress response system, as well as the interface between the HPA axis and other systems critical for maintaining health, such as immune functioning.[436,460,510,562,563] Keenan and colleagues postulated that a primary cause of disparities in maternal and child health among Black Americans is likely due to a disproportionate amount of stress experienced by this group.[436] As noted above, stress experienced not only by the individual, but also by past generations, can impact health status through epigenetic and other mechanisms. Policies, systems, and societal norms must address historical and current racial trauma as well as implement strategies to decrease the burden of toxic stress for minorities and marginalized communities.

Factors considered SDOH can exacerbate intergenerationally transmitted biological and behavioral risks, but are not generally considered to be transmitted themselves, due to their external nature. An effective public health and policy response to ACEs and toxic stress must include strategies to address the SDOH that perpetuate cycles of trauma, poor health, and negative social outcomes (see **Part II**).[564]

Historical and cultural trauma

The impacts of an individual's early exposure to adversity and stress may be passed through several generations. Recent scientific advances have begun to uncover the mechanisms of this longer-range intergenerational transmission.[303,414,565,566] Studies, reviews, and commentaries have evaluated the offspring of survivors of the Holocaust,[476,565,567] Native American genocides,[568-571] 9/11,[572,573] and slavery.[574-576]

These studies highlight the intergenerational transmission of adversity through direct biological mechanisms, including those discussed in this report, as well as political, economic, environmental, and social/ecological pathways, rather than simply through effects of the parent's emotional state and behaviors.[577] These studies also provide a valuable frame to expand from a focus solely on the transmission of ACEs from an individual to their offspring to that of historical trauma passed from one generation to the next. Bringing the lens of historical trauma to trauma work "creates an emotional and psychological release from blame and guilt about health status, empowers individuals and communities to address the root causes of poor health, and allows for capacity-building unique to culture, community, and social structure."[577] Recognizing that current and historical trauma—including the murder and enslavement of Black and Native Americans—can leave biological imprints on the health of current and subsequent generations, adding to the moral imperative and obligation to heal these harms.

CONCLUSION

ACEs and other early life stressors cause a chicken-egg cycle of intergenerational risk for toxic stress and poor health outcomes. However, emerging science is illuminating what was formerly the black box of toxic stress, highlighting mechanisms between ACEs, toxic stress, and health. In this way, science offers new opportunities to more precisely interrupt the intergenerational cycle of ACEs and toxic stress, and to promote an intergenerational cycle of health. The skills children need to be resilient and healthy can all be learned from attuned, engaged, and nurturing adults. Evidence suggests that early intervention can improve brain, immune, and genetic regulatory control of development and is therefore critical for improving outcomes for individuals at risk for toxic stress.[579-585] Treatment of toxic stress in adults may serve to prevent transmission of neuro-endocrine-immune-metabolic and genetic regulatory disruptions in offspring. This section highlights the importance of a multigenerational and multidisciplinary approach that promotes caregiver healing, family resilience, and safe, stable, and nurturing relationships to break the cycle. Curbing the intergenerational transmission of ACEs and toxic stress requires a public health approach utilizing a coordinated, multisector strategy to advance prevention, early detection, and interventions (see **Part II**).

RECOMMENDATIONS

Prevention

1. Raise national awareness through communication, policy, and action efforts, that ACEs and toxic stress can be passed down from generation to generation—but so can protective factors.
2. Community and ecological action: collaborate across child-serving sectors to create accountable communities and collective, equitable action.
    a. Highlight transmission of protection and resilience.
    b. Interventions at any point are primary prevention for the next generation.
    c. Patience and perseverance: recognize that if it takes time to cause dysregulation, it can take time to reverse it.
    d. Biologically based approaches to policy, advocacy, and interventions, including trauma-informed care, strength-based approaches, and attention research-based stress-mitigation strategies; if ACEs and toxic stress can increase risk for poor health in one generation, promoting relational health will decrease ACEs and toxic stress in the next.
    e. Focus on reducing racism and bias everywhere, including in the delivery of healthcare, as a key highlighted goal for primary prevention.
3. Family and multi-generational approach.
    a. Supporting caregivers in treating impacts from their own ACEs.
    b. Family-focused therapies, such as Child-Parent Psychotherapy,[586,587] are two-generation treatment approaches which address ACEs for both caregiver and child. (See **Tertiary Prevention Strategies in Healthcare**

in Part II for further description of these and other evidence-based therapies.)

Practice transformation

1. Universal screening: ensuring universal screening for cumulative adversity and risk of toxic stress in the preconception, prenatal, and postnatal periods.
2. Promote relational health and safe, stable, and nurturing relationships, which are known to mitigate effects of parental adversity, both during childhood and into adulthood.
   a. Support programs such as Centering Parenting[588] and the CDC's Legacy for Children,[589] which provide the proactive social supports to promote positive parenting and positive child health outcomes, rather than waiting for the child's ACE score to rise.
   b. Implement sufficient social supports for young parents and families.
3. Effective referral systems: strengthening referral systems to help children, adults, and families access appropriately targeted services can interrupt or mitigate toxic stress physiology.
4. Comprehensive service array: comprehensive services to address ACEs, toxic stress, and accompanying SDOH that can be coordinated through a primary care home (especially in rural and underserved communities) for both children and adults, can interrupt the intergenerational transmission of ACEs.
5. Payment for services.
   a. Secure public (e.g. Medicaid) and private insurer payment for routine screening and treatment for toxic stress in every state.
   b. Explore payment reform such that preventative interdisciplinary primary care is reimbursed at rates comparable to those paid for disease care and procedural services.

Research and innovation

1. Advance the science to measure, mitigate, and treat the effects of ACEs and toxic stress in children and adults. Enhance understanding of clinically viable biomarkers for diagnosing and monitoring toxic stress, as well as biologically precise therapeutic targets for treatment of toxic stress. In research, identify consistent measures of toxic stress to be able to compare across studies.
2. Increase research on interventions that heal toxic stress and improve

health.

a. Evaluate impacts of interventions on neuro-endocrine-immune-metabolic and genetic regulatory disruption, health outcomes, and measures of health.

b. Increase focus on researching which interventions work best in what circumstances, for which populations, and for which health conditions.

3. Promote a strengths-based research framework that studies how to proactively build relational health that not only buffers adversity when it occurs, but also promotes the social-emotional and cognitive skills to be resilient in the future.
4. Utilize machine learning and big-data computational analyses to identify how timing, severity, and predisposing factors contribute to differences in generational patterns of health outcomes. More precisely evaluate effects of exposure timing, moderating impacts, and the cumulative effects of adversity and resilience factors.

Of note, all recommendations made are subject to the budget approval process.

Establishing Causality Between ACEs and Poor Health Outcomes

The Bradford Hill Criteria are widely used by the scientific community to establish causal inference from observational data.[590] Since their original publication in 1965, these criteria have been updated to incorporate modern molecular methods and data integration to strengthen the determination of causality.[591] These nine criteria can be definitively applied to the association between Adverse Childhood Experiences (ACEs) and poor health outcomes.[5]

1. STRENGTH.

The stronger the association between the exposure and outcome, the more likely it is to be causal.

There are strikingly strong associations between ACEs and many of the leading causes of death in the United States, ranging from 1.4 times the risk for diabetes to 37.5 times the risk for suicide attempt in those with four or more ACEs.[2] Individuals with four or more ACEs are two to three times as likely to develop ischemic heart disease, stroke, chronic obstructive pulmonary disease (COPD) and cancer, and 11 times as likely to develop Alzheimer's disease or other dementias, compared to those with no ACEs.[2,16,17,30] While the most robust associations are between ACEs and adverse neuropsychiatric outcomes, the links to adverse immune, metabolic, and cardiovascular outcomes are also quite strong,[2,3,5,30] equaling or exceeding the effects of other known causal factors. For example, the association between ACEs and ischemic heart disease equals or exceeds the effects of smoking and hypertension, depending on the dose (number of ACEs), and persists even after adjusting for traditional risk factors.[592-594]

2. CONSISTENCY.

If multiple studies involving a variety of populations, locations, and methods demonstrate a consistent association, it is more likely to be causal.

Findings from the Behavioral Risk Factor Surveillance System (BRFSS), which collects ACEs data from 42 states, show consistent associations between ACEs and poor health.[13] These associations are further corroborated by global data from at least 17 countries.[2] The physiological effects and clinical consequences of ACEs are also consistent across study designs, from the original retrospective cohort ACE Study,[3] to prospective cohort studies,[39,595] to animal models in a variety of species.[306,596] There is also consistency across clinical, physiologic and molecular outcome measures. For example, the impact of ACEs and risk or protective factors on immune function has been documented clinically as increased risk of certain infections and autoimmune disorders,[190,191] physiologically as impaired immune responsiveness to vaccination,[597] and molecularly as alterations in inflammatory markers such as C-reactive protein, fibrinogen, and proinflammatory cytokines.[340] Together, these findings reinforce a consistent association between ACEs and immune dysregulation.

3. SPECIFICITY.

If the exposure leads to only one outcome, then the association is more likely to be causal.

While it was previously thought that the association between ACEs and numerous health conditions undermined the criteria of specificity,[5] advances in science now point to the toxic stress response[6,23,60] as a single, highly specific mechanistic outcome of ACE exposure that consequently increases the risk of multiple negative health outcomes. Just as discovery of the role of the human immunodeficiency virus (HIV) in immune impairment shed light on the pathways that give rise to the many clinical manifestations of acquired immunodeficiency syndrome (AIDS), so too understanding of the toxic stress response sheds light on the mechanistic pathways underlying the associations between ACEs and myriad adverse health outcomes.

4. TEMPORALITY.

The exposure must precede the onset of the outcome in order for the association to be causal.

The original ACE Study was based on adult participants' recollection of their ACE exposures,[3] which makes it challenging to establish temporality with certainty due to recall bias. However, multiple long-ranging birth cohort studies have since linked antecedent ACEs to the subsequent development of a variety of adverse health outcomes.[39,595,598-600] Prospective data showing that ACE-associated psychopathology in early adulthood mediates mid-life psychopathology also helps establish temporality.[599] A prospective study showed that childhood maltreatment predicts adult inflammation in a life-course study.[176]

5. BIOLOGICAL GRADIENT.

If there is a dose–response relationship between the exposure and outcome, the association is more likely to be causal.

The literature has consistently shown a dose-response relationship between the number of adversities experienced and almost all poor health and social outcomes studied.[3,5,13,30] For example, while individuals with four ACEs have double the risk of ischemic heart disease compared to those with none, those with seven or eight ACEs have more than triple the risk.[592] Similarly, compared to those with zero ACEs, individuals with one ACE have about 1.5 times the risk of respiratory disease, and those with four or more ACEs have more than 2.5 times the risk.[30]

6. PLAUSIBILITY.

If there is a conceivable mechanism for the relationship given the current body of scientific knowledge, then the association is more likely to be causal.

There are clear mechanisms through which ACEs harm health. ACE exposure in the absence of adequate buffering relationships and environments can lead to the toxic stress response, which is characterized by prolonged activation of the stress response via the hypothalamic-pituitary-adrenal (HPA) and sympatho-adreno-medullary (SAM) axes, leading to dysfunction of the neurologic, endocrine, immune, and metabolic systems and changes in DNA regulation.[6,12,60,319] These physiologic derangements can lead to a multitude of poor clinical outcomes. By affecting specific parts of the brain, such as the mesocorticolimbic system (reward centers),[6] toxic stress can also lead to health-harming behaviors, such as substance use, overeating, and sexual risk-taking.

7. COHERENCE.

If the cause-and-effect story makes sense given the information available to the scientific community, then the association is more likely to be causal.

The effects of ACEs on health fit with current knowledge of the biology of toxic stress, particularly when those ACEs occur during critical and sensitive periods of development in the absence of sufficient buffering relationships and environments.[23,47] The toxic stress response is defined in a 2019 consensus report by the National Academies of Science, Engineering, and Medicine as the "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."[23] It includes neurologic, endocrine, immune, metabolic, and genetic/genetic regulatory derangements, and each mechanistic pathway involved coheres with the range of health consequences linked to ACEs via toxic stress.

8. EXPERIMENT.

If manipulation of the exposure leads to changes in the outcome, then the association is more likely to be causal.

While it would be unethical to introduce childhood adversity to demonstrate the cause-and-effect nature of ACEs and toxic stress, both natural experiments and animal studies have demonstrated a dose–response relationship between dose of adversity experienced and severity of outcomes.[2-5,13,16,29,30,63,64,85] Natural experiments, such as the 1998 Quebec Ice Storm and the Dutch Hunger Winter, show that prenatal exposure to stress leads to increased stress responsiveness and physiologically and clinically apparent changes in the immune, metabolic, and cardiovascular systems,[421,601] coherent with the effects of ACEs and toxic stress. Populations who have experienced the atrocities of war, such as Nazi prison camp refugees and Eastern Serbians exposed to civil war, have shown a higher incidence of autoimmune hyperthyroidism, which is coherent with the association between ACEs leading to toxic stress, and immune dysfunction.[602] Similarly, animal studies of rats and of rhesus monkeys demonstrate that experimental exposure to high doses of adversity, particularly during early development, leads to neuro-endocrine, immune, metabolic, and genetic regulatory disruption.[306]

Conversely, there is robust experimental evidence that safe, stable, and nurturing relationships and environments can buffer the toxic stress response and mitigate the effects of ACEs.[603,604] The Bucharest Early Intervention Project, a randomized controlled trial among institutionalized infants and toddlers,[605] showed that early and stable placement in high-quality foster homes improved physiological and clinical outcomes in physical development,[606] brain structure and electrical activity,[579,607] and neuropsychiatric symptoms.[608,609] These findings are supported by many animal models. For example, Meany and colleagues demonstrated that rat pups raised by more "attentive" mothers showed improved performance on cognitive tasks and better regulated stress responses as adults than those raised by less attentive mothers, and that these outcomes were associated with changes in epigenetic regulation of stress response pathways. Further, experimental manipulation in which the pups were switched at birth revealed that these findings, including epigenetic markers, were associated with the care of the rearing mother, even if the pups' biological mothers were less attentive.[306] A population-based study documented that adults reporting ACEs were 72% less likely to experience depression or poor mental health in adulthood if they also experienced positive childhood experiences (PCEs), defined as feeling safe to talk about feelings with your family, feeling supported in difficult times, having at least two non-parental adults to rely on, and having a sense of belonging in school or the community.[41] A study of US school-age children with ACEs similarly documents the mitigating effect of building family resilience and parent–child connection to substantially reduce the negative association of ACEs with diminished child resilience and lack of interest and engagement in learning and school.[604]

9. ANALOGY.

If the exposure is similar to another exposure that has strong evidence for causing the outcome, then the association is more likely to be causal.

High doses or long courses of corticosteroids are well documented to cause adverse health effects, such as impaired growth, delayed puberty, high blood sugar, obesity, hypertension, and neuropsychiatric symptoms. In fact, these effects are sufficiently predictable that clinical guidelines have been developed for monitoring and preventing them.[610] Thus, it is paradigmatically consistent that toxic stress, which leads to chronic dysregulation of cortisol (a natural corticosteroid) and other stress hormones, may cause similar hormonal, metabolic, cardiovascular, and neuropsychiatric outcomes in individuals who have experienced ACEs.[86]

In summary, rigorous application of the Bradford Hill Criteria strongly supports a causal association between ACEs, development of the toxic stress response, and a host of negative health and social outcomes.

Other potentially traumatic childhood experiences have been identified that may also increase the risk for toxic stress. These other potential traumatic childhood experiences incorporate the role of the community and social environments and recognize the experiences of diverse populations beyond the original ACE Study. Some of these risk factors are poverty, discrimination (particularly racial discrimination), food and housing insecurity, interpersonal and community violence, bullying, parental absence, death of a family member, child separation from the family, living in foster care, and justice system involvement.[2,53-61] They can coexist with and amplify the impacts of ACEs. We must continue to comprehensively evaluate and address other sources of early adversity to ensure that all children thrive in homes, communities, and social environments that are safe, stable, and nurturing.

The Economic Costs of ACEs and Toxic Stress

Adverse Childhood Experiences (ACEs) such as child abuse, neglect, and household challenges (like family member incarceration or intimate partner violence) are very common, affecting 62% of California adults by age 18 years. Approximately 16% of Californians report experiencing four or more ACEs.[27] ACEs are associated in a dose-response fashion with numerous poor health and social outcomes over the life course, including at least nine of the 10 leading causes of death nationally.[2,16,17,29,30,85]

The consequences of ACEs also create significant costs for systems and for individuals and families. For health, this includes costs to healthcare systems, like increased utilization of services for health conditions that could be prevented or mitigated, and the costs to society and individuals, who lose productive, healthy years of life.[13,63,64] They also include costs from lost economic productivity, school failure and noncompletion, learning and developmental problems requiring interventions like special education, involvement in criminal justice, child welfare, and public support service systems.[16,555,611-616]

ESTIMATES OF HEALTH COST IMPACTS

Studies estimating economic costs of health conditions often look at healthy years of life lost due to ill health and premature death across populations. A commonly used measure is disability-adjusted life years (DALYs), which is the sum of years of life lost due to premature death and to disability for people living with the

DISABILITY-ADJUSTED LIFE YEARS

The sum of years of life lost due to premature death and to disability for people living with a health condition or its consequences.

ACE-ATTRIBUTABLE FRACTION

Excess risk of disease due to ACEs exposure specifically is called the ACE-attributable fraction for that disease or condition.

health condition or its consequences. Sometimes analysts use studies of the value people place on reducing their risk of dying to assign a monetary value to a DALY. Another way costs are calculated for health risks like ACEs starts with estimating the proportion of common diseases or health conditions that are thought to be caused by, or attributable to, exposure to the risk factor (in this case, ACEs). This excess risk of disease due to ACEs exposure specifically is called the ACE-attributable fraction for that disease or condition. Because many factors contribute to diseases and health conditions, ACE-attributable fractions are used to estimate costs due to the proportion of that condition thought to arise from exposure to ACEs specifically.

In North America and Europe, the health consequences attributable to ACEs in 2017 resulted in an estimated annual cost of $1.3 trillion.

In a 2019 systematic review and meta-analysis of studies comparing risk data in individuals with ACEs to those without, Bellis and colleagues calculated the relative risk for 10 major causes of ill health and risk factors for poor health outcomes associated with ACEs leading to toxic stress, including cancer, diabetes, cardiovascular disease, respiratory disease, anxiety, depression, harmful alcohol use, illicit drug use, smoking, and obesity (known as ACE-Associated Health Conditions, AAHCs). The fraction of these AAHCs attributable to ACEs ranged from 7.5% to 41.1%. Significantly, in North America, 30% of cases of anxiety and 40% of cases of depression were attributable to ACEs. Costs were calculated based on the DALYs using the human capital method, which assigns a monetary value to reduced productivity due to ill health and premature death. Costs due to cardiovascular disease attributable to ACEs were substantially higher than for the other causes of ill health included in the study. Costs went up with total number of ACEs experienced; 77–82% of costs resulted in those who had experienced two or more ACEs. For North America and Europe, the health consequences attributable to ACEs in 2017 resulted in an estimated yearly loss of 37.5 million DALYs, at a cost of $1.3 trillion, representing 3.6% of gross domestic product (GDP) for North America and 2.7% for Europe.[64]

A study by Miller and colleagues focusing on 2013 data for California estimated personal healthcare spending (using patient health system encounters), health burden measured in DALYs, and costs based on monetized DALYs. The annual (2013) healthcare burden and the resulting monetary costs of the ACE-attributable fraction of eight AAHCs (asthma, arthritis, chronic obstructive pulmonary disorder [COPD], depression, cardiovascular disease, smoking, heavy drinking, and obesity) totaled $112.5 billion, with $10.5 billion in personal healthcare spending and $102 billion in years of productive life lost due to early death and disability. This includes an estimated loss of 434,313 DALYs, or healthy years of life, for that year. Specifically, on average, each adult with a history of ACEs cost an additional $589 in annual healthcare expenses, and 0.0224 DALYs valued at $5,769. Costs rose with the number of ACEs experienced. However, since there are more adults with fewer than four ACEs, while healthcare costs for people with four or more ACEs were more than double the costs for those with just one ACE ($818 versus $407 per person per year), most (64%) of the health costs resulted from adults exposed to fewer ACEs. For example, adults exposed to one ACE accounted for 24% of the total health costs (**Table 5**).[63,617]

ESTIMATES OF COST BEYOND HEALTH IMPACT

To estimate costs associated with ACEs and toxic stress in sectors beyond health burden and healthcare, we must look at studies of child abuse and neglect, which account for five of the 10 ACEs (physical, emotional, and sexual abuse, and physical and emotional neglect). For example, Fang and colleagues reported that US lifetime systems-level costs for child abuse and neglect cases substantiated by Child Protective Services (CPS) were $4.5 billion in child welfare, $3.9 billion in criminal justice, and $4.6 billion in special education (based on 2008 data).[611] A California-specific study from Safe & Sound estimated annual (2017) state costs due to substantiated child abuse and neglect at $919 million in education, $787 million in welfare, and $545 million in criminal justice, along with $13 billion in lost economic productivity—or $15.3 billion total for these areas. The report also estimates $3.8 billion in healthcare costs and $207 million in fatalities, totaling $19.3 billion for the overall annual cost of substantiated child abuse and neglect cases in California.[555] And these are presumably underestimates, because they do not include cases that were not reported, investigated, and substantiated. More importantly, many ACEs do not qualify for reporting or investigation, but they nevertheless result in health problems, unfulfilled potential, and a myriad of other costs. A robust assessment of systems-level costs associated with all ACEs is challenging and has not been done.

Other studies give us an idea about some of the costs that go beyond the costs discussed above. For example, a study by Miller and colleagues on alcohol and drug use—which can be an ACE in itself (if it occurs in another family member) as well as an outcome or AAHC—estimated annual costs to the state of California at $52.6 billion from alcohol and drug use leading to illness, injury, crime, traffic collisions, and public prevention efforts.[616] While the costs due to ACEs are only a portion of this (Bellis and colleagues described ACE-attributable fractions for North America of 27.9% for harmful alcohol use and 41.1% for illicit drug use[64]), they are still quite high, and the Miller study shows impacts that go well beyond health-related costs.

Another study estimated the cost of childhood exposure to crime, including both direct victimization, and exposure to family and community crime. Though this study includes crimes arising from experiences not included in the original 10 ACEs (e.g., exposure to crime in the community, in addition to the traditional ACEs of child abuse and neglect, witnessing intimate partner violence, and having a family member who is incarcerated), it provides estimates of the broad and costly impact of childhood exposure to crime. Annual US costs were estimated at $458 billion, when considering impact on lifetime prevalence of physical and mental health problems, life productivity, educational outcomes, criminal justice involvement, and substance use.[618]

While these studies on the costs of alcohol and drug use and the costs of crime aren't limited to the ACE-attributable costs, they provide some understanding of the broad impacts beyond health-associated costs, and they reveal the limits of existing methods to evaluate the indirect, lifetime, and intergenerational costs associated with ACEs. Also, because ACEs tend to co-occur,[3] studying the cost of a single or only some ACEs doesn't provide an accurate estimate. Future studies

Study source/ region	Risk category	Annual cost estimates	Notes
Bellis et al., 2019[64] North America and Europe	ACEs	$1.3 trillion (lost productivity)	Cost estimates of reduced economic productivity due to ill health and early death (measured in DALYs).
Miller et al., 2020[63] California	ACEs	$102 billion (health burden) $10.5 billion (education)	Cost estimates of health burden due to ill health and early death (based on monetized DALYs) and personal healthcare spending.
Safe & Sound, 2019[555] California	Child Abuse and Neglect (5 of 10 ACEs)	$13 billion (lost productivity) $3.8 billion (health burden) $919 million (education) $787 million (welfare) $545 million (criminal justice)	Cost estimates for support systems and individuals for child abuse and neglect cases substantiated by CPS.

Table 5. *Summary of studies estimating annual costs for ACEs and child abuse and neglect*

that include all ACEs and consider cost impacts across many domains will add to understanding of the cost impact of ACEs.

SUMMARY

Annual health burden and healthcare costs attributed to ACEs in California have been estimated at $112.5 billion (2013).[13,63] Annual cost estimates across other sectors are currently limited to studies of child abuse and neglect, with an estimate of $15.3 billion for California (2017) for lost economic productivity, education, criminal justice, and welfare costs.[555]

Actual costs for ACEs and toxic stress are likely higher than what has been estimated to date. Current studies have focused primarily on health costs, and on only a fraction of relevant AAHCs. Ongoing and future studies on the costs of ACEs could include total costs associated with illness and disability from all AAHCs, lost economic productivity, school failure and noncompletion, learning and developmental problems requiring interventions like special education, involvement in criminal justice, child welfare, and public support service systems, all shown to be higher in those with significant ACEs, toxic stress, and/or AAHCs.[2,16,17,34-38,555,611,613]

The studies discussed do demonstrate that, in the areas considered, ACEs cost California and the US billions of dollars each year; and they indicate that even moderate reductions in ACEs would yield significant gains for people's health and well-being and significant reductions in money spent by state and federal support systems. For example, the Bellis study discussed above estimates that just a 10% reduction in ACE prevalence could equal an annual savings of one million DALYs, or $56 billion, in North America, considering health and productivity costs alone.[64] Significant savings could be made when the downstream impacts of ACEs are prevented or ameliorated through early screening and more intentional treatment.

PART II

The Public Health Approach for Cutting Adverse Childhood Experiences and Toxic Stress in Half Within a Generation

Primary, Secondary, and Tertiary Prevention of ACEs and Toxic Stress: An Overview

A comprehensive statewide path to reducing the burden of Adverse Childhood Experiences (ACEs) and toxic stress by half in a generation requires a coordinated cross-sector approach to prevention, early recognition, and early, evidence-based intervention for ACEs, toxic stress, and their associated negative impacts on health and social outcomes.[23,24,31,619] In other words, an effective response to ACEs and toxic stress requires prevention at all three levels: primary, secondary, and tertiary.[24,25] None of these strategies is sufficient alone, and each extends the reach of the others. The synergistic effect of primary, secondary, and tertiary prevention is illustrated by the United States' response to the human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) epidemic. Coordinated efforts for public awareness and prevention, testing for early detection, and effective treatment were all necessary for achieving a reduction in the AIDS mortality rate of more than 87% in a generation (from 50,628 deaths in 1995 to 6,465 deaths in 2015).[620]

This report will use this three-part framework to outline sector-specific strategies and impacts, and highlight opportunities for cross-sectoral collaboration, in the sections that follow. This purpose of this section is to define and give examples of the three levels of prevention, to lay the groundwork for the sections to come.

PRIMARY PREVENTION

Primary prevention efforts target healthy individuals and aim to prevent harmful exposures from ever occurring. These include efforts to change or establish structural and systemic conditions to prevent 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. Broad primary prevention efforts include vaccinations to prevent specific infectious diseases and the fluoridation of water to prevent tooth decay and caries.[621] In the case of HIV prevention, primary prevention includes promoting public education, condom use, and needle exchange practices to prevent exposure to HIV during sex or injection drug use in healthy, susceptible individuals.[622]

For ACEs and toxic stress, primary prevention strategies are designed to reduce the likelihood of ACEs and other risk factors for toxic stress from ever occurring. By increasing buffering factors and reducing the dose of adversity, primary prevention promotes the experience of stressors as positive or tolerable—involving brief or time-limited activation of the biological stress response, in ways that do not lead to longer-term changes to neuro-endocrine-immune-metabolic or genetic regulatory systems and promote risk for chronic disease—rather than toxic.[6]

Primary prevention of ACEs and other risk factors for toxic stress involves investments in cross-sector policies and programs that promote stable, safe, and nurturing relationships and environments and other resilience-enabling factors. It is grounded in the developmental and ecological sciences and incorporates a life-course perspective with multiple structural levels (e.g., individual, family, neighborhood, community, systems/policies/laws). These proactive interventions are needed to (1) raise awareness about the risks of ACEs and toxic stress and the effectiveness of buffering interventions, (2) support positive parenting and relationship norms, (3) strengthen individual, family, and community resilience, and (4) reduce the incidence and impacts of poverty, structural racism, environmental toxins, and other contextual conditions that contribute to and exacerbate ACEs and toxic stress.[23,31]

Based on a comprehensive public health framework, primary prevention strategies are rooted in ensuring broad public awareness[31] and supported by effective upstream policy and systems changes, such as assuring social, educational, and economic opportunities for all, support of social safety net programs, and proactive actions that promote equity, including anti-racist frameworks.[23,24,31,42,564,619] They should also include specific policy and programmatic efforts to enable access to high-quality home visiting programs, early childcare, early education, and economic and legal supports for families.[31] Another crucial element in preventing and reducing the intergenerational transmission of adversity is the provision of cross-sectoral buffering supports during the preconception, prenatal, and early parenting years, including economic supports and skill-based parenting and family relationship

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programs.[31] In addition, surveillance mechanisms[2] are necessary for monitoring and acting on the regional and local population-level prevalence of ACEs and impacts of toxic stress. Universal ACEs-aware, trauma-informed policies, trainings, and infrastructure coordination efforts within and across sectors, including first responders, healthcare, public health, social services, early childhood, education, and justice, are needed to maximally leverage existing investments, reduce retraumatization, facilitate ease of navigation for families and service providers, and advance equity.[623-628]

SECONDARY PREVENTION

Secondary prevention efforts target individuals who have experienced an exposure and aim to prevent the development of symptoms, disease, or other negative outcomes. They facilitate early detection and intervention within the first ('subclinical') stages of disease or undesired social outcomes in order to stop or slow its progression.[24,25] Examples of the importance and efficacy of secondary prevention strategies are abundant in healthcare. The United States Preventive Services Task Force (USPSTF) recommends newborn screening to detect metabolic diseases right at birth so proper treatment can be initiated without risking long-term damage, as well as age-appropriate periodic screening for different cancers (e.g., breast, cervical, and colorectal) so that they can be caught early and treated.[629] Since the implementation of routine mammography for breast cancer screening, death from breast cancer has declined by 40%, with 375,900 deaths averted between 1989 and 2017.[630] In the example of HIV, secondary prevention includes HIV testing, which enables identification of asymptomatic individuals and facilitates treatment to prevent the development of opportunistic infections.[622,631-634]

For ACEs and toxic stress, secondary prevention is particularly crucial. Once ACEs and other risk factors of toxic stress occur, early detection, and early, evidence-based interventions are imperative to prevent toxic stress physiology from manifesting. Early action is "easier to implement, more effective, and less costly" than that implemented later in life.[23] Early detection of ACEs and other risk factors for toxic stress provide an opportunity to strengthen existing protective factors, initiate

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early buffering interventions, and ultimately prevent toxic stress physiology and downstream consequences, such as earlier-onset, more severe ACE-Associated Health Conditions (AAHCs) or toxic-stress-related social consequences (see the next section, **Primary and Secondary Prevention Strategies in Healthcare**, for further details).[6-12]

TERTIARY PREVENTION

Tertiary prevention efforts target individuals who have already developed a disease or social outcome, and aim to lessen the severity, progression, or complications associated with that outcome. For instance, intensive rehabilitation programs can optimize function after injury, and chemotherapy and radiation therapy can reduce cancer progression. Tertiary prevention of HIV consisted of monitoring for and treating opportunistic infections in the 1980s, but since then, investments in basic, clinical, and translational research on HIV biology have yielded the modern era of more than 25 sophisticated antiretrovirals. Optimal treatment with these medications can now keep patients living long, healthy lives (see **TIMELINE OF HIV/AIDS PROGRESS**).[634]

Tertiary prevention of toxic stress involves optimizing outcomes in those who have already developed clinical evidence of a toxic stress response. Moreover, tertiary prevention of toxic stress in one generation can equate to biologically and behaviorally mediated primary prevention of toxic stress in the next (see **Intergenerational Transmission of Adversity** in Part I and **Tertiary Prevention Strategies in Healthcare** in Part II for details about mechanisms). Resilience-optimizing and toxic-stress-mitigating interventions for those with AAHCs and other consequences of toxic stress include enhanced supportive relationships, high-quality and sufficient sleep, nutrition, exercise, mindfulness practices, access to nature, and when needed, mental and/or behavioral health care, as crucial parts of treatment.[635]

Of note, these same strategies can also promote primary and secondary prevention of toxic stress, but their impacts depend on the characteristics of the target population: they are considered primary when applied to healthy individuals and

TERTIARY PREVENTION

Tertiary prevention efforts target individuals who have already developed a disease or social outcome, and aim to lessen the severity, progression, or complications associated with that outcome. For instance, intensive rehabilitation programs can optimize function after injury, and chemotherapy and radiation therapy can reduce cancer progression.

secondary when applied to at-risk individuals who have not yet developed toxic stress physiology. Enhanced biomedical research into specific therapeutic targets for toxic stress, its potential subtypes, and particular AAHCs is an important component of both secondary and tertiary prevention. In other sectors, these strategies often take the form of systems and processes that prevent further harm from befalling someone who has toxic-stress-related outcomes and is particularly vulnerable to further impacts. Tactics include de-escalation and restorative justice practices in the criminal justice system, or an individualized education program (IEP) for students exhibiting symptoms of toxic stress in the education sector. The sections that follow will put these strategies into context for a number of sectors, including healthcare, public health, social services, early childhood, education, and justice.

TIMELINE OF HIV/AIDS PROGRESS [636,637]

1981 The first known case of HIV/AIDS. CDC issues reports on young men with rare pneumonia and Kaposi's sarcoma, a rare cancer, later found to be associated with AIDS.

1982 CDC establishes the term AIDS. The first United States (US) Congressional hearings on AIDS are held.

1983 The World Health Organization (WHO) holds its first meeting on the global impacts of AIDS and begins international surveillance. The US Public Health Service recommends prevention of HIV through safer sexual contact and blood transfusions.

1984 Dr. Robert Gallo of the National Cancer Institute and Dr. Luc Montagnier of the Pasteur Institute announce discovery that HIV is a retrovirus.

1985 The US Department of Health and Human Services (HHS) and WHO host the first International AIDS Conference. Blood banks begin screening donated blood for HIV after the US Food and Drug Administration (FDA) approves the first HIV antibody test.[638] The US Public Health Service issues its first recommendations for preventing perinatal transmission of HIV.[639] Ryan White, an Indiana teenager who contracted HIV through blood transfusions, is barred from school due to unfounded fears of spreading HIV—he goes on to raise public awareness about AIDS stigma and discrimination.

TIMELINE OF HIV/AIDS PROGRESS

1986 US Surgeon General Koop issues a Surgeon General's Report on AIDS, calling for public education on how HIV is spread, and for condom use to prevent the transmission of HIV.[640] An Institute of Medicine report provides national HIV strategy recommendations, including the importance of public education.[641]

1987 The FDA approves zidovudine, or AZT, as the first antiretroviral drug.[642] The FDA adds HIV prevention as a new indication for male condoms. The AIDS Memorial Quilt is displayed for the first time on the National Mall in Washington, DC. CDC launches the first AIDS-related television and radio public service announcements (PSAs), "America Responds to AIDS."

1988 WHO declares World AIDS Day. The US National Institutes of Health (NIH) establishes the Office of AIDS Research and the AIDS Clinical Trials Group. US Health Omnibus Programs Extension (HOPE) Act of 1988 authorizes use of federal funds for HIV/AIDS prevention, education, and testing. US Surgeon General C Everett Koop and CDC mail brochure "Understanding AIDS" to all US households, giving facts on HIV transmission. Comprehensive needle exchange programs are established in Tacoma, Washington; New York City, New York; and San Francisco, California.

1989 CDC issues its first guidelines for prevention of Pneumocystis carinii pneumonia (PCP), a common manifestation of AIDS.[643]

1990 The Ryan White Comprehensive AIDS Resources Emergency (CARE) Act of 1990 is enacted by Congress,[644] providing funds for community-based care and treatment services for HIV/AIDS.

1991 International Council of AIDS Service Organizations[645] forms as a global network of non-governmental and community-based organizations. The red ribbon is introduced as the international symbol of AIDS awareness.

1992 The FDA licenses the first rapid (10-minute) HIV test.

1993 President Clinton establishes the White House Office of National AIDS Policy. Congress enacts the NIH Revitalization Act, giving the Office of AIDS Research oversight over all NIH HIV/AIDS research, and establishing guidelines for more intentional inclusion of women and minorities.

1994 AIDS becomes the leading cause of death for all Americans ages 25 to 44 years (through 1995). The US Public Health Service recommends the use of AZT by pregnant women to reduce perinatal transmission of HIV by approximately 2/3.[646] The FDA approves an oral HIV antibody test, the first non-blood-based test of its kind.

1995 The FDA approves the first protease inhibitor, saquinavir, to reduce HIV burden in infected people.[647] CDC issues the first guidelines for prevention of opportunistic infections in HIV-infected persons, and a report on syringe exchange programs as a prevention

TIMELINE OF HIV/AIDS PROGRESS

strategy. The first National HIV Testing Day is held.

1996 The number of new AIDS cases diagnosed in US declines for the first time, with HIV no longer the leading cause of death for all Americans ages 25-44 years, but remains so for Black Americans in this age group. The FDA approves the viral load test, the first HIV urine test, the first HIV home testing and collection kit, and the first non-nucleoside reverse transcriptase inhibitor, nevirapine. Congress reauthorizes the Ryan White CARE Act. AIDS awareness ad campaigns launch that target the general public, not only those at high risk.

1997 AIDS-related deaths in US decline by more than 40% compared to prior year, largely due to highly active antiretroviral therapy (HAART). FDA approves Combivir, a tablet combining two ARV drugs, making it easier to take.

1998 The first large-scale human trials for an HIV vaccine begin. HHS issues the first national guidelines for the use of antiretroviral therapy in adults. The Minority AIDS Initiative[648] is created, after Black American leaders declare a "state of emergency."

1999 President Clinton announces Leadership and Investment in Fighting an Epidemic for increased funding to address the global epidemic.

2000 CDC forms the Global AIDS Program.[649] Congress reauthorizes the Ryan White CARE Act for the second time.

2001 The World Trade Organization announces the Doha Declaration, which promotes access to generic HIV medications in developing countries.[650] The first National Black HIV/AIDS Awareness Day in the US is observed.

2002 HIV is the leading cause of death worldwide among those aged 15-59 years. The Global Fund to Fight AIDS, Tuberculosis and Malaria[651] begins operations. The FDA approves OraQuick Rapid HIV-1 Antibody Test, the first rapid finger prick test.

2003 President Bush announces the President's Emergency Plan for AIDS Relief (PEPFAR), a five-year, $15 billion initiative to address HIV/AIDS, tuberculosis, and malaria in countries heavily impacted by HIV. WHO announces the "3 by 5" Initiative,[652] intended to bring treatment to 3 million people by 2005. The first National Latino AIDS Awareness Day in US is observed.

2004 The FDA approves OraQuick Rapid HIV-1 Antibody Test for use with oral fluid. The Joint United Nations Programme on HIV/AIDS (UNAIDS) launches the Global Coalition on Women and AIDS to raise the visibility of the epidemic's impact on women and girls.

2005 WHO, UNAIDS, the US government, and the Global Fund to Fight AIDS, Tuberculosis, and Malaria join efforts to increase availability of antiretroviral drugs in developing countries. The first National

TIMELINE OF HIV/AIDS PROGRESS

Asian and Pacific Islander HIV/AIDS Awareness Day in the US is observed.

2006 CDC releases revised HIV testing recommendations for healthcare settings, recommending routine HIV screening for all adults, ages 13-64, and yearly screening for those at high risk. Congress reauthorizes the Ryan White CARE Act for third time. The first National Native HIV/AIDS Awareness Day and the first National Women and Girls HIV/AIDS Awareness Day in the US are observed.

2007 WHO and UNAIDS issue new guidance recommending "provider-initiated" HIV testing in healthcare settings.

2008 Congress reauthorizes PEPFAR for an additional five years at up to $48 billion. The first National Gay Men's HIV/AIDS Awareness Day in the US is observed.

2009 President Obama launches the Global Health Initiative[653] to address health in low- and middle-income countries, with PEPFAR as a core component. The first National Caribbean American HIV/AIDS Awareness Day in the US is observed.

2010 Obama Administration releases the first comprehensive National HIV/AIDS Strategy for the US. President Obama signs comprehensive health reform, the Patient Protection and Affordable Care Act (ACA), which provides new health insurance opportunities for millions, including people with HIV. The first large international clinical study (iPrEx) on pre-exposure prophylaxis (PrEP) shows efficacy of this strategy.[654]

2011 A large, multinational study (HPTN 052) of serodiscordant, mostly heterosexual couples shows early treatment of HIV-infected persons greatly reduces transmission to negative partners.[655] HHS launches 12 Cities Project, focusing resources on areas with the highest HIV/AIDS burden in the country.[656]

2012 The FDA approves OraQuick In-Home Test, the first rapid test using oral fluid that can be bought over-the-counter, results of which are obtained at home. The FDA approves the use of Truvada (emtricitabine/tenofovir disoproxil fumarate) for reducing risk of HIV infection in uninfected individuals at high risk, making it the first HIV treatment to be approved for PrEP.

2013 UNAIDS reports that since 2005, deaths related to AIDS have declined by almost 30%. WHO releases new guidelines recommending earlier use of antiretrovirals, and antiretroviral therapy for children under 5 with HIV, pregnant and breastfeeding women with HIV, and HIV-positive persons with uninfected sexual partners. The US Preventative Services Task Force (USPSTF) gives routine HIV screening an A grade, indicating that "there is high certainty that the net benefit is substantial."[657]

2014 Major Affordable Care Act reforms enacted, improving healthcare coverage for many people with and at risk for HIV in US.

2015 WHO announces "treat all"

TIMELINE OF HIV/AIDS PROGRESS

recommendation, calling for HIV treatment as soon as possible following diagnosis to optimize outcomes. Congress lifts restrictions, under certain circumstances, for the use of federal funds to cover syringe services for HIV outbreaks related to injection drugs.

2017 The United Nations and partners announce a pricing agreement towards the first affordable, generic, single-pill HIV treatment regimen in low- and middle-income countries.

2020 CDC publishes an association between increased PrEP coverage and decreased HIV diagnosis rates and re-releases its HIV Risk Reduction Tool.[658] More than 25 options for HAART now exist.[634]

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.[619] 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.[659] 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.[660,661] It is therefore beneficial for all patients, providers, and staff.[662,663]

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:[659,664]

- **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:[659,664]

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.[23,31,47] 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.[23,31,47] Promoting family strengths and healthy parenting is fundamental to preventing ACEs as well as to the mitigation of and healing from impacts of ACEs.[23]

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.[41,43,44,97,604,665,666] 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.[667] 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.[604,667] 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.[41,43,44,97,604,665,666]

PCEs can coexist with ACEs and can reduce the risk that ACEs will lead to toxic stress and associated negative outcomes.[41,43-45,97,604,665,666] 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.[668-672] 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.[41,604] They are also substantially less likely to experience positive relationships and social connection as adults.[41] 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.[673] Many science-based tools and resources are available for healthcare providers on the Harvard Center on the Developing Child website.[674] Other sources of specific educational messaging and tools include the American Academy of Pediatrics' (AAP's) Connected Kids: Safe, Strong, Secure Clinical Guide[675] and the Healthy Outcomes from Positive Experiences (HOPE) websites.[676]

Adult care providers also play an important role in primary prevention of ACEs and toxic stress.[23] 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.[2] 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.[677-679] Many ACE-Associated Health Conditions (AAHCs) in adults are ACE risks for the next generation (such as violence, mental illness, and substance use),[2] and AAHCs can enhance family stressors, including disability and financial impacts due to lost productivity.[63,64,680] 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[23] (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.[681] 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.[682]

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:[23,31,619]

- Optimizing social-emotional and other learning at home, such as through the Talk. Read. Sing.®[683] or Reach Out and Read[684] 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).[685]

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.[686-688]

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).[689] 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.[690-693] 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).[31,690,691,694,695]

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.[31]

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,[696] 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.[31] 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.[31]

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,[697] 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.[698] 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 (NASEM), 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.[7,23,31] 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.[699] 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,[700] asthma in school-age children,[701] delayed menarche in teenage girls,[702] and cardiovascular disease in adults.[207]

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.[703]

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 ≥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.[23,603,704]

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).[705] However, intergenerational transmission of ACEs can be reduced through interventions such as positive parenting skill-building and treating parental AAHCs.[553] 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.[706] Prenatal providers can also help parents space births, which may reduce the risk of child maltreatment[707] by preventing unintended pregnancies, which is a risk factor for abuse and neglect behaviors in both parents.[708] 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.[679]

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.[2] 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.[63,64,680] 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.[31]

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.[709-712] 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**[713] and **love is respect**[714]), documenting referrals in the patient's chart to facilitate follow-up, discussing harm reduction strategies, and planning close follow-up.[715] This approach has been shown to improve patient knowledge and decrease reproductive coercion and abuse.[715,716]

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.[717,718] 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.[699]

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.[41] 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.[604] Many studies show that reinforcing existing buffering relationships and environments can mitigate the impacts of ACEs.[41,43,45,62,97,696] 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.[45] 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).[45] 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%.[44] 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**).[32] 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%.[32] 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.[56,722] 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,[723] 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.[2]

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.[724] 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.[2,3,5,15,16,30,613] While the prevalence of toxic stress is unknown, exposure to childhood adversity is well established to be mechanistically linked to toxic stress,[6,12,60,319] 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-

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%[¥]	37.2% 38.6%[¥]
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*[s]
% *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%¥	5.9%¥ 7.9%¥	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%

% *All California children*[s]
% *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.*[39]

[s]*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.*

[¥]*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**).[6,23,603,725,726] 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,[56,722,727-733] adult primary care,[734,735] family medicine,[736] and prenatal care.[678,679] 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.[737]

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.[6,60] The physiological stress response is characterized as either positive, tolerable, or toxic.[6,7] 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.[719] 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.[720] 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.[630] 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.[630] 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.[721]

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.*[26]

as possible because adversity can become biologically embedded as early as the prenatal period,[421] and the signs of toxic stress can manifest as early as infancy.[700]

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.[699] 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.[56] 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.[738]

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).[56,678,727-730,734-736] 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.[678,697,728,729,739,740] Studies also suggest that screening does not significantly extend visit times (<5 minutes),[736] and may even reduce them.[730,731] 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.[6,12,60,319] 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."[23] 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.[6,7,23] 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).[86] 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,[86] discussed further in **The ACEs Aware Initiative**.[86] The National Pediatric Practice Community on ACEs (NPPC) has put forward similar algorithms for assessment and response.[741] 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.[7,23,31]

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.[64] More than 75% of the costs were attributed to individuals with two or more ACEs.[64] The study suggested that reducing ACE prevalence by just 10% could save $105 billion annually, considering just the 10 AAHCs included in the study.[64] As referenced in **Principle 1**, the cost of AAHCs in California is similarly enormous.[63] While further studies are needed, current evidence suggests that screening and intervention for toxic stress may be associated with improved healthcare utilization.[697,739,740]

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.[3,5,13,30] 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.[3] 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.[742] Children should be rescreened periodically to monitor for additional ACEs.[743] 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,[56,678,722,728-731,734,735,739] 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.[422]
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[678] 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[729] 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,[376] hypertension,[212] chronic obstructive pulmonary disease exacerbations,[372] and poor birth outcomes.[394] 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.[212,376] Acute stressors are also associated with increased incidence of ACEs, such as child abuse[362] and intimate partner violence,[396] and with new or recurrent health conditions that in parents may serve as ACEs, including substance use disorders[385] and mental health exacerbations.[360,362,383,744,745] 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,[403] and

IMPLICATIONS OF COVID-19

children without social supports were at greater risk of persistent post-traumatic stress symptoms related to disasters.[364]

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[86] 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**,"[746] 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.[361,383] 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.[747] 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.[748]

Tertiary Prevention Strategies in Healthcare

This section's goal is to offer strategies and interventions to reduce the impact of the toxic stress response, once these physiological processes are already underway. There is an urgent need for healthcare providers to be familiar with the toxic stress response, the ways in which it can alter physiology, and evidence-based or promising practices for treatment. While the American Heart Association and other entities have increasingly recognized Adverse Childhood Experiences (ACEs) as a significant risk factor for chronic disease,[749] few, if any, clinical treatment guidelines incorporate strategies for mitigating the toxic stress response.

This section summarizes current science and clinical practice for supporting individuals with positive ACE screens (i.e., those who are assessed to be at intermediate or high risk for toxic stress). It offers information on interventions that target the underlying biological mechanisms of toxic stress to improve neuro-endocrine-immune-metabolic functioning and ACE-Associated Health Conditions (AAHCs). Overall, the goal is to highlight tools and interventions that can be used in the primary care setting, as well as strategies for trauma-focused partnerships and referrals. Moving forward, evidence-based treatment guidelines to address the role of toxic stress physiology in the treatment of AAHCs are necessary, such as for asthma, autoimmune disease, cardiovascular disease, and mental health disorders.

DIAGNOSIS

As discussed in the previous section, 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. Of important note, there currently exist no widely agreed upon clinical diagnostic criteria for toxic stress, and the toxic stress response is not listed in the International Classification of Diseases (ICD). Although the biological mechanisms of toxic stress are well supported by a consensus of scientific evidence, further research is necessary to determine whether the toxic stress response is best characterized as a condition, a disorder, or a disease.

In the absence of clinical diagnostic criteria, the combination of ACE score and the presence or absence of AAHCs may serve as a somewhat crude, but useful, proxy for the likely presence of a toxic stress response. Pending the development of confirmatory diagnostic criteria and/or biomarkers, the evidence supports characterizing a patient as being at low, intermediate or high risk of manifesting a toxic stress response. The ACEs and Toxic Stress Risk Assessment Algorithms (**Figures 8 a,b**) for pediatric and adult care were created by a team of expert researchers and clinicians, led by the Office of the California Surgeon General, to assist providers who screen for ACEs in assessing risk for toxic stress.[86]

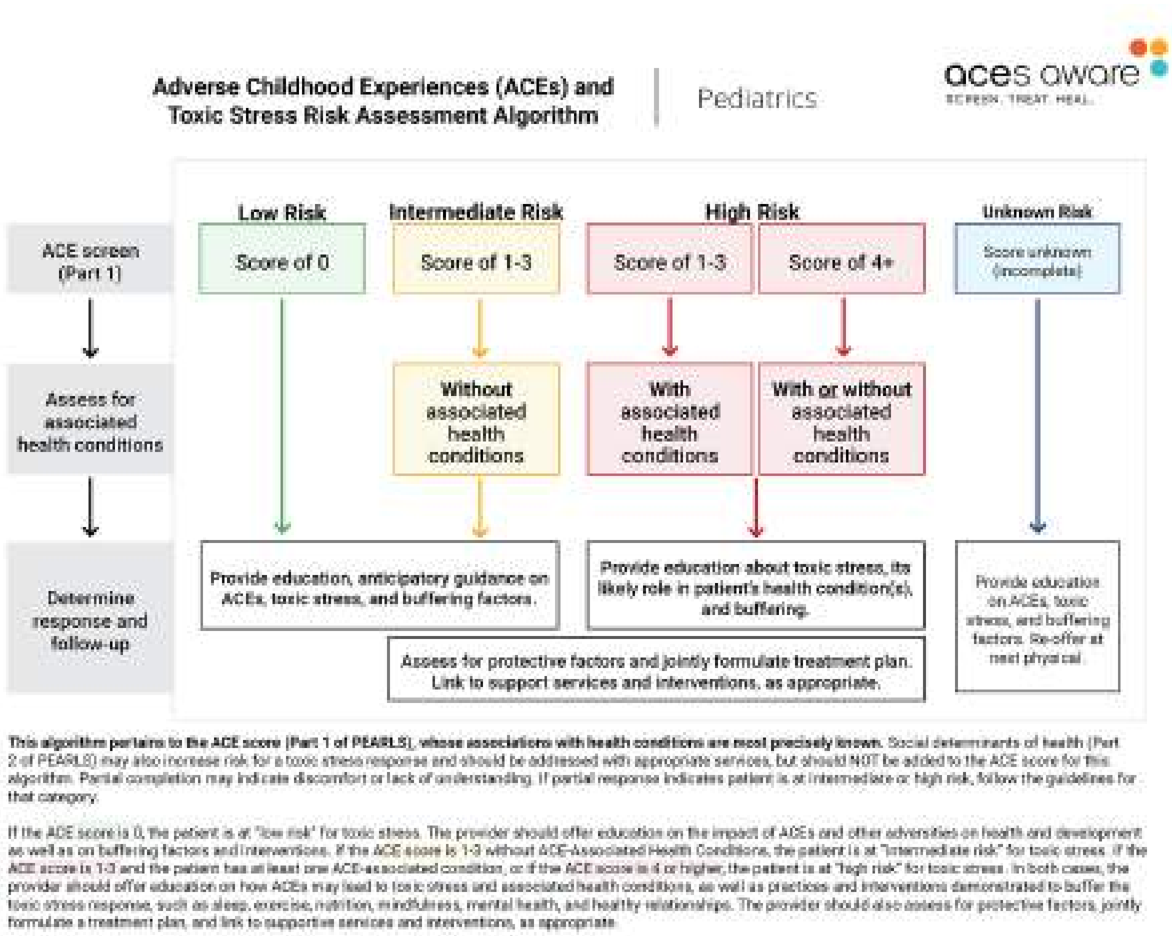


Figure 8a. *ACEs and toxic stress risk assessment algorithm for pediatrics. Reproduced with permission from ACEs Aware.*[86]

CLINICAL RESPONSE

Anticipatory guidance, interventions, and referrals should start with addressing any immediate safety concerns, and attention to the key principles of trauma-informed care (TIC), reviewed in the last section (**Primary and Secondary Prevention Strategies in Healthcare**).

This section on tertiary prevention offers research-based tools that are associated with mitigation of toxic stress. The strategies that follow can also be used as a framework for a meaningful and supportive approach that emphasizes strengths and intervention options for managing toxic stress. For example, an adult patient found to be at low risk of toxic stress (ACE score of 3, no associated symptoms or

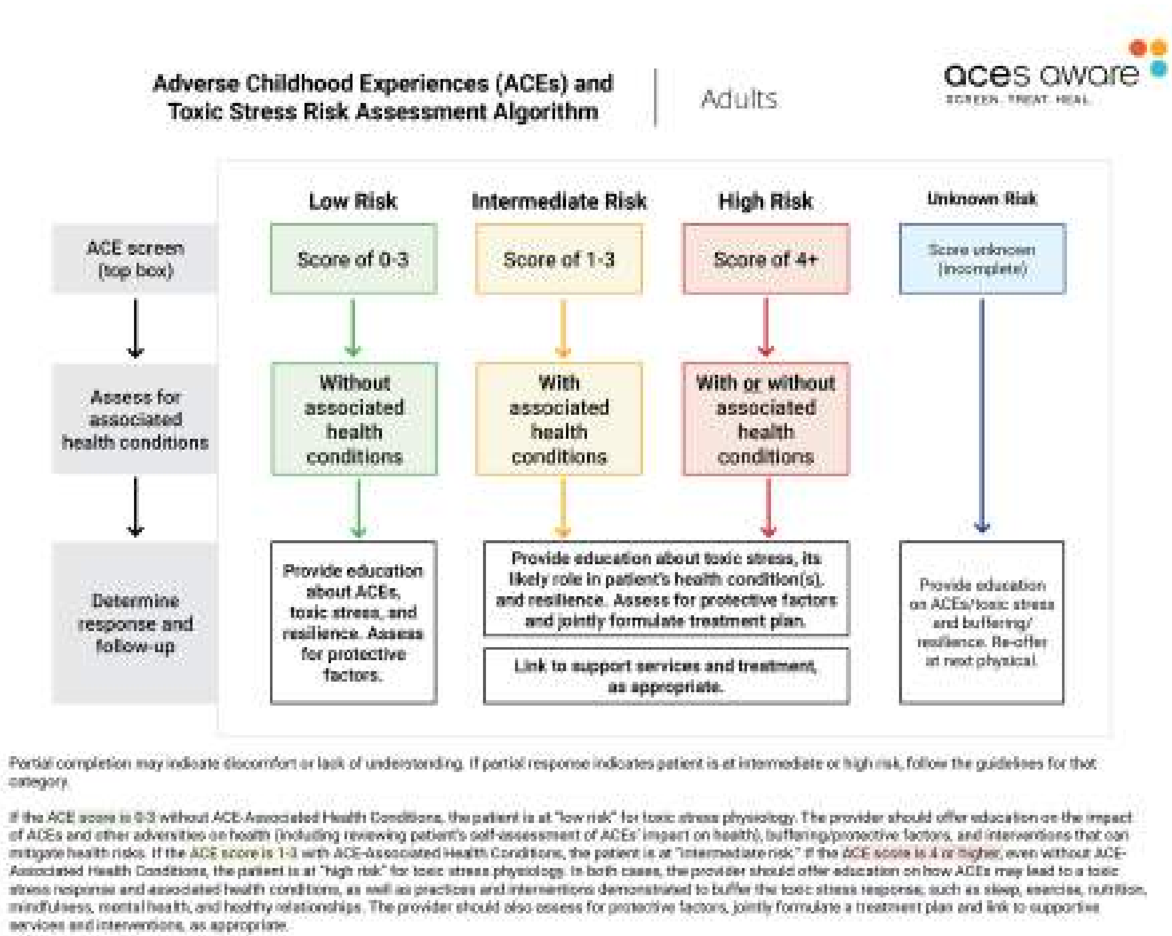


Figure 8b. ACEs and toxic stress risk assessment algorithm for adults. Reproduced with permission from ACEs Aware.[86]

Figure 9. *Employing the evidence-based strategies for toxic stress regulation can help patients reduce stress and build resilience. Reproduced with permission from ACEs Aware.*[26]

conditions) and with a number of protective factors may not need any additional interventions or referrals beyond patient education. However, a patient determined to be at intermediate risk of toxic stress (ACE score of 1, with symptoms of depression and poorly controlled asthma) and with limited social supports may benefit from specific interventions that target the toxic stress response, as well as referrals for community and/or mental health resources.

The stress-mitigation strategies listed below can be used as a framework for patient education and as an adjunct to usual care for AAHCs, as they have all been shown to reduce stress hormones, reduce inflammation, and enhance neuroplasticity[603,750-759]—key mechanisms to counteract the toxic stress response and improve overall health and well-being. These strategies offer an integrative approach to ACEs and toxic stress intervention:

- Healthy relationships
- High-quality, sufficient sleep
- Balanced nutrition
- Regular physical activity
- Mindfulness and meditation
- Access to nature
- Behavioral and mental healthcare

HEALTHY RELATIONSHIPS

Relational health is a relatively new term used to highlight the growing body of science detailing the importance of relationships to health and well-being.[102,544-546,549,551,760,761] Research shows that relationships can buffer stress and reduce, or in some cases, eliminate the negative health impacts associated with ACEs.[604,762]

HPA axis and cortisol

A growing body of research is identifying the positive impacts of relational health on neuro-endocrine-immune-metabolic function. In rats and primates, nurturing maternal interactions inhibits hypothalamic-pituitary-adrenal (HPA) axis reactivity in the presence of stressors.[750,763] Responsive caregiving mediates improved cortisol reactivity in children, and is associated with reduced health impacts of ACEs.[750,751]

Cardiovascular reactivity and autonomic nervous system

Social support is associated with lower blood pressure and a decreased risk for cardiovascular disease.[764] Supportive relationships have been shown to buffer stress-induced cardiovascular reactivity and are associated with lower plasma and urinary catecholamine (stress hormone) levels.[765]

Immune function

Social support and Positive Childhood Experiences (PCEs) have also been associated with decreased asthma symptoms and improved immune responses, including inhibiting inflammation, providing protection against infection, and promoting wound healing.[668-672] Social support can predict natural killer cell activity and helper T cells in HIV-positive individuals,[764] and has also been linked to decreased susceptibility to common cold.[764] Greater social integration has shown a dose-dependent association with reduced susceptibility to clinical illness and viral-specific antibody levels across two viruses.[762] Another study by the same group found that hugging had a stress-buffering, immune-protective effect and explained 32% of the attenuating effect of support on infection risk.[766] Relational health has also been associated with decreased markers of inflammation.[764]

Oxytocin

One mechanism by which supportive relationships are believed to lead to health-protective effects is through release of the hormone oxytocin. Oxytocin is produced in the hypothalamus and enhances bonding, inhibits the stress response, protects against stress-induced cell death, has anti-inflammatory effects, enhances metabolic homeostasis, and protects vascular endothelium.[671,672,767-769] It is released in high quantities during childbirth and lactation and is most widely used clinically for augmentation of labor.[767,770]

The amygdala (the brain's threat detector) has oxytocin receptors, allowing oxytocin to inhibit the amygdala-induced stress response, thereby inhibiting both the sympatho-adreno-medullary (SAM) and HPA axes, which constitute the fight-flight-or-freeze pathways.[767] Oxytocin has been associated with reductions in anxiety and stress, and can modulate trust and social memory.[767] Oxytocin has been suggested to inhibit stress-hormone-related neuronal cell death in the hippocampus, a brain structure involved in memory.[768] Oxytocin also appears to be involved in safety learning and extinguishing fear when safe[771] and has been shown to support interoceptive (internal awareness) sensitivity and lower somatic problems in children.[772] The tend-and-befriend response to stress, possibly more prominent in females, may also be linked to oxytocin release.[773,774]

Oxytocin has been investigated as a potential therapeutic agent for several AAHCs. Research to date is mixed, but suggests that oxytocin may support cardiovascular health, including reversing atherosclerosis associated with heart disease,[769] promoting weight loss, metabolism of sugar and fat, insulin sensitivity,[775] mitigating post-traumatic stress disorder (PTSD), antisocial symptomatology,[776-779] strengthening immune defense, inhibiting inflammation, and promoting wound healing.[671,672]

However, oxytocin is also associated with increased self-versus-other distinction,[780] which can increase us-versus-them thinking and lead to greater sensitivity to social threats.[780,781] Increases in hostility, aggression, and parasympathetic response to interpersonal threat have also been associated with oxytocin.[780,782] Further research on potential therapeutic uses of oxytocin to mitigate toxic stress is warranted.

Assessment of relational health

While there are a number of validated, research-based tools to evaluate attachment and relational health, there are very few short, dynamic screens available for easy use in primary care clinical practice. While tools such as the Protective Factors Survey may be useful, providers are also encouraged to have an open conversation with their patients about relational health and specifically ask about perceived social support (Do you feel you have someone who understands and believes in you, who you could talk to when you are upset?), received social support (When needed, do you have someone that can give you emotional, financial, or material support—for example, a car ride to the clinic?) and social integration (Do you feel you belong and are part of a group/community?). If relational health issues are identified, the strategies and programs presented below can support healthy relationships and connections within the community. Referrals to these needed resources can be included with other referrals.

Relational health in pediatrics

There are a number of programs that have been developed to support the child–caregiver relationship that can be used in the pediatric primary care clinic setting.[783,784] Universal primary prevention, including routine anticipatory guidance about relational health and developmentally appropriate play such as Talk. Read. Sing.[785] and clinic programs such as Reach Out and Read,[786,787] have been recommended by the American Academy of Pediatrics. Key components of high-quality programs include opportunities for parents and patients to network with and receive support from peers who have been in similar situations, engaging fathers, and treating parents and patients as equal partners.[553,788]

Of note, the intergenerational pattern observed with ACE transmission reflects that children with high ACEs often have parents with high ACEs. Some dyadic or two-generation interventions specifically target addressing parental trauma as a means to improve child outcomes. Targeted interventions to repair strained relationships include Attachment and Biobehavioral Catch-up (ABC), Child-Parent Psychotherapy (CPP), and Parent-Child Interaction Therapy (PCIT).[699,789-791]

These interventions have been associated with improvement in various markers of neuro-endocrine-immune-metabolic regulation, including cortisol, epigenetic regulation, and brain development.[603,792,793] ABC has been found to improve child attachment, cortisol levels, emotion regulation, executive functioning, as well as increased parent sensitivity to their child.[789] CPP has been associated with improvements in child behavioral problems and child traumatic stress disorder symptoms,[587] as well as protecting against telomere shortening.[492] PCIT has been shown to decrease negative parent–child interactions,[791] and to reduce child aggressive behavior and cortisol levels.[792]

A systematic review of interventions in pediatric care to improve ACE-related child outcomes found that multicomponent interventions including parenting education, mental health support, and social service referrals were associated with improvements in parent–child relationship and behavioral and mental health problems.[794]

Adolescents and adults

Difficult relationships during childhood may affect the ability to make meaningful and trusting personal connections or engage in group activities. If indicated, referral for individualized mental health therapy may help patients overcome issues with trust and safety, and develop skills to form healthy relationships. (See the subsection on Mental and Behavioral Health below.)

Providing education about healthy relationships can help patients and caregivers understand the normal and expected reactions to ACEs and toxic stress so that they can better regulate themselves and respond to others in challenging situations. The patient–provider relationship can be a model for the healthy relationships providers hope to promote for their patients. This includes supporting self-care for healthcare providers to reduce burnout and compassion fatigue.

KEY TAKEAWAYS: HEALTHY RELATIONSHIPS

> Key aspects of relational health include having safe, stable, and nurturing relationships and environments.

> Relational health has been associated with improved mental, cognitive, cardiovascular, and immune health, and has been shown to buffer the stress response system.

> Difficult relationships during childhood may affect the ability to make meaningful and trusting personal connections or engage in group activities.

> Patients and clients may be encouraged to connect with supportive relatives, friends and community activities.

> Improving relational health requires an individual, family and community approach.

> The patient-provider relationship can be a model for the healthy relationships providers hope to promote for their patients.

> Self-care for health providers is an essential component of trauma-informed clinical care.

SLEEP

Sleep disturbances are among the most common and nonspecific outcomes of childhood adversity.[795,796] Stress can cause increased, decreased, or disordered sleep,[795-797] and children and adults with a history of ACEs may be more vulnerable to the effects of subsequent stressors due to sensitization of the stress response.[798-800] A systematic review of ACEs and sleep disorders found associations between family conflict in childhood and insomnia at 18 years of age, as well as between child sexual abuse and sleep disturbances.[796] Nightmares are one of the intrusion symptoms involved in PTSD diagnosis; however, additional disruptions in sleep have also been noted. Researchers are currently investigating the development of criteria for "trauma-associated sleep disorder" (TASD), which would include nightmares, disruptive nocturnal behaviors (moaning, screaming, tossing, turning, or thrashing), increased heart rate, more rapid breathing, and sweating.[797]

Poor sleep is linked with poor health outcomes. Disordered or reduced sleep duration is associated with heart disease, hypertension, obesity, diabetes, cancer, decreased cognitive performance, depression, anxiety, inflammatory diseases, infection risk, and all-cause mortality.[752,753,801-804] In children, poor sleep is associated with impairments in neurocognitive development, social emotional skills, physical health, and family functioning.[805] Understanding the mechanistic pathways linking trauma, disordered sleep, and poor health outcomes can help direct interventions.

Neuroendocrine pathways

Normal sleep increases growth hormone, prolactin, and melatonin, and supports memory consolidation.[752,753,802,804] Healthy sleep also allows for the normal circadian rhythms of cortisol levels and supports decreases in sympathetic nervous system (SNS) output.[752,753] Adversity and toxic stress may impair sleep by dysregulating cortisol and SNS activity.[752,753,806] The reverse has also been found: profound sleep loss can activate the fight-flight-or-freeze system.[752] Disruptions in sleep are associated with altered levels of cortisol,[804] as well as increases in norepinephrine, epinephrine, and blood pressure.[752]

Poor sleep alters other endocrine and metabolic functions. Sleep deprivation can increase appetite and caloric intake.[804] It is also associated with elevated insulin and blood glucose levels and altered brain glycogen.[804] In adolescents, short sleep has been independently associated with insulin resistance.[807]

Immune pathways

Sleep deficiency disturbs immune system homeostasis and is associated with chronic, low-grade inflammation.[752,802] Healthy sleep is associated with a reduced risk of infection, improved infection outcomes, and improved response to vaccination.[802] It is associated with early increases in inflammatory markers needed for healthy immune function, while later in sleep, counterregulatory processes develop.[752] Natural killer cell activity increases over the course of sleep, as do inflammatory markers IL-6 and TNF, which can affect immune response.[752] Unhealthy alterations in sleep are associated with altered immune cell counts and dysregulation of these inflammatory markers.[752]

It is important to note that immune activation may also disrupt sleep.[802] In animal studies, IL-1, TNF, and PGD2 promoted non-REM sleep and at high doses, may suppress REM sleep.[802] Research is still exploring how these domains of stress regulation are interrelated.

Assessment of sleep

While there are validated sleep-assessment tools, such as the Pittsburgh Sleep Quality Index and the Insomnia Severity Index, the most pragmatic approach for a busy clinic may be to highlight four key elements: patient satisfaction with sleep, whether patients feel restored and rested when they wake up, whether they have trouble falling asleep initially, and whether they have trouble staying asleep or falling back to sleep if they wake up in the middle of the night.[752] Sleep diaries, sleep apps, actigraphy (wearable devices), and polysomnography can be used when more data is needed, especially if there is concern for obstructive sleep apnea or sleep-disordered breathing.[752]

Behavioral strategies

Interventions to support healthy sleep can decrease stress and improve health outcomes. Generally, behavioral techniques and education about healthy sleep habits (also known as sleep hygiene) are first-line interventions.[808,809] These include eliminating electronics, caffeine, alcohol, and exercise close to bedtime; creating a sleep routine; using the bed for sleep (and, for adults, sex) only; and getting out of bed if one cannot sleep.[810] A meta-analysis of sleep interventions for adults without diagnosed sleep disorders found that cognitive and behavioral interventions, including relaxation practices, sleep hygiene, and exercise improved sleep quality.[811] In addition, the triad of healthy nutrition, exercise during the day, and sleep has been shown to reduce the risk of developing neuropsychiatric disorders.[812]

A consistent bedtime routine improves sleep, child mood, emotional behavioral regulation, mother's self-reported mood, school readiness, and literacy outcomes (especially when reading is part of the bedtime routine); it has been associated with decreased bedtime tantrums (and associated improvements in marital satisfaction) and can be a buffer against parenting stress.[805,813,814] Bedtime routines can create a sense of predictability and stability known to support trauma healing and resilience building.[815] Bedtime routines can include feeding (for infants and children), bath, massage, reading books, rocking, prayer, singing, and listening to music.

It is important to note that children with neurodevelopmental, mental health, or trauma-related conditions may need different or more flexible bedtime routines than neurotypical children.[813] For example, children and adults experiencing nightmares, anxiety, depression, or fear may need specific coping strategies such as a night light, a weighted blanket, and relaxation techniques. Efforts to have a traumatized child sleep-train or "cry it out" may increase fear, isolation, and trauma reactions. Medical providers can remind parents about their ability to buffer the threat-response system and encourage them to discuss fears and solutions openly with their child.[704]

Behavioral therapies

- Parent-child groups, parenting classes, and case management in infancy and early childhood are associated with improved sleep schedules at age three years.[816]

- Meditation, tai chi, yoga, and exercise have been shown to improve sleep quality.[752,817-819]
- Cognitive-behavioral therapy (CBT) has been associated with reduced insomnia and decreased markers of inflammation.[752] In addition, there is a specific CBT protocol for insomnia, CBT-I.[810]
- Imagery rehearsal therapy and exposure, relaxation, and rescripting therapy, both of which involve rescripting and rehearsing changes to a recurrent nightmare, have been shown to decrease recurrent nightmares.[820,821]
- Medications such as melatonin or prazosin may be indicated in some cases.[821-827] Physicians and patients can together determine whether medication is an appropriate option.
- Given that inflammation can aggravate healthy sleep, studies are currently being done to evaluate the effectiveness of immune therapies for sleep. For example, TNF-α blockers have been shown to improve sleep.[828]

KEY TAKEAWAYS: SLEEP

> Sleep disturbances in childhood and adulthood are common outcomes of childhood adversity.

> Poor sleep is associated with increased risk for heart disease, obesity, diabetes, cancer, decreased cognitive performance, depression, anxiety, inflammatory diseases, infection risk, and all-cause mortality.

> Healthy sleep can improve neurological, endocrine, metabolic and immune regulation and is associated with improved health outcomes.

> Healthy sleep habits include eliminating electronics, caffeine, alcohol, and exercise close to bedtime, creating a sleep routine, using the bed for sleep (and, for adults, sex) only, and getting out of bed if one cannot sleep.

> Children with neurodevelopmental, mental health, or trauma-related conditions may need different or more flexible bedtime routines than neurotypical children, including a night light, a weighted blanket, relaxation techniques, or conversations with a trusted adult about strategies to address specific worries.

> Meditation, yoga, and exercise during the day can also improve sleep.

> For people with significant sleep disturbances additional assessment and interventions may be indicated, including medications and cognitive-behavioral therapies.

NUTRITION

ACEs have been linked to increased risk of obesity, insulin resistance, and diabetes, as well as eating disorders such as anorexia nervosa and bulimia.[829-832] In one study of girls, child sexual abuse was associated with increased risk of obesity (odds ratio, OR: 2.6; 95% confidence interval, CI: 1.1–6.4) and extreme weight-loss behaviors (OR: 2.2; 95% CI: 1.0–4.7), and parental unemployment was associated with obesity (OR: 3.5; 95% CI: 1.2–9.6) and being underweight (OR: 3.6; 95% CI: 1.1–11.6).[830] In another study, a dose-response effect was noted between child trauma subtypes and the severity of eating disorder symptoms.[831] Among people with eating disorders, several systematic reviews found a higher prevalence of ACEs.[833-836]

Bidirectional relationship

There is a bidirectional relationship between nutrition and stress: malnutrition/undernutrition can activate the physiologic stress response, and, conversely, stress can affect food behavior, digestive processes, and metabolism.[837] Calorie restriction has been associated with increased cortisol levels and reduced white blood cells (lymphocytes), or lymphopenia.[838] Interestingly, alleviation of the stress rapidly reverses the lymphopenia.[838] Maladaptive nutritional coping strategies, including preference for high-fat and high-sugar foods, can lead to increased inflammation or infection risk.[837] Patients with eating disorders have been found to have either greater basal cortisol levels or greater cortisol reactivity.[838] Additionally, obesity is associated with physiological stress, chronic inflammation, and oxidative stress.[838] As an example of the interrelated pathways between food and stress, one study found food insecurity was linked to maternal perceived stress and increased fat intake, while pre-pregnancy body mass index (BMI) was associated with food insecurity status.[839]

Stress affects food behavior

Norepinephrine and epinephrine are released as part of the threat response and affect metabolic functions, including increasing glucose mobilization, insulin resistance, and glucagon secretion and decreasing gut motility and gastric emptying.[74,839,840] Glucagon, in turn, decreases appetite.[74] Glucocorticoids, however, have been shown to stimulate appetite, especially for carbohydrates and fat.[74,837,841] High-fat and high-sugar diets can temporarily decrease the cortisol response and feelings of anxiety and stress,[837,839] potentially reinforcing this pattern of eating as a way to calm an overactive threat response system, and promoting risk for diabetes, cardiovascular disease, obesity, and other diet-related health effects.

Researchers have identified different time courses for the impacts of neurotransmitters; norepinephrine and epinephrine act in seconds to minutes, while glucocorticoids act in hours to days.[74] Thus, it may be that decreased appetite occurs early in the stress response, and increased appetite occurs in the later phase. Researchers suggest that many of the glucocorticoids' actions are to help prepare the individual for future threats and that the effects of glucocorticoids on appetite and metabolism may support future stress reactions.[74,842] Thus, under- and overeating may both be neurobiological adaptations to stress.

Neuroendocrine and immune impacts

Diet can directly affect the immune system.[840,843] For example, produce with residual pesticides, fast food, and overly processed foods are pro-inflammatory.[844-847] The Western diet (high in red and processed meat, saturated fats, and refined grains) has been associated with increased inflammatory markers compared to diets with greater fruit, vegetables, fish, and whole grains.[840]

The Mediterranean diet, which emphasizes olive oil, fish, whole grains, fresh fruit, and vegetables, has been associated with reduced inflammation and decreased risk for depression, cardiovascular disease, diabetes, and total mortality.[843] Olive oil use has been associated with lower biomarkers of inflammation.[843]

Assessment

Given the complex and interconnected nature of diet, nutrition, stress, eating disorders, and obesity, measuring BMI and weight alone are not sufficient to assess nutritional status.[848] Patient completion of a 24-hour food recall or a food diary (which can be supported with downloadable apps) can be useful clinical techniques.

Interventions

Given the literature identifying the strong link between stress, nutrition, and neuro-endocrine-immune-metabolic functioning, an adequate and balanced diet, as well as nutritional supplementation, may help support regulation of the toxic stress response.

It is important to consider from the outset how patient education around diet and weight is given. Nutritional counseling for patients found to be at intermediate or high risk for toxic stress should include consideration of the biological drive for high-fat, high-sugar foods and the complex interplay between food, stress, and neuro-endocrine-immune-metabolic function. Any implication that dietary choices and weight gain are due solely to lack of willpower and poor personal choices is not biologically accurate. A trauma-informed approach can help decrease blame and shame and identify a more comprehensive strategy to treat eating disorders or obesity as part of a toxic stress phenotype.

Trauma-informed strategies to support healthy eating habits include helping patients identify healthy forms of high-fat, high-energy foods, such as nuts, yogurt, fish, and avocados, and offering strategies to increase use, including storing them in easily accessible places (while putting the junk food in hard-to-reach places or gradually eliminating it). Recognizing that toxic stress can lead to inflammation, medical providers may consider offering patient education about anti-inflammatory diets, such as those high in fruits and vegetables, and low in pro-inflammatory foods, such as fast food and overly processed foods.

Several researchers have highlighted the importance of specific nutritional interventions in decreasing stress and inflammation.[849,850]

Polyunsaturated fats

Polyunsaturated fats support brain function, cell membrane transport, and production of neurotransmitters.[837] Omega-3 fatty acids are in fish, walnuts, and flaxseed and have been found to block NF-kappaβ, decrease TNF-α, and decrease oxidative stress.[844] Diets low in omega-3 fatty acids have been associated with higher levels of anxiety and depression in pregnancy.[851,852] Nutritional supplementation with omega-3 fatty acids has been found to lower norepinephrine, adrenocorticotropic hormone, plasma cortisol, and body temperature in response to an endotoxin challenge, compared to a placebo.[844] Two specific omega-3s, eicosapentaenoic acid and docosahexaenoic acid, have both been shown to decrease stress-related depression, anxiety, violence, and aggression.[838]

In double-blind, randomized, placebo-controlled studies, nutritional supplementation with omega-3 fatty acids for children was associated with improved child behavior and decreased aggression and intimate partner violence among parents, but did not impact child maltreatment.[853,854] Omega-6, found in refined vegetable oils, competes with omega-3 for the same receptors and may interfere with omega-3 uptake. Omega-6 intake has been associated with increases in inflammatory markers IL-1, TNF-alpha, and IL-6.[844]

Breastfeeding

Breastfeeding is associated with decreased infection risk, improved cognitive development, decreased postpartum depression, and may facilitate mother–child bonding.[805,848,850] Responsive feeding practices can improve child development even more when combined with nutritional support.[850] In addition, eating meals with family and community can be a source of cultural and relational support.[704]

While there is much promise, further research is needed to provide specific recommendations for diet or nutritional supplementation as a way to improve neuro-endocrine-immune-metabolic function in the setting of ACEs and toxic stress.

KEY TAKEAWAYS: NUTRITION

- ACEs and toxic stress have been associated with obesity, insulin resistance, diabetes, and eating disorders such as anorexia.
- Stress can increase or decrease appetite.
- Stress can increase craving for high-fat and high-sugar foods.
- The Western diet (high in red and processed meat, saturated fats, and refined grains) has been associated with increased inflammation.
- Diets with greater fruit, vegetables, fish, and whole grains have been associated with decreased inflammation and improved health.
- Patients may be encouraged to consider healthy forms of high-fat, high-energy foods, such as nuts, yogurt, fish, and avocados when craving high-fat, high-sugar foods.
- Patients should be encouraged to use habit formation strategies to increase intake of anti-inflammatory foods (fruits, nuts, vegetables) by storing them in easily accessible places (while putting the junk food in hard-to-reach places).

PHYSICAL ACTIVITY

Physical activity is known to improve health, including reducing risk of cardiovascular disease, diabetes, mental health disorders, and all-cause mortality.[855-859] Health benefits include those potentially mediated by improvements in neuro-endocrine-immune-metabolic functioning.

Neurologic impacts

Ample research demonstrates the positive effects of physical activity on brain health. Exercise releases proteins such as brain-derived neurotrophic factor (BDNF) and metabolites such as lactate, which can cross the blood-brain barrier and may support brain health.[754,860] A meta-analysis found that higher exercise intensity and longer durations were associated with higher acute increases of BDNF and/or changes in BDNF basal level.[861] BDNF is a potential link between physical activity and brain health, and is associated with neuronal growth and improved neuroplasticity.[861,862] Interestingly, there appears to be a dose–response relationship between aerobic exercise and BDNF levels, but not between strength training and BDNF levels.[863]

Exercise training increases hippocampal perfusion and hippocampal volume, specifically the anterior, left, and right hippocampus.[864-866] Physical activity increases hippocampal white matter volume, neurogenesis, synaptic plasticity, and blood flow.[581] Child maltreatment has been associated with decreased hippocampal volumes in adults.[867] Further research is needed to evaluate whether physical activity interventions can reverse this change.

Physical activity is associated with improved memory and attention, cognition, academic achievement, and psychosocial functioning; however, studies are not uniform in the type, intensity, or frequency of exercise needed to achieve these outcomes.[581,754] A meta-analysis of 36 studies, including 12,820 total records of adults over 50 years, found that 45 to 60 minutes of at least moderate-intensity physical exercise improved cognitive function (effect size, or group difference, of 0.29).[868] Improvements in mental health and pain perception associated with exercise may be due to increasing dopamine and endogenous opioid levels.[754]

Endocrine impacts

Physical activity itself can represent a physiologic stressor, and can stimulate the acute stress response, activating the HPA axis and the SNS.[869] Thus, it is not surprising that physical activity is associated with increases in cortisol, catecholamines, and growth hormone.[869] Increases in cortisol can occur in endurance and resistance exercise, but more so with vigorous or high-intensity physical activity.[869] In a study of 12 endurance-trained males who cycled at low, moderate, or high intensity, cortisol levels increased significantly only in response to high-intensity exercise.[870]

Other key changes in hormone levels can occur during exercise. Epinephrine levels generally increase with physical activity, while studies are mixed as to the norepinephrine response.[869] Growth hormone increases immediately with endurance or resistance exercise and decreases when activity stops.[869] Nutrition, sleep, gender, prior exercise, physical fitness, environmental conditions, exercise intensity, and duration can all affect the magnitude of growth hormone release.[869] Insulin levels decrease during exercise, allowing for greater glucose production and release to prevent hypoglycemia.[869]

There seems to be a paradox: exercise can elicit the stress response, but it also confers many health benefits. There are a number of possible explanations. First, some stress is helpful and can build protective immunity, increase mental and physical performance, and improve health and well-being.[871] Thus, physical activity may promote improved regulation of the stress response and a shift toward the positive stress response, and away from toxic stress.[872] Physical activity may also help metabolize the increased energy associated with anxiety or perceived (but not actual) threats. For example, a child who has experienced ACEs and is hyper-aroused and hypervigilant at school may be more activated by perceived threats and have trouble sitting still. Brief physical activity breaks may help the child release the excess energy and regulate the threat-response system.

Immune impacts

Physical activity has been associated with overall improved immune system function.[754,873] A single bout of moderate to high-intensity exercise has been associated with increased immune cell counts and cytokine levels during exercise and decreased lymphocytes and antibody response for a period after exercise.[874] This may lead to a general anti-inflammatory effect of regular exercise over time.[875] The reductions in immune cell counts after exercise have also been associated with immune cell mobilization, heightened immune surveillance, and increased immune system regulation, leading to the potential for enhanced overall immune competency across the lifespan.[876] While intense, long-duration, elite-level physical activity has been associated with immune suppression and increased infection risk, moderate-intensity exercise has been associated with decreased upper respiratory tract infections.[875,877]

Additional mechanistic pathways

Physical activity may help individuals affected by ACEs by increasing resilience factors such as skill development, self-regulation, problem-solving abilities, and a sense of agency.[878,879] Physical activity may also support healthy relationships. For adolescents, team sport participation has been shown to decrease the odds of receiving a diagnosis of depression (aOR 0.76), having current depressive symptoms (aOR 0.85), or anxiety (aOR 0.70). Stratified analysis found similar results among males; however, for females, team sport participation was associated only with decreased anxiety.[880] Exercise can improve sleep, which can also improve immune function.[752]

Physical activity, hormones, obesity, and weight loss

A large review by Hansen and colleagues found that cortisol levels may increase more in obese individuals than in lean individuals following exercise, while epinephrine and growth hormone release may be lower.[869] It is hypothesized that the lower epinephrine levels may be due to a blunted SNS response.[869] Unfortunately, rates of fat breakdown (lipolysis) are also lower in obese subjects, which may be related to the decreased growth hormone levels.[869] In addition, hyperinsulinemia is more likely to persist in obese individuals during and after exercise, further blunting fat breakdown.[869] Taken together, these findings suggest that weight loss and stress relief through physical activity may be more difficult for obese individuals than for lean individuals. There is also limited data on whether long-term exercise alone can reverse these hormonal changes for obese individuals.[869]

Interventions

- Moderate-intensity aerobic exercise three times a week for a minimum of nine weeks has been shown to improve depression.[881]
- Low mood and stress have been identified as barriers to exercising; professional support may help patients overcome these barriers.[882]

- Among patients with PTSD, physical activity may reduce depressive symptoms, PTSD symptoms, anxiety, and stress.[883]
- Physical activity interventions for anxiety were more effective when they included supervised exercise, moderate- or high-intensity exercise, and exercise at a fitness center rather than at home.[884]
- Programs that couple physical activity with self-regulation skills, such as martial arts and yoga, may lead to more improvements in executive functioning.[885]
- Gamification strategies, such as the Behavioral Economics Framingham Incentive Trial, which gamified step goals, can help improve activity levels.[886]

Overall, physical activity is a valuable tool in helping to mitigate the health consequences of ACEs and toxic stress. Medical providers can discuss the stress-related health benefits of physical activity, identify strategies to support moderate-intensity aerobic exercise, and suggest team sports, fitness centers, supervised individual or group activities, and/or combined practices such as yoga or martial arts.

KEY TAKEAWAYS: PHYSICAL ACTIVITY

> Physical activity is associated with improved memory and attention, cognition, academic achievement, psychosocial functioning, and immune function.

> Physical activity may help promote the positive stress response, metabolize increased energy associated with anxiety or stress, and increase resilience factors.

> Physical activity may also support healthy relationships—for example, through coaching and team sport participation.

> Brief physical activity breaks may help release excess energy and regulate the threat-response system.

> Moderate-intensity aerobic activity, for longer durations, at a frequency of three times or more a week, has been associated with improved health outcomes.

> Activities that combine physical activity with self-regulation skills and breathing techniques, such as martial arts and yoga, may also be beneficial.

> Low mood and stress have been identified as barriers to exercising; professional support may help patients overcome these barriers.

MINDFULNESS PRACTICES

Complementary and alternative medicine (CAM) use is common in the United States, with a 2007 study finding that 40% of adults and 11% of children had used such therapies within the past 12 months.[887] In adults, the most commonly used CAM therapies were non-vitamin, non-mineral natural products, deep-breathing exercises, meditation, chiropractic or osteopathic manipulation, massage, and yoga.[887] While the evidence is strongest for mindfulness and meditation, an expanding body of literature has indicated that other approaches, including yoga, acupuncture, breathing techniques, and neurofeedback, may be promising practices to support healing from ACEs and toxic stress.[888-894]

Mindfulness has been defined as nonjudgmental, moment-to-moment awareness that involves attention, intention, and a kind attitude.[889,895,896] Mindfulness originates in ancient Buddhist practices; however, secular versions, including mindfulness-based stress reduction (MBSR) and mindfulness-based cognitive therapy, are increasingly used to reduce stress and improve health.[889,897] MBSR is an eight-week program with weekly two-and-a-half-hour in-person (and now also virtual) sessions with daily home practice; it was originally designed to support cancer patients but has been adapted for general use and implemented across the country.[889] Shapiro and colleagues refer to a process of "re-perceiving" in which mindfulness produces a shift in perspective that allows for more flexibility in behaviors.[896] Mindfulness may increase the space between perception of threat and one's response, as described by Holocaust survivor and psychologist Viktor Frankl: "Between stimulus and response, there is a space. In that space lies our freedom and our power to choose our response. In our response lies our growth and our happiness."[898]

A rapidly growing body of research shows that mindfulness practices can support trauma healing and regulation of stress, emotions, and behavior for children[726,755,899-904] and adults.[726,756,897,905-910] Mindfulness has been shown to be helpful for people with ACEs and trauma,[726] PTSD,[726] anxiety and depression,[726,897,905,906,911-913] executive functioning disorders,[726,912,914] pain management concerns,[897,915] attention-deficit/hyperactivity disorder (ADHD),[916] sleep problems,[917,918] and parental stress.[726] It has also been shown to decrease shame and increase acceptance, self-compassion,[919,920] and empathy.[921,922] Mind-body therapies improve mental health problems,[902,923] including depression and anxiety.[924]

Mechanisms

The literature is still emerging; however, the science suggests that mindfulness may support trauma healing via regulation of the stress response[755,756] and improved functionality and connectivity among regions of the brain involved in attention, self-referential thinking, and emotional regulation.[726,912,914,925,926] Mindfulness may offer cognitive and behavioral flexibility in the face of stressful events and increase one's ability to tolerate uncomfortable emotions.[896,897]

Neuroendocrine impacts

Functional magnetic resonance imaging (fMRI) studies suggest that mindfulness involves the brain's frontal regions, primarily the medial frontal cortex, including the anterior cingulate cortex, as well as the cortical midline structures, insula, amygdala, and the hippocampus.[926] Mindfulness may act on the attention networks in the brain and improve the default mode network processes, thus supporting self-referential thinking.[925,926]

From a stress-reduction perspective, mindfulness has been associated with decreased cortisol levels, although there have been some conflicting reports.[897] In one study, 38 adults were evaluated before and after a three-month yoga/meditation retreat and on average, were found to have decreased depression and anxiety, increased BDNF, and increased morning cortisol.[927] Mindfulness has also been associated with decreased sympathetic activation, lower blood pressure,[897] and improved parasympathetic activity, with increasing heart rate variability.[928] Many studies have linked mindfulness programs with self-reported decreases in stress levels and in maladaptive responses to stress.[726,755,929-931]

Cardiovascular disease

Transcendental meditation (TM) was associated with decreased carotid atherosclerosis in Black Americans with hypertension (compared to those who received only health education)[909] and reduced exercise-induced myocardial ischemia in patients with coronary artery disease.[932] In a study of 201 Black men and women with coronary artery disease, TM was associated with a reduced risk of mortality, myocardial infarction, and stroke, and these changes were found in association with lower blood pressure and psychosocial stress factors.[933]

Immune function

Mindfulness has been associated with improved immune function.[726,897,907] A meta-analysis suggests that mindfulness can influence markers of inflammation, cell-mediated immunity, and biological aging. However, there is substantial heterogeneity across studies and the need for more research.[934]

Interventions

As always, interventions can start as self-care for providers. Mindfulness has been found to decrease provider stress and burnout,[935-938] improve patient-centered care,[939,940] increase empathy,[941] improve patient satisfaction,[942] and reduce implicit bias.[943] Mindfulness is also associated with decreased parental stress and an improved caregiver–child relationship.[755]

The American Heart Association reports that, given the low costs, low risks, and potential benefits, meditation could be considered an adjunct to routine treatments for cardiovascular disease.[910] Use of online and downloadable apps for mindfulness has been demonstrated to improve stress, resilience, and mental health symptoms[922,944] and is associated with lower blood pressure.[945]

As noted above, other mind-body practices, including tai chi, yoga, acupuncture, breathing techniques, massage therapy, and neurofeedback, show promise to support healing from ACEs and toxic stress.[752,805,888-894,946] Discussions combined with motivational interviewing techniques can help determine which practice might best support each patient.

KEY TAKEAWAYS: MINDFULNESS PRACTICES

- Mindfulness has been defined as nonjudgmental, moment-to-moment awareness that involves attention, intention, and a kind attitude.
- Mindfulness has been shown to be helpful for people with ACEs and trauma, PTSD, anxiety and depression, executive functioning issues, pain management issues, ADHD, sleep problems, and parental stress.
- Research shows that mindfulness practices can support trauma healing and regulation of stress, emotions, and behavior for children and adults.
- Mindfulness has been shown to decrease shame and increase acceptance, self-compassion, and empathy.
- Mindfulness has been associated with improved cardiovascular and immune health.
- Mindfulness has been found to decrease provider stress and burnout, improve patient-centered care, increase empathy, improve patient satisfaction, and reduce implicit bias.
- Mindfulness also decreases parental stress and improves the caregiver–child relationship.
- Mindfulness-based stress reduction (MBSR) is an eight-week program with weekly sessions and daily home practice. Programs are available through work wellness programs, hospitals, community organizations, and online.
- Online and downloadable apps for mindfulness are also available.
- Other mind-body practices, including tai chi, yoga, acupuncture, breathing techniques, massage therapy, and neurofeedback, can also support healing from ACEs and toxic stress.

EXPOSURE TO NATURE

Nature can come in many forms, including local, state, or national parks, green spaces around work or school environments, playgrounds, and even indoor plants. Importantly, access to natural environments can improve health.

Interacting with nature is associated with decreased diabetes, depression,[947] heart rate and blood pressure,[948] heart disease,[949] and mortality.[948,950-952] Walkable green space in a city was associated with longer life for senior citizens in Tokyo.[953] In a randomized controlled study of 90 patients recovering from surgery, plants and flowers in the hospital rooms were associated with lower blood pressure, lower ratings of pain, anxiety, and fatigue, and higher room satisfaction.[954] Similarly, patients who had a room with a view looking out on a natural scene had shorter hospital stays and required less pain medication.[955]

Adding green spaces in low-resourced communities has been associated with reduced crime and violence, improved perception of safety, increased social connections, and reduced depressive symptoms.[947,956,957] Conversely, losing trees has been associated with increased crime and worse health, including increased cardiovascular and respiratory deaths.[952,957,958] Nature most likely improves health for children and adults with toxic stress by directly calming the stress response system, as well as by increasing healthy behaviors such as physical activity, mindfulness, and relational health. Parks and exposure to nature have been shown to increase play and physical activity, and to decrease screen time.[959] Nature may also increase opportunities for relationship and connection and improve sleep.[757,758] Studies also document improvement in family functioning and attachment,[757,960] and increase in social ties.[758]

A study of park prescriptions at a pediatric primary care clinic in a city found that they increased park visits and physical activity, and were associated with decreased perceived stress, loneliness, and cortisol levels.[757] Another study by the same author found that counseling children and families about nature was associated with greater time spent in nature and decreased parental stress.[757] Time in nature has been associated with decreased SNS activity and increased parasympathetic nervous system activity.[758] Nature has also been linked to decreased blood glucose levels and reduced inflammatory cytokines and NK cells.[758] A small study of 30 subjects found that images of urban scenery were associated with activation of the hippocampus and amygdala (both of which are involved in stress pathways), while rural scenery images were associated with activation of the anterior cingulate, globus pallidus, putamen, and caudate nucleus (involved in empathy, impulse control, and proprioception pathways).[961]

Interacting with nature may improve cognitive functioning and attention.[758,960,962] In a study of 547 adults, connectedness to nature was associated with improved psychological well-being, meaningfulness, and energy.[963] Another study had 12 students wear mobile devices that recorded brain electrical activity (via an EEG), and walk through three different neighborhoods in Edinburgh: a populated, urban shopping district, a path through trees and fields, and a busy commercial district.

Transitioning from the shopping district to the green space was associated with decreased arousal and frustration, and an increase in brain electrical patterns associated with a meditative state.[964]

Access to nature is, unfortunately, not equal. Low-income neighborhoods often have fewer trees, parks, and green spaces.[959,965,966] In a study of 890 caregivers at an urban pediatric federally qualified health clinic, 17% felt that "access to green spaces/parks/playgrounds" was an unmet social need.[965] In addition, the study found significantly increased odds that access to nature was an issue for families living at or below the poverty line.[965] This social inequality in access to green space may be a mechanism by which disadvantaged communities experience poorer outcomes in the face of high stress and adversity. In addition, adversity is demonstrated to interact with air quality, resulting in poorer lung function for children in high-stress environments for a given level of air pollution.[967] Similarly, a study done in northwest Florida found that stroke mortality was associated with lower incomes, increased pollution, and decreased green space.[968]

The experience of being in nature is also not the same for all populations. Both current and historical racism within park systems and natural spaces have contributed to feelings of lack of safety and inclusion for some communities of color.[969] Historically, "redlining" policies forced minorities to live in locations that often had less green space.[970] Extra efforts must be made to support historically marginalized communities, including Black and other minority Americans, in feeling safe and welcome in nature.

There are many ways that nature has been used as a therapeutic modality, including nature prescriptions, wilderness therapy, adventure-based programs, and ecotherapy.

Tools for improving nature usage and access

- Providers can discuss the important link between health and nature and encourage time in nature as a health intervention.
- Park prescriptions can be used in primary care clinics as a way to start a conversation about nature, encourage park usage, and demonstrate the link between nature and health; see parkrx.org.[971]
- Hospitals, schools, and workplaces may be encouraged to increase indoor and outdoor green space.
- Providers can recognize that there may be cultural, community, and policy barriers to equal access to nature. Access to nature is a social justice health issue.
- Patients may be referred to ecotherapy, wilderness therapy, or adventure-

based treatment programs.

KEY TAKEAWAYS: EXPOSURE TO NATURE

- Nature can come in many forms, including parks, local green spaces, playgrounds, and even indoor plants.
- Access to these natural environments can improve health.
- Adding green spaces in low-resourced communities has been associated with reduced crime and violence, improved perception of safety, increased social connections, and reduced depressive symptoms.
- Interacting with nature is associated with decreased diabetes, depression, heart rate, blood pressure, and mortality.
- Nature is associated with calming the stress response system and increasing healthy behaviors such as physical activity, mindfulness, and relational health.
- Social inequality in access to green space may be a mechanism by which disadvantaged communities experience poorer outcomes in the face of high stress and adversity.
- Both historical and current racism within park systems and natural spaces as well as "redlining" practices have contributed to feelings of lack of safety and inclusion for some communities of color. Extra efforts must be made to support Black Americans and other minorities in feeling safe and welcome in nature.
- Providers may encourage time in nature as a health intervention.
- Increased indoor and outdoor green space should be encouraged.
- Providers may consider park prescriptions, ecotherapy, wilderness therapy, or adventure-based treatment programs.

MENTAL AND BEHAVIORAL HEALTHCARE

Individuals requiring mental health and substance abuse services represent a special population with particularly high risk for ACE exposure and toxic stress.[972,973] Mental and behavioral healthcare can help patients build skills and capacities for resilience, directly address trauma-related symptoms, and scaffold with medications as necessary, all in the context of safe, supportive, and trusting relationships.[973] Integrated primary care and behavioral health and team-based care represent clinical best practices for addressing the range of outcomes associated with toxic stress. Multidisciplinary teams may include primary care providers, mental or behavioral health providers, care coordinators and navigators, social workers, or others, such as peer supports. This section offers an introduction to the various aspects of mental and behavioral healthcare that can support healing from toxic stress.

It is important for mental and behavioral health systems to be trauma-informed and include a recognition of the science of ACEs and toxic stress. Multidisciplinary care should include bidirectional flow of information, as ACEs are risk factors not only for mental and behavioral but also for non-neuropsychiatric health conditions. Just as primary care providers may refer patients in need to a mental or behavioral health provider, so too can mental and behavioral health providers who, in the course of treatment, learn of a patient's history of ACEs or other risk factors for toxic stress, can encourage and/or refer patients to seek trauma-informed care for other AAHCs. Increased communication across disciplines, integration of services, and shared treatment plans can improve access and care for individuals with high risk of toxic stress.

There is a vast body of literature linking various behavioral and mental health therapies with improved outcomes, and summaries of best practices can be found in the National Academies of Sciences, Engineering, and Medicine's report, Fostering Healthy Mental, Emotional, and Behavioral Development in Children and Youth: A National Agenda, the US Surgeon General's Report, Addiction in America, and resources from the National Child Traumatic Stress Network (NCTSN), the Substance Abuse and Mental Health Services Administration (SAMHSA), and the California Evidence-Based Clearinghouse for Child Welfare (CEBC).[974-978] As with treatment of other AAHCs, the treatment approach for mental and behavioral sequelae of toxic stress should incorporate strategies to mitigate the toxic stress response. There is not yet sufficient evidence to determine whether mental health interventions are warranted for patients at intermediate or high risk of toxic stress, but who do not have mental or behavioral symptoms. Few cross-disciplinary research studies have addressed whether these therapies are reliably associated with clinical improvement of physical health outcomes. The limited research available, however, does indicate that psychological interventions can improve both the mental and the physical health consequences of toxic stress.[603,759,979] Continued multidisciplinary research in this area should be a priority.

A recent Cochrane review evaluated psychological interventions for parents of children and adolescents with chronic illnesses, and while there were a limited number of high-quality studies, CBT for the parents showed promise in decreasing children's medical symptoms.[980] The Creating Opportunities for Personal Empowerment (COPE) for Asthma program, which incorporated cognitive-behavioral skills-building for children with asthma and anxiety, found reductions in self-reported symptoms of anxiety and increased child management self-efficacy and asthma illness representations.[981]

In a randomized controlled trial of 437 adults with recently diagnosed heart disease, patients who received traditional care plus CBT had a 41% lower rate of a

Therapy	Ages	General Description
Child-Parent Psychotherapy	Birth to 6 years	Dyadic intervention for young children and their caregivers that supports family strengths and relationships.[586,587,994]
Parent-Child Interaction Therapy	2 - 12 years	Dyadic parent training treatment that emphasizes improving the quality of the parent-child relationship and interactions.[995-997]
Cue-centered therapy	8 - 18 years	Protocol of 15 sessions through which children and caregivers learn about traumatic stress, how to cope rather than avoid, and the value of verbalizing their life experiences.[998,999]
Trauma-focused cognitive behavioral therapy (TF-CBT)	Verbal children and adults	A structured, short-term treatment model for children and adults who have experienced trauma.[1000-1002]
Eye movement desensitization reprocessing (EMDR)	Verbal children and adults	Focuses on helping clients resolve unprocessed traumatic memories.[1003-1005]
Family systems therapy	Verbal children and adults	Supports resolving family conflict or issues.1[006,1007]
Cognitive processing therapy	Adolescents and adults	A type of CBT, generally 12 sessions, that helps modify maladaptive thinking related to their trauma.[1008]
Prolonged exposure therapy	Adolescents and adults	A CBT approach that helps clients gradually approach their memories, feelings, and situations of trauma.[1009]

Evidence-based trauma therapies.

recurrent cardiovascular disease event and 45% fewer heart attacks than patients who received traditional care alone.[982]

Neuro–endocrine–immune–metabolic function

CBT is based, at least in part, on the concept that thought can influence emotions and behavior. Thus, CBT may help improve patient awareness of negative thoughts, behaviors, and feelings about their disease, increase compliance with medical recommendations, and support healthy self-care behaviors.[983] Cognitive therapy may enhance prefrontal cortex function and inhibit amygdala activation.[984] A study of both trauma-focused cognitive-behavioral therapy (TF-CBT) and eye movement desensitization and reprocessing (EMDR) found improvements in PTSD symptoms correlated with alterations in bilateral temporal lobe connectivity.[985]

A systematic review found that psychosocial interventions for children were associated with improved cortisol regulation.[759] Boparai and colleagues found that a number of behavioral and mental health interventions, including Attachment and Biobehavioral Catch-Up (ABC), Strong African American Families (SAAF), and CPP, were associated with improvement in various markers of neuro-endocrine-immune-metabolic regulation, including cortisol, epigenetic regulation, and brain development.[603] CPP has also been found to be effective in treating depression and PTSD, decreasing stress, and improving self-efficacy in both parents and children with high ACE scores.[96,586,587,699,986] CPP has also been shown to protect against the telomere shortening associated with trauma, suggesting the intervention slowed, stopped, and, for some children, reversed the cellular "wear and tear" of early adversity.[492]

Who needs therapy?

Generally, individuals who have trauma-related mental or behavioral health symptoms (e.g., depression, anxiety, anger management concerns, and alcohol or other substance misuse or dependence) should be offered evidence-based and trauma-appropriate mental or behavioral health services. Mental health therapy can be used in combination with the other strategies for toxic stress mitigation. Of note, routine mental health referrals for all patients who have experienced ACEs are not recommended or indicated by current evidence. Those who manifest non-neuropsychiatric manifestations of toxic stress, such as immunologic, inflammatory, cardiovascular, or metabolic conditions, may benefit from mental health interventions. However, more research is needed.

Trauma therapy

Just as in other fields, mental health practitioners have specialties and can be trained and certified in various mental health modalities. It is important to help individuals who have experienced ACEs connect with therapists who can provide trauma-focused services. Trauma-trained mental health practitioners should have certification or expertise in at least one of the evidence-based trauma therapies.

Given that the client–therapist relationship is critical to helping establish new patterns of trust and safety, individuals interested in mental health therapy are encouraged to interview therapists before starting therapy. Similarly, if therapy does not seem to be helping, one should consider trying a different therapist or different treatment modality before giving up on mental health therapy altogether.

The CEBC and the NCTSN both offer searchable databases of mental health therapies. Below are a few examples of evidence-based therapies demonstrated to support healing for children and adults affected by trauma and toxic stress.[725,987-993]

Developmental and behavioral pediatrics (DBP)

Pediatricians specializing in DBP have broad expertise in developmental and behavioral assessments and in supporting children and families address identified concerns. DBP can support multidisciplinary care and offer evidence-based strategies and interventions to help children with ACEs and toxic stress.[1010]

Psychiatry

Psychiatrists can provide critical support for children and adults with severe trauma symptoms, especially when they understand the biology of toxic stress. For children, it is important that psychiatrists recognize the developmental consequences of trauma, can differentiate trauma from oppositional defiant disorder or ADHD, and are sensitive to issues of polypharmacy.[704]

Medications

Medications can be important adjunctive treatment for addressing the sequelae of ACEs and toxic stress. It is important for prescribing clinicians to consider how medications might best be utilized in concert with other treatment modalities (including all stress mitigation strategies) that will ultimately lead to sustained healing. Monitoring and avoiding polypharmacy are especially important in at-risk groups such as children in foster care.

Medications for mental health diagnoses are often prescribed by primary care providers, given limitations in access to psychiatry support; however, advocacy and public policy efforts should be made to ensure adequate access to all forms of mental health support, including psychiatry.

- Selective serotonin reuptake inhibitors (SSRIs) are a class of antidepressants that may be helpful in the treatment for acute stress disorder, non-combat PTSD (such as motor vehicle accidents, childhood and adult sexual assault, and other interpersonal traumas), and associated anxiety and depression.[1011]
- There are no drugs, including antidepressants, that have been found to specifically treat PTSD symptoms in children.[1012-1016]
- Prazosin, an α-1 adrenergic antagonist, is a promising treatment option for PTSD-related nightmares and sleep disruptions for adults and children.[1011,1017]
- Clonidine and guanfacine are alpha-2 agonists that may help children and adults with intrusive and hyperarousal symptoms associated with PTSD.[1018,1019] For traumatized youth and adults, guanfacine may help calm the fight-flight-or-freeze response while enhancing prefrontal cortex inhibition of the

amygdala.[1018,1019]

- Psychiatric medications are thought to act primarily by altering neurotransmitters such as dopamine and serotonin within the brain, but emerging research shows they may also support healing by improving autonomic nervous system regulation[1020] and immune system regulation.[752]

Access to mental healthcare

A 2018 online survey of 5,000 Americans found that while the need for mental health services is high (over half of respondents considered or sought mental health services), access to care (not quality of care) was the biggest hurdle in addressing mental health needs.[1021] Access is an even greater barrier for Black, Latinx, and Asian Americans.[1022] The cost of mental health services can also be a barrier to care, especially for those who are uninsured or privately insured.[1023,1024]

Engagement in therapy

Many people who are referred to mental health therapy do not initiate or maintain services, and racial/ethnic minorities are much less likely (by 20–50%) to engage in mental health services.[1025] Barriers to starting and staying in therapy include access, transportation issues, fear of stigmatization, uncertainty of what to expect, lack of culturally and linguistically congruent providers for racial/ethnic minorities, and length of wait until first appointment.[1026-1028] For children and adolescents, contributing factors included family attitudes, flexibility and availability of services, stigma, and degree of coordination and integration of care.[1029] Both outreach and integrated care have been found to improve engagement.[1029] A focus on the therapeutic alliance, person-centered care, peer support, and culturally and linguistically congruent care are also important.[1028,1030] Care coordination, navigators, and integrated behavioral health services can also help improve engagement and access to care.[1031]

CULTURAL COMPETENCE

Cultural competence includes framing mental health services in culturally relevant ways, allowing for complexity of issues based on culture, gender, class, national origin, and race, being respectful of cultural preferences around personal space and touch (such as hugging), recognizing cultural issues around power and control, and interpreting mental health symptoms and emotions in the context of culture. While cultural competence has been used to describe an approach or skill set for understanding another person's culture, cultural humility recognizes that one may never fully understand another's culture and offers a framework for personal accountability, ongoing learning, and challenging of barriers that impact marginalized communities.

Cultural considerations

Addressing cultural competence, sensitivity, and humility must be an individual practice, as well as a priority for improving systems and policy more broadly. Linguistic and cultural congruence between provider and patient is critical in addressing health equity and highlights the need to advance a more culturally and linguistically diverse mental health provider workforce.[1028] **Cultural competence** includes framing mental health services in culturally relevant ways, allowing for complexity of issues based on culture, gender, class, national origin, and race, being respectful of cultural preferences around personal space and touch (such as hugging), recognizing cultural issues around power and control, and interpreting mental health symptoms and emotions in the context of culture.[1032] While cultural competence has been used to describe an approach or skill set for understanding another person's culture, cultural humility recognizes that one may never fully understand another's culture and offers a framework for personal accountability, ongoing learning, and challenging of barriers that impact marginalized communities.[1033] A systematic review of models for professional training on cultural competence among mental health practitioners found that none of the studies evaluated patient experience and outcomes.[1034] Thus, it is important for individual patients and referring clinicians to identify mental and behavioral health providers who demonstrate cultural sensitivity and humility. Further, on a systems level, there is a need to increase parity and leadership of underrepresented minorities in the mental health workforce.

Integrated behavioral health models

For patients with neuropsychiatric symptoms, integrating behavioral and mental health with primary care improves outcomes and is a critical element in addressing toxic stress physiology.[1035] Studies have shown that integrated services can decrease healthcare utilization,[552] and improve mental and behavioral health outcomes, including depression, panic disorder, substance dependence, chronic pain, and medication adherence.[1036] A meta-analysis of 31 studies with over 13,000 patients found that integrated care improved behavioral health outcomes.[1035] A more recent meta-analysis of integrated care models for children found improved quality of life and cost savings compared to usual care.[1037] Further multidisciplinary research is needed to explore how integrated behavioral health may improve physical health outcomes.

Care coordination and care management

Care coordination is a team-driven activity that can help organize and integrate services as well as support children and adults navigating across clinics, health systems, and services.[1038] The Center for Health Care Strategies and the Agency for

Healthcare Research and Quality define care management this way:

> "Care management programs apply systems, science, incentives, and information to improve medical practice and assist consumers and their support system to become engaged in a collaborative process designed to manage medical/social/mental health conditions more effectively. The goal of care management is to achieve an optimal level of wellness and improve coordination of care while providing cost effective, non-duplicative services."[1039]

A study found that the medical home model, including having a personal provider, a usual source for medical care, family-centered care, and having effective care coordination, was associated with improved child well-being (as measured by the child well-being index).[1040] A study of 11 high-income countries (Australia, Canada, France, Germany, the Netherlands, New Zealand, Norway, Sweden, Switzerland, United Kingdom, and the United States), demonstrated that the United States lags behind the other nations in care coordination, with almost one in 10 adult patients reporting poorly coordinated care.[1041]

Substance abuse

The treatment of substance use disorder is greatly enhanced when comorbid mental health problems are simultaneously addressed.[1042] Studies have shown that adding trauma-focused therapy to substance use disorder treatment can improve outcomes.[1043-1045] SAMHSA has developed in-depth toolkits for understanding, implementing, and integrating treatment for trauma, traumatic (or toxic) stress, and substance abuse.[1046,1047]

KEY TAKEAWAYS: MENTAL AND BEHAVIORAL HEALTHCARE

- Mental and behavioral healthcare can help patients build skills and capacities for resilience, directly address trauma-related symptoms, and scaffold with medications as necessary, all in the context of a safe, supportive, and trusting clinical relationship.
- Mental and behavioral health systems should be trauma-informed and include a recognition of the science of ACEs and toxic stress.
- Mental and behavioral health providers who, in the course of treatment, learn of a patient's history of ACEs or other risk factors for toxic stress, can encourage and/or refer patients to seek trauma-informed care for AAHCs.
- Multidisciplinary care should include bi-directional flow of information as high ACEs are a risk factor for numerous mental, behavioral, and physical health conditions.
- Studies suggest that behavioral and mental health programs can improve physical health and neuro-endocrine-immune-metabolic dysregulation; however, more multidisciplinary research is needed.
- Individuals who have trauma-related mental or behavioral health symptoms (e.g., depression, anxiety, anger-management concerns, and alcohol or other substance misuse or dependence) should be offered evidence-based and trauma-appropriate mental health services.
- Limited access to mental healthcare is a serious issue in the Unites States. Barriers are even greater for Black, Latinx, and Asian Americans.
- The cost of mental health services can also be a barrier to care, especially for those who are uninsured or privately insured.
- Multidisciplinary teams, integrated behavioral and mental healthcare within the primary care setting, care coordination, and medical home models may help address some barriers to care.
- Linguistic and cultural congruence between provider and patient is critical in addressing health equity and highlights the need to advance a more culturally and linguistically diverse mental health provider workforce.
- Medications for mental health issues are often prescribed by primary care providers, given the limited access to psychiatry support; however, public policy efforts should be made to ensure adequate access to all forms of mental health support, including psychiatry.

MANDATED REPORTING

The goal of ACE screening and trauma-informed care is to identify risk and protective factors before a reportable event occurs, and provide support, scaffolding, coping strategies, and stress buffering skills to prevent future ACEs. However, ACE screening may uncover active or recent neglect or abuse that must be reported to Child Protective Services (CPS) or law enforcement to ensure the safety of a child. While a mandated report will most likely cause stress for the patient and the provider, it is important to remember:

1. Not all positive ACE screens require mandated reporting. Further

discussion with the patient and family are needed to further assess. If in doubt, a provider can call the CPS hotline and receive guidance as to whether a report is required.

2. Addressing the safety needs of the child can protect the child from further harm.
3. Not all CPS reports result in removal. In 2018, nationally, CPS received approximately 4.3 million referrals (regarding 7.8 million children), and approximately 150,000 children received foster care services.[1048]
4. CPS and law enforcement can offer additional services to support the child and family. Differential response is an example of a CPS program that offers resources and supports to the family.
5. A trauma-informed approach to mandated reporting can lessen the stress and even bolster the patient–provider relationship through the process.

Applying the principles of trauma-informed care to mandated reporting can help decrease some of the uncertainty and loss of control associated with the process.[1049,1050]

1. **Safety.** Provide a private and safe space for the patient to disclose and discuss next steps. The clinician taking a few moments or deep breaths, if needed, can be helpful to achieve a state of being calm and reassuring for the patient. Of note, the clinician doesn't need to get all the details of the adverse event, just enough information to know whether there is a suspicion of neglect or abuse. CPS and/or law enforcement will hopefully arrange for a formal forensic interview to get details in a professional and trauma-informed manner. It is ideal to have a mental health provider or social worker involved in supporting the patient through the process.
2. **Trustworthiness and transparency.** Provide information about the process of reporting and give clear indications of what to expect. Explain confidentiality around the process and who may or may not find out. The CPS hotline worker is a good resource about some of these aspects of confidentiality and process to report back to the patient.
3. **Peer support.** Offer to connect the patient to an advocate on the phone or support group.
4. **Collaboration, empowerment, voice, and choice.** Depending on the age of the patient and the situation, consider offering to let the patient listen to and be part of the call to report. Ask if they would like anyone else to be with them for any part of the discussion or the call itself.
5. **Attention to cultural, historical, and gender issues.** It is important to

consider cultural and historical differences in parenting styles and customs when considering a suspicion of abuse and neglect. It is also important to recognize that boys and men can be sexually abused, that women can be perpetrators, and that lesbian, gay, bisexual, and transgender children are at increased risk for neglect and abuse.[15,1051-1054]

CONCLUSION

There are a number of evidence-based and promising tools, strategies, interventions, and treatment measures that can help support children and adults identified as being at intermediate or high risk for toxic stress. Primary care providers can use strategies for buffering the toxic stress response—relational health, sleep, nutrition, physical activity, mindfulness, access to nature, and mental and behavioral health—to offer assessment, patient education, specific intervention strategies, and referrals for patients at increased risk. This is an integrated, bio-psycho-social approach that allows for multidisciplinary treatment efforts.

ACE screening involves assessing for the triad of *adversity* (ie, ACE score), clinical manifestations of *toxic stress* (ie, AAHCs), and *protective factors*.[699] Many tools have been presented throughout this section that can be used to assess for strengths and protective factors within each of the stress-buffering strategies. Within each strategy, intervention and referral suggestions are also offered that the primary care provider can use in conjunction with mental health providers and/or community supports. Health plans and providers should work to identify local resources that are available for referral for ACEs prevention and toxic stress mitigation, as well as to address additional social determinants of health such as housing and food insecurity. As a starting point, clinic administrators and staff can inquire with health plans as to whether any community organizations may already be involved in such efforts, such as through Medi-Cal's Whole Person Care pilots and/or the Health Homes Program. Additional guidance related to the state's efforts toward supporting a Network of Care around ACE screening and response is forthcoming. Tools such as such as Aunt Bertha, FINDConnect, and ONE Degree can also help connect patients to needed resources.[1078-1080] Follow-up may need to be more frequent for patients who are at intermediate or high risk of toxic stress to monitor for signs and symptoms of dysregulated neuro-endocrine-immune-metabolic systems.

This report recognizes that meaningful and supportive conversations between patients and providers are a critical first step to addressing ACEs and toxic stress. This section is intended to bring awareness of existing evidence-based and promising practices available to be deployed in the primary care setting, in addition to community-based interventions and referral options. With advances in neuroscience, we now know that the brain continues to grow and rewire itself at all ages throughout life. Thus, interventions and acquisition of new skills can be utilized throughout the life course to improve patient outcomes. Overall, providers can use the key strategies for mitigating the toxic stress response along with a trauma-informed approach to further assess and treat children and adults impacted by ACEs.

While this report highlights current science-based interventions for mitigating the toxic stress response, it also recognizes that advances in treatment are necessary to achieve the bold goal of cutting ACEs and toxic stress in half in a generation. Investments in basic science and clinical and translational research are needed to improve diagnostic precision and treatment efficacy for toxic stress and its potential subtypes, and to identify more precise therapeutic targets.

Case Study

Attention–Deficit/Hyperactivity Disorder

Attention-deficit/hyperactivity disorder (ADHD) is the most common neurobehavioral disorder in childhood and can include symptoms of hyperactivity, inattention, and impulsivity.[1055] ADHD and toxic stress can present with similar symptoms, and a diagnosis of ADHD has been associated with higher ACE exposure.[1056] Diagnosis of ADHD is based on symptoms as defined in the Diagnostic and Statistical Manual of Mental Health Disorders, fifth edition (DSM-V). Toxic stress is defined by physiologic derangements in the biological stress response and concomitant neuro-endocrine-immune-metabolic and genetic regulatory dysregulation. Therefore, it has yet to be determined whether toxic stress predisposes for ADHD, or whether the ADHD-like symptom profile of toxic stress may represent a separate disease entity. Further research to confirmatively establish diagnostic criteria for toxic stress will aid in answering this question, which may have implications for treatment.

Clinically, the standard treatment for ADHD includes therapy in combination with medications. Psychostimulants such as methylphenidate, amphetamine, and atomoxetine, which stimulate catecholamine signaling, are the best known and most widely used medications for ADHD treatment.[1055,1057] For many patients with ADHD (and without toxic stress), deficits in the neurotransmitters norepinephrine and dopamine contribute to symptoms, and this treatment effectively increases attention, working memory, and performance. However, for children experiencing toxic stress who have prolonged activation of the stress response system, this course of treatment may not be the most effective first-line intervention because catecholamine signaling is already too high. Treatment with an α2-adrenergic receptor-activating drug such as guanfacine, which opposes the actions of catecholamine signaling, mitigates effects of toxic stress on attention by directly improving prefrontal cortex functions like executive function and attention.[1018,1058-1060] Importantly, pharmacological treatment for ADHD is most effective when applied in conjunction with other interventions targeted at reducing environmental risk factors, addressing underlying toxic stress physiology by utilizing stress-buffering strategies, and behavioral therapy.

Case Study

Asthma

As discussed in the **Biological Embedding of Toxic Stress** section in Part I, asthma is a chronic, relapsing inflammatory disease that is more prevalent in people with high ACEs.[229,1061] It is characterized by episodic shortness of breath, cough, wheezing, and/or chest tightness. Toxic stress-related inflammation and airway constriction can mediate this increased disease burden. Children experiencing adversity are more likely to be exposed to factors associated with increased incidence and severity of asthma, such as indoor air pollutants like tobacco smoke and living in communities near highways.[1062,1063,1064] Prolonged activation of the stress response is also directly associated with increased risk of asthma. Children with clinical biomarkers of toxic stress physiology were found to have 5.5-fold reduction in glucocorticoid receptor mRNA and 9.5-fold lower β2-adrenergic receptor mRNA levels in one study.[231] Such biological changes decrease the sensitivity of the lung to the actions of glucocorticoids like prednisone and bronchodilators like albuterol, the two standard elements of treatment for acute asthma exacerbations. Thus, these "standard" treatments may be less effective for children with toxic stress and asthma.[230]

Treatment considerations for children whose asthma may be associated with toxic stress are thus different from children without toxic stress. Shared decision-making, the desired norm in all healthcare contexts, also improves self-management in people with asthma and leads to improved outcomes.[1065] Identifying and removing or mitigating sources of stress may improve responses to standard treatments. For example, a study of 150 children (9–17 years) with physician-diagnosed asthma found that parental perspective-taking was associated with children having smaller inflammatory responses to stimulation by non-specific, asthma-specific, and viral analogue ligands, and a greater sensitivity to the anti-inflammatory effects of glucocorticoids.[670] Additional steps to mitigate underlying toxic stress, such as the key intervention strategies described above, may help normalize physiology, thus increasing efficacy of standard treatments. These findings are reflected in draft consensus statements on ACEs, toxic stress, and asthma by the National Committee on Asthma and Toxic Stress, which recommends social support, exercise, mindfulness practices (meditation, yoga, tai chi, hypnosis), exposure to nature, and nutritional approaches, in addition to standard asthma management practices.[1066-1077]

Primary, Secondary, and Tertiary Prevention Strategies in Public Health

The public health sector's long-standing mission is to promote and protect the health and well-being of entire populations, to seek to prevent disease and injuries before they happen, and to mitigate health consequences once disease, injury, or disaster does strike. In general, the professional field is led by the network of national, state, and local governmental public health agencies and supported by a wide range of academic, public, and private partners conducting research, implementing and evaluating population-level interventions and advocating for public health solutions. The public health field emphasizes a broad perspective that includes the social, economic, and political determinants of health and recognizes and prioritizes the non-medical contextual factors influencing health outcomes. To carry out its mission, the public health field strives to deliver 10 essential public health services:[1081,1082]

1. Assess and monitor population health, factors that influence health, and community needs and assets;
2. Investigate, diagnose, and address health hazards and root causes;
3. Communicate effectively to inform and educate about health, factors that influence it and, how to improve it, for the public at large, and for specific sectors about their roles in prevention, early detection, and treatment;
4. Strengthen, support, and mobilize communities and partnerships to improve health, including strong cross-sector referral networks and community partnerships to respond to health risks;
5. Create, champion, and implement policies, plans, and laws that impact health, including equitable access to resources needed for health promotion, prevention of health risks, and to early identification and treatment of recognized health conditions;
6. Utilize legal and regulatory actions designed to improve and protect the public's health;
7. Assure an effective system that enables equitable access to the individual services and care needed to be healthy, including for primary, secondary, and tertiary prevention of health risks;

8. Build and support a diverse and skilled public health workforce, including training for sector-specific personnel to understand their role in preventing and intervening on health risks, and strategies for cross-sector coordination, including across the justice, healthcare, public health, social services, early childhood, and education sectors;
9. Improve and innovate public health functions through ongoing surveillance, evaluation, research, and continuous quality improvement—in the field of toxic stress, these include the work of consortia such the Bay Area Research Consortium on Toxic Stress and Health; the JPB Research Network on Toxic Stress, and the PALS research network;[1083-1085] and
10. Build and maintain a strong organizational infrastructure for public health.

These essential public health services provide the framework for public health to protect and promote the health of all people in all communities. Specifically, the framework utilizes a systematic approach to problem-solving with four general components:

1. Define and monitor the health problem to be prevented or mitigated,
2. Assure widespread adoption of known effective prevention principles and strategies,[1086-1088]
3. Develop and test further prevention strategies, and
4. Identify and seek to reduce risks and increase protective factors at each social-ecological level (individual, relationships, community, and society) across the life cycle.[1089]

This framework also offers a roadmap for public health work to address Adverse Childhood Experiences and toxic stress through primary, secondary, and tertiary prevention strategies. For example, public health surveillance (i.e., tracking health and disease patterns over time) and epidemiologic study (i.e., investigating risk and protective factors and evaluating effectiveness of interventions) provide critical data to inform policy, program, and practice decisions at all prevention levels. In 2008, California became the first state to include the ACE module, adapted from the ACE Study by Kaiser Permanente and the Centers for Disease Control and Prevention (CDC), in the state's Behavioral Risk Factor Surveillance System (BRFSS).[1090] Since then, most states have integrated an ACE module into their BRFSS.[1091] California currently collects ACE information on eight out of the 10 ACEs (neither type of neglect is included) in the BRFSS every other year (so far, 2009, 2011, 2013, 2015, 2017, and 2019).[27] In December 2012, California added ACEs as an indicator for "Healthy Beginnings" in the *Let's Get Healthy California* report.[1092] The BRFSS ACEs module collects information based on adult recollections of their childhood experiences during the first 17 years of life and allows California to compare ACE prevalence with population-level data on other health outcomes, such as heart disease, cancer, and stroke.

However, because the BRFSS ACE module is based on adults' recollections of their childhoods, it is a lagging indicator of ACE exposure that doesn't provide direct information about the current status of ACEs in California's children. Therefore, public health surveillance seeks additional data sources to expand its monitoring of child adversity. The National Survey of Children's Health (NSCH), a population-based survey conducted by the US Census Bureau on behalf of the Maternal and Child Health Bureau of the Department of Health and Human Services, provides the most direct and timely assessment of childhood resilience and adversity.[1093] It asks about five of the original 10 ACEs; in total, the NSCH uses a set of eleven family, economic, and community indicators to ask parents about current adverse experiences to which their children (ages 0–17) have been exposed.[1094] The NSCH confirms that childhood adversity is common among California children. 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 ACE 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%.[32]

The Maternal Infant Health Assessment (MIHA) survey adds an intergenerational perspective on early hardships and adversities, and asks about four of the original 10 ACEs, among eight total adversities. MIHA surveys postpartum women (15 years and older) who deliver a live birth about their own childhood hardships prior to age 14 and their contemporaneous challenges during the current pregnancy. It is a collaborative effort of the Maternal, Child, and Adolescent Health Division and the Women, Infant, and Children Division of the California Department of Public Health and the Center on Social Disparities in Health at the University of California, San Francisco. According to the 2013–2014 MIHA survey, one in four California women with a recent birth (25%) experienced two or more childhood hardships before age 14. Among young mothers ages 15–19, one-third (33%) experienced two or more hardships as children, compared with fewer than one-fifth (19%) of mothers ages 35 and older. Statewide, an estimated 34% of postpartum women living at or below the federal poverty guideline were exposed to at least two childhood hardships, more than double the estimate (16%) for women with higher family incomes (above 200% of the federal poverty guideline).[1095] See **Appendix A** for a summary comparison of the three kinds of ACE surveys used in California.

Taken together, these three public health surveillance data sources provide a rich and conceptually related perspective that looks at child adversity across the lifespan, and useful data to inform and facilitate interventions. However, more timely community-level data are needed to provide detailed, integrated, and real-time information on risk and protective factors to inform policymakers and local community action. In addition, a more robust state and local data infrastructure is needed to move from population-level data to actionable community and clinical data on prevalence, treatment resources, and treatment implementation and efficacy to improve the assessment and treatment of toxic stress, including tracking locally relevant clinical data on rates of ACE-Associated Health Conditions (AAHCs) and available cross-sector services to address toxic stress.[1096]

Public health practitioners also serve as catalysts and conveners to align stakeholder efforts to pursue the multi-level, multi-faceted approaches, promote cross-sector collaboration, community engagement, and increased efficiency in implementing effective, evidence-based interventions and policies to build healthy communities and enhance equity in outcomes. A collaborative "collective impact" approach can mobilize efforts around the shared goal of reducing ACEs and toxic stress in half within a generation and recognizes the power of aligning cross-sector agency actors and community partners in mutually reinforcing policy, systems, and programmatic change activities.

CONCEPTUAL FRAMEWORKS FOR UNDERSTANDING AND ADDRESSING ACEs AND TOXIC STRESS

The public health field has also developed several conceptual models that provide insights and capture the complexities of understanding the wide range of childhood adversities and addressing toxic stress. As characterized by the World Health Organization's (WHO) framework, for example, social determinants of health (SDOH) are identified as "the conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life."[1097] These macro forces often create the context in which families struggle and children are challenged with the traditional ACEs (10 categories of child abuse, neglect, and household challenges) and other risk factors for toxic stress.[3-5]

One of the most comprehensive conceptual models for understanding SDOH is the framework from California's own Bay Area Regional Health Inequities Initiative (BARHII), which is focused on reducing health inequities.[1098] As highlighted in the

BARHII model (**Figure 10**), the public health approach identifies the structural social, economic, cultural, and institutional forces that shape the living conditions through which the odds for optimal early child development are set. These structural drivers are grounded in the inequitable distribution of power, money, and resources. They create the structural stratifications that shape income, education, occupation, housing, gender, and race/ethnicity social hierarchies, exposure to adversities like violence and environmental toxins, as well as the dominant social norms that support these hierarchies.

Public health embraces health equity as a foundational guiding principle, and seeks the eradication of unjust and remediable differences in health among and between social groups.

Health inequities are the unjust and avoidable differences in health status seen within and between population groups. They are conceptualized as the result of past discriminatory actions and present-day policies, laws, practices, and procedures within government, institutions, and businesses: systems that, whether deliberate or inadvertent, shape the unequal distribution of these determinants. Examples include displacement and gentrification, loss of economic engines or jobs, school funding formulas, toxic exposures, the criminalization of mental illness and substance abuse, and targeted enforcement of immigration laws.[1099] Thus, public health embraces health equity as a foundational guiding principle, and seeks the eradication of unjust and remediable differences in health among and between social groups.

These public health and health equity approaches thus compel us not only to address the impacts of ACEs and other childhood adversities at the individual and family levels, but equally importantly for large-scale systemic change and

SOCIAL DETERMINANTS OF HEALTH

Social determinants of health (SDOH) are identified as "the conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life."[1097]

HEALTH INEQUITIES

Health inequities are the unjust and avoidable differences in health status seen within and between population groups.

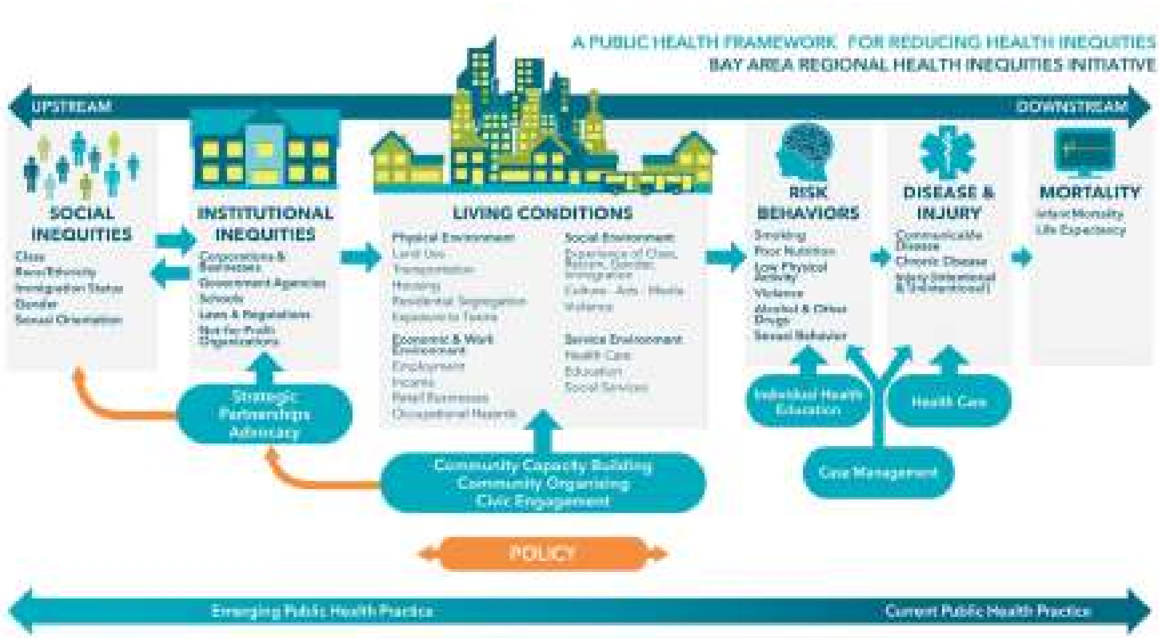


Figure 10. A public health framework for reducing health inequities. Reproduced with permission from the Bay Area Regional Health Inequities Initiative (BARHII).[1098]

prevention of these impacts, to focus on the social, economic, and policy contexts in which people live, grow, learn, and work (see **THE BUILT ENVIRONMENT AND SMART GROWTH**).[23]

At each stage of the life course and at each societal level, public health posits three types of prevention interventions—primary, secondary, and tertiary—*all* of which are needed to achieve a meaningful degree of prevention and change. The factors that are highlighted below pertain primarily to the structural conditions that need to be addressed, at the level of primary prevention, to reduce or eliminate systemic risks for ACEs and toxic stress.

Poverty

Poverty is one of the most powerful and well documented socioeconomic determinants of health, as well as a known risk factor for ACEs and independently, for toxic stress.[10,23,31,60,61,178,510,1100,1101] It increases family stresses and creates child adversities that, in turn, can trigger toxic stress and negative child health and social outcomes, especially when exposure to poverty begins early or is deep or prolonged.[1102] Further research has documented some of the potential underlying mechanisms through which spatially concentrated neighborhood disadvantage acts to produce bio-physiological consequences. For example, analyses from the Fragile Families and Child Well-being Study have found that neighborhood disadvantage was associated with shorter telomere length for both Black and

White mothers, but with a unique role of racial segregation.[1103] (Telomeres are protective sequences of DNA capping the ends of chromosomes that shorten over time. Chronic stress exposure leads to accelerated telomere length shortening,

THE BUILT ENVIRONMENT AND SMART GROWTH

The health and well-being of California's populations are shaped in large part by the policies and programs that inform land use and planning, housing, transportation, economic development and infrastructure. These **built environment** factors profoundly influence how well the state is able to address health and access to opportunity for all Californians, particularly low-income residents.

The public health field plays an important role in ensuring that communities have healthy environments that support healthy behaviors and reduce risk of harmful exposures. For example, changes to the built environment are considered a promising strategy for creating population-wide access to stress-buffering factors such as nutrition and physical activity. The characteristics of our communities, such as proximity of facilities, street design, density of housing, and availability of public transit and of pedestrian and bicycle facilities, play a significant role in promoting or discouraging physical activity.

A public health approach to reducing ACEs and toxic stress includes addressing these structural forces and building community resilience factors that strengthen the capacity to mitigate the stress response and counteract the negative effects of ACEs. Implementation of positive environmental changes such as transit-oriented development and increased active transportation (walking, biking, and public transportation) can improve access to health-promoting factors, especially for vulnerable or historically disenfranchised communities.

The **California Health in All Policies (HiAP) Task Force** was established in 2010 through Executive Order S-04-10.[1154] It was charged with identifying strategies to improve the health of Californians while advancing existing goals around air and water quality, natural resources and land protection, affordable housing availability, infrastructure, public health, sustainable communities, and climate change. The HiAP initiative is a collaborative approach designed to improve the health of Californians by incorporating health, equity, and sustainability considerations into policymaking across sectors. The approach recognizes that chronic illness, climate change, health inequities, and rising healthcare costs are interrelated and influenced by policies, programs, and investments across sectors. HiAP, at its core, is an approach to addressing the social determinants of health that are the key drivers of health outcomes and health inequities.

which has been linked to increased susceptibility to and faster progression of aging-related diseases.)[12,310-314] However, despite this theoretical basis and the growing literature on the impact of neighborhood conditions, income, and social position, there is limited empirical evidence on how, where, and for whom these effects influence childhood development and health, making it hard to translate into policy-friendly actions.[1104]

Using the California Poverty Measure, the Public Policy Institute of California reports that in 2018, 17.6% of Californians (about 6.8 million) lacked enough resources to meet basic needs ($34,200 per year for a family of four, on average).[49] Families with children have even higher rates of poverty, at 18.8%, representing about 1.7 million children. Another 17.6% of California residents live in near poverty (up to one and a half times above the official poverty level). Poverty is often present despite family members working full-time. In California, 79% of poor children lived in families with at least one working adult. There are also significant disparities in child poverty among different racial/ethnic groups. In 2018, the percentage of Latinx children in poverty was 22.9%, nearly double that of White (12.8%) children. The poverty rates among Black (18.2%) and Asian American/Pacific Islander (15.9%) children were also high.[49]

Racism and discrimination

The American Academy of Pediatrics (AAP) recently recognized historical and institutionalized racism as a crucial SDOH.[681] AAP outlines three levels through which racism operates: (1) institutional, (2) personally mediated, and (3) internalized. According to the Prevention Institute's framework,

> "On a community level, institutional racism, expressed through the implicitly or explicitly discriminatory policies and practices of social institutions (e.g., governmental organizations, schools, banks, and courts of law), has segregated communities of color from health-promoting resources and exposed these communities to health threats like environmental hazards, disinvestment, and violence."[1105]

Increased cumulative adversity over the lifetime related to interpersonal and structural racism is documented to lead to increased biological "weathering" involving neuro-endocrine-immune-metabolic dysregulation and accelerated aging.[12,58,404,556,557,563,681,1106,1107] For example, analyses of data from the Coronary Artery Risk Development in Young Adults Telomere Ancillary Study documented that racial discrimination contributes to accelerated physiologic weathering and health declines among Black Americans through multiple negative impacts on biological systems, including telomere attrition.[1107] This has implications for susceptibility to acute and chronic health conditions (for example, see **COVID-19:INTERSECTIONS WITH PLACE AND RACE**).

Historical redlining, the practice of making it difficult to lend money to people in neighborhoods with a higher proportion of people of color, is one way in which systemic racism has contributed to both social and environmental stressors.[1108] Institutional and personally mediated racism can result in trauma and chronic stress, as well as internalized racism and a diminished sense of self in youth of color.[681] In California, the complex, cumulative health impacts of racism are manifest across the life span, resulting in disproportionately lower life expectancy based on race and place. In Oakland, for example, a Black child who lives in the low-income flatlands will, on average, die 14 years earlier than a White child who lives in the affluent hills.[1098]

There are other examples of oppression and discrimination that also produce adverse individual and community impacts. For example, lesbian, gay, bisexual, and transgender individuals report experiencing disproportionately higher prevalence of ACEs (e.g., parental abuse)[15,1051] and public discrimination and violence. Gender-nonconforming individuals also report higher levels of family and community abuse, and poorer health and well-being.[1109,1110]

COVID-19: INTERSECTIONS WITH PLACE AND RACE

It is now well established in the United States that racial and ethnic populations have been disproportionately affected by coronavirus disease 2019 (COVID-19) in hospitalizations, ICU admissions, and deaths.[1111] Nationally, for example, Black residents are more than twice as likely to die of the coronavirus as their White counterparts. In California specifically, minority populations have disproportionately high coronavirus death rates, relative to their percentage of the California population: 1.3 times as high for Black, 1.2 times for Latinx, and 1.7 times for Pacific Islander Californians.[1112] A number of factors likely contribute to these inequalities. First, this differential coronavirus impact has been exacerbated by the socioeconomic inequalities documented above that contribute to the co-occurring health conditions (e.g., asthma, chronic obstructive pulmonary disease, diabetes) that increase the risks of serious disease and death from COVID-19. Black and Latinx populations are disproportionately located in neighborhoods with more poverty, air pollution, and extreme heat, less access to healthcare and food, and experience higher unemployment than white neighborhoods. Jobs are often low-wage and, related to COVID-19, are more likely to be deemed "essential," with many working as hospital and emergency support staff, security guards, bus drivers, and delivery drivers. Workers in these roles are more likely to be exposed to the coronavirus and pass it on to friends and family, especially if

COVID-19: INTERSECTIONS WITH PLACE AND RACE

they are living with multiple family members in small or densely packed homes. In addition, a recent study confirmed and strengthened the finding that increased chronic multi-air-pollutant exposure, even at levels below expected impact thresholds, is associated with higher COVID-19 mortality rates when controlling for known socioeconomic and behavioral health influences.[1113] The study models suggested an increase in the respiratory hazard index that was associated with a 9% increase in COVID-19 mortality. Although differing in magnitude, this association held for individual hazardous air pollutants, acetaldehyde, and diesel particulate matter. All these factors make these residents more vulnerable to the coronavirus.

In addition, once exposed, it is known that members of marginalized communities face increased risk of serious infection and death, for complex reasons. For example, Black Americans have a higher risk of morbidity and mortality from COVID-19 due to greater rates of pre-existing chronic conditions that promote more serious infection (such as heart disease, high blood pressure, chronic lung diseases, diabetes, or kidney disease), decreased access to care, and increased cumulative adversity over the lifetime, leading to increased biological "weathering" and accelerated aging, which are known risks for greater complications from COVID-19.[12,58,404,556,557,563,681,1106,1107]

COVID-19 Responses

A recent Johns Hopkins COVID-19 update provides an example of how some states have implemented measures that specifically aim to address the racial and ethnic disparities related to COVID-19:[1114] Black residents in Michigan, who represented 15% of the state's population, represented 29.4% of cases and 40.7% of deaths at the beginning of the pandemic. In September, Black residents represent just 8.2% of cases and 9.9% of deaths. Michigan credited its Coronavirus Task Force on Racial Disparities for this decrease in racial disparities. The Task Force implemented several targeted initiatives, including widespread distribution of masks and enhanced testing in communities of color.

In October of 2020, California became the first state to launch an equity metric as part of the state's reopening plan. In order to advance to the next less restrictive tier, each county is required to meet an equity metric or demonstrate targeted investments to eliminate disparities in levels of COVID-19 transmission, depending on its size. The California Health Equity Metric was designed to help guide counties in their continuing efforts to reduce COVID-19 cases in all communities and requires more intensive efforts to prevent and mitigate the spread of COVID-19 among Californians who have been disproportionately impacted by the pandemic. To facilitate an equitable

COVID-19: INTERSECTIONS WITH PLACE AND RACE

reopening, California also invested in a state-run testing laboratory capable of doubling statewide coronavirus testing capacity, launched in November of 2020. California Health and Human Services Secretary, Dr. Mark Ghaly, specifically targeted bringing greater testing capacity to the communities most impacted, along with contact tracing and supports for quarantining: "We've been tracking the disproportionate impact of COVID on communities of color, on older Californians, on people who are living in more crowded living conditions... and this represents an opportunity to get one of those key tools in there to reduce transmission."[1115]

Michigan and California's efforts are examples of targeted measures to mitigate the elevated risks faced by racial and ethnic minorities.

Distressed neighborhoods with underinvestment

Sufficient data already exist to identify neighborhoods where economic, physical, social, and educational capital are insufficient to counter these stresses and provide necessary protective factors to buffer children from ACEs and other childhood adversities. Multiple studies have shown that neighborhood characteristics (e.g., segregated and concentrated poverty) affect the level of violence, crime and delinquency, education performance, psychological distress, and various health problems. The stressors of living in neighborhoods with inadequate or inequitable access to economic and educational opportunities are indicative of community-level trauma. Researchers have highlighted that:

> "Distressed neighborhoods are places where families are under the greatest stress and ACEs in the home are more likely to occur. They also are places where there are more environmental hazards, such as exposure to lead, mold, and airborne pollutants, which jeopardize health. They are places where families often must struggle to find safe and supportive environments outside the home for their children to grow and explore the world."[1116]

This often means families who live in distressed neighborhoods face a higher cumulative dose of adversity and a lower cumulative dose of buffering relationships and environments, resulting in increased allostatic load (the cumulative biological impacts of repeated exposure to adversity) and increased risk for toxic stress.[60,61,1101] In terms of health inequalities, it has been further demonstrated that "place and race are highly intertwined and the poorest neighborhoods often are racially segregated and distant from sources of economic opportunity and support."[1116] Thus, distressed neighborhoods create the conditions in which ACEs and other child adversities are more likely both to occur and to have more severe consequences. These conditions contribute to cumulative allostatic load and development of the toxic stress response.[6,10,12,61,178,1100,1101,1116-1118]

Environmental pollution exposure

Children who are highly exposed to adversity, including ACEs, often also have higher exposure to environmental toxicants like air pollution, heavy metals, and toxic chemicals.[1119] Low-income communities and communities of color in the United States often reside in neighborhoods with worse air quality and greater environmental hazards.[1120] Specifically, schools in California attended by Latinx, Black, or low-socioeconomic-status students are more likely to be close to a heavily trafficked highway than those attended by White students.[1121] The result is that children of color are more likely to be exposed to higher levels of traffic-related airborne pollutants. Lead is another example of a specific environmental exposure that can interact with toxic stress, with similar detrimental impacts on the brain and nervous system, including lower IQ (see LEAD EXPOSURE).[1122-1124] Exposures to lead and other toxic stressors (like ACEs) together can result in enhanced neurotoxicity.[170]

In California, neighborhood districts that were historically classified as being "non-desirable" (with a D rating) have been documented to have higher diesel exposures (39.7 kg/day, compared to 22.6 kg/day) than districts with an A rating. These districts also have a higher proportion of people of color—only 18% of "non-desirable" districts consisted of non-Hispanic White people, compared to 67% in other districts. These districts, in turn, have more asthma-related emergency department visits (15.6 per 100,000 population, age-adjusted, 95% confidence interval, CI, 8.8-23.3) than "desirable" districts.[1125]

As another example, in utero exposure to both stress and air pollution can increase oxidative stress, which may affect the development of the fetal lungs, including increased airways inflammation and simplification of the normally complex lung structures.[235,236] An increased risk of asthma was found in children co-exposed in utero to fine particulate matter ($PM_{2.5}$) and maternal stress (odds ratio, OR 1.15; 95% CI, 1.03-1.26) during the phase of lung development when many of the peripheral airways important in asthma develop (the canalicular phase).[233] In childhood, air pollutants and stress interactions are associated with changes in specific inflammatory mediators that are associated with worse asthma outcomes, including interleukin-5, IgE (allergic-type antibodies), and eosinophil counts (allergic-type immune cells, AIR POLLUTION AND ASTHMA).[1126]

PRIMARY PREVENTION STRATEGIES

The public health field recognizes that ACEs and other child adversities, and resultant toxic stress, are preventable, and that primary, secondary, and tertiary

AIR POLLUTION AND ASTHMA

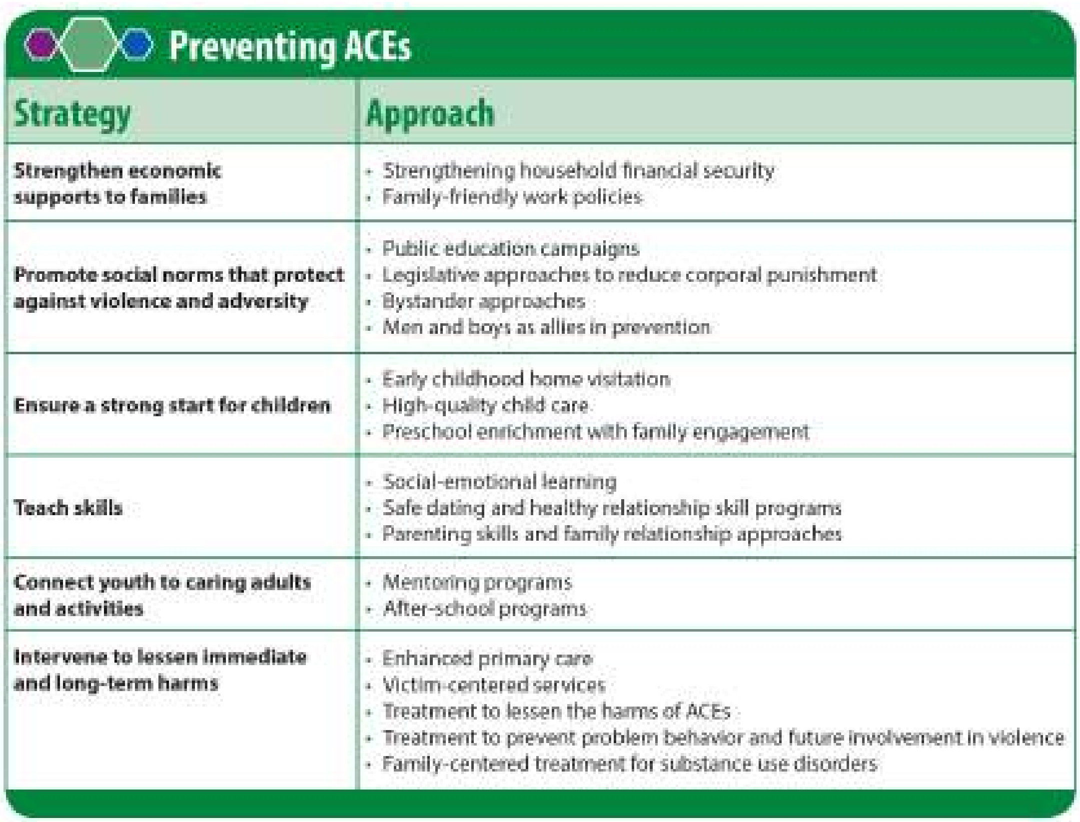
Air pollution is also associated with decreased lung function growth and both development and exacerbation of childhood asthma. Exposure to and impacts of air pollution are inequitably distributed in ways that mirror the populations at greatest risk for ACEs and toxic stress. For example, living near or attending a school near a heavily trafficked highway is associated with an increased risk of children developing asthma or bronchitis. Asthma incidence is highest for children growing up in poverty (10.2% of children below the poverty line compared to 5.4% of those at greater than 4.5 times the poverty line) and in non-Hispanic Black children (14.2%, compared to 6.8% of non-Hispanic white children).[1142]

The impacts of air pollution on asthma also interact with total exposure to adversity or buffering factors. Children who grow up in households with greater psychosocial stress are more susceptible to the detrimental effects of air pollution on asthma outcomes. In a birth cohort followed from pregnancy, exposure to nitrogen dioxide, a common traffic-associated air pollutant, was associated with increased risk of developing asthma (OR 1.63, 95% CI 1.14, 2.33), but only in those children who also experienced higher levels of intimate partner violence (IPV) (one of the original ACEs) and community-level violence (an additional risk factor for toxic stress).[1143] Children whose parents are stressed and are exposed to air traffic pollution have larger decreases in lung function (~5% decrease)[967] and increased risk of asthma (hazard ratio 1.5; 95% CI 1.16-1.96)[232] than those without both risk factors. Higher parental stress interacted with exposure to nitric oxide, nitric dioxide, and total oxides of nitrogen to more strongly reduce lung function in children with asthma in households with high parental stress. For example, FEV1 was reduced by 4.5% in high-stress households after exposure to a 21.8 ppb increase in total oxides of nitrogen at home.[967]

prevention strategies must work synergistically to improve outcomes at public health scale. Primary prevention approaches require cross-sector collaboration working “upstream” on the structural determinants of health to prevent child adversity from happening in the first place. Primary prevention interventions address the fundamental root causes of health status, such as housing security, economic supports, community development funds, living wage policies, family-friendly business policies, access to education, and employment opportunities. They tend to have the greatest population health impact because these social and economic stratification structures shape the whole population’s access to and opportunities for employment, mobility, success, and health. They reduce the overall dose of adversity and enhance access to buffering resources, should exposure to ACEs occur.

The CDC created the Essentials for Childhood (EfC) initiative to focus on the primary prevention of ACEs, and more specifically, of child abuse and neglect.[619] The initiative focuses on raising awareness and commitment to promote safe, stable, nurturing, relationships, and environments and creating the broader societal conditions for healthier children and families through policies and programs (i.e., changing social norms).[1127] California was selected for five-year CDC grants in both 2014 (among five states chosen) and 2019 (among seven states) and has made significant progress towards these aims.[1128,1129] The CDC's suite of technical materials, including the EfC Technical Package, highlights the growing body of scientific evidence supporting primary prevention strategies and approaches for effective prevention of ACEs (**Figure 11**).[1130,42]

In order to focus more attention at the community level, the Prevention Institute (PI) developed a useful framework for detailing the dynamics of community adversity



Preventing ACEs

Strategy	Approach
Strengthen economic supports to families	• Strengthening household financial security • Family-friendly work policies
Promote social norms that protect against violence and adversity	• Public education campaigns • Legislative approaches to reduce corporal punishment • Bystander approaches • Men and boys as allies in prevention
Ensure a strong start for children	• Early childhood home visitation • High-quality child care • Preschool enrichment with family engagement
Teach skills	• Social-emotional learning • Safe dating and healthy relationship skill programs • Parenting skills and family relationship approaches
Connect youth to caring adults and activities	• Mentoring programs • After-school programs
Intervene to lessen immediate and long-term harms	• Enhanced primary care • Victim-centered services • Treatment to lessen the harms of ACEs • Treatment to prevent problem behavior and future involvement in violence • Family-centered treatment for substance use disorders

***Figure 11**. Strategies and approaches to preventing ACEs. Note: All but the last strategy listed represent primary prevention approaches; the last item represents secondary and tertiary prevention. Reproduced under open access from the CDC.*[1130]

Figure 12. *Community symptoms of trauma. Reproduced with permission from the Prevention Institute.*[1099]

and resilience and developing strategies to address and prevent community adversity.[1099] Community symptoms of adversity are displayed in Figure 12. At the community level, adversity manifests in three interrelated clusters: people (the social-cultural environment), place (the physical/built environment) and equitable opportunity (the economic environment).

In response to the community symptoms, a framework for creating community solutions and resilience is shown in Figure 13. In the context of community adversity, building resilience means putting the conditions in place in which the community can heal from past traumas and be protected against the impact of future adversity. The successful implementation of strategies for community healing build on existing community assets and are dependent on community engagement that connects young people and adults together in a supportive community.

Strengthening economic supports

The state budget (2019–2020 and 2020–2021) put forward by Governor Newsom and the California legislature has made significant investments in promoting a "parents' agenda" to make life easier for California families.[1131,1132] It has begun to expand the reach and coverage of existing economic support mechanisms to increase the economic well-being of families and children. These include the state Earned Income and Child Tax Credits (EITC and CTC), CalWorks (cash assistance for families with children, including a suite of economic support opportunities like job skills, child care, and educational supports), CalFresh (California's main food

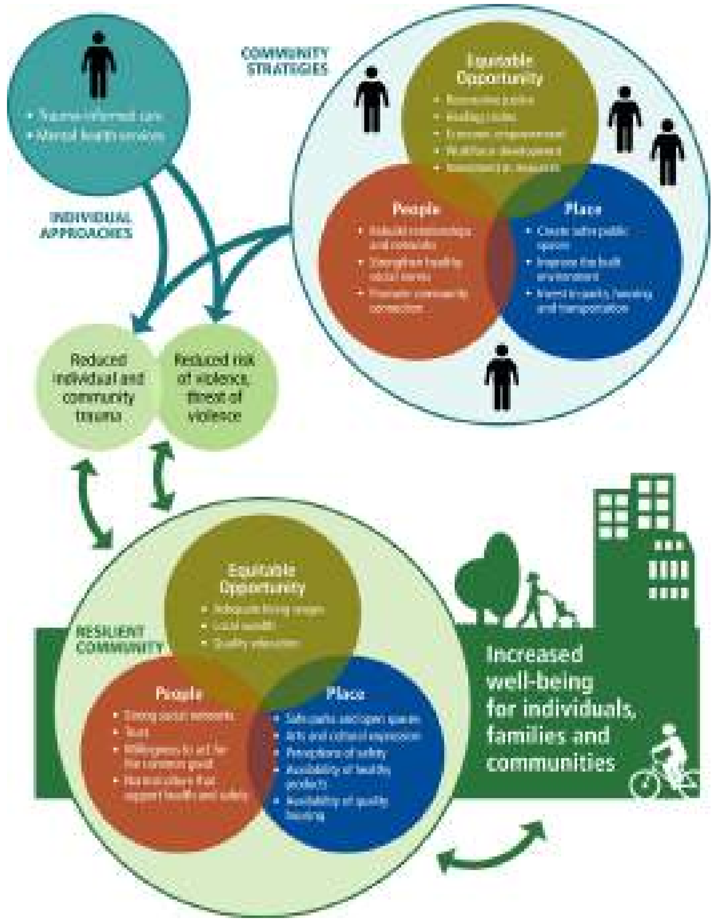


Figure 13. *Promoting community resilience: from trauma to well-being. Reproduced with permission from the Prevention Institute.*[1099]

assistance program), and financial/economic literacy training (e.g., the Economic Empowerment grants of the Office of Child Abuse Prevention, Department of Social Services). Paid family leave is an economic strengthening policy available to parents who need time to bond with a new child entering their life either by birth, adoption, or foster care placement. It also provides benefits to individuals who need to take time off work to care for a seriously ill family member. Paid family leave is an important policy strategy for primary prevention of ACEs and toxic stress in that it both strengthens economic supports and facilitates parent–child bonding. California was the first state in the nation to implement a comprehensive paid family leave program (in 2004) and has continued to expand its reach. Additional federal food and nutrition policies and programs that address child poverty include the Supplemental Nutrition Assistance Program (SNAP) and the Special Supplemental Nutrition Program for Women, Infants and Children (WIC). (See **Primary, Secondary, and Tertiary Prevention Strategies in Early Childhood**

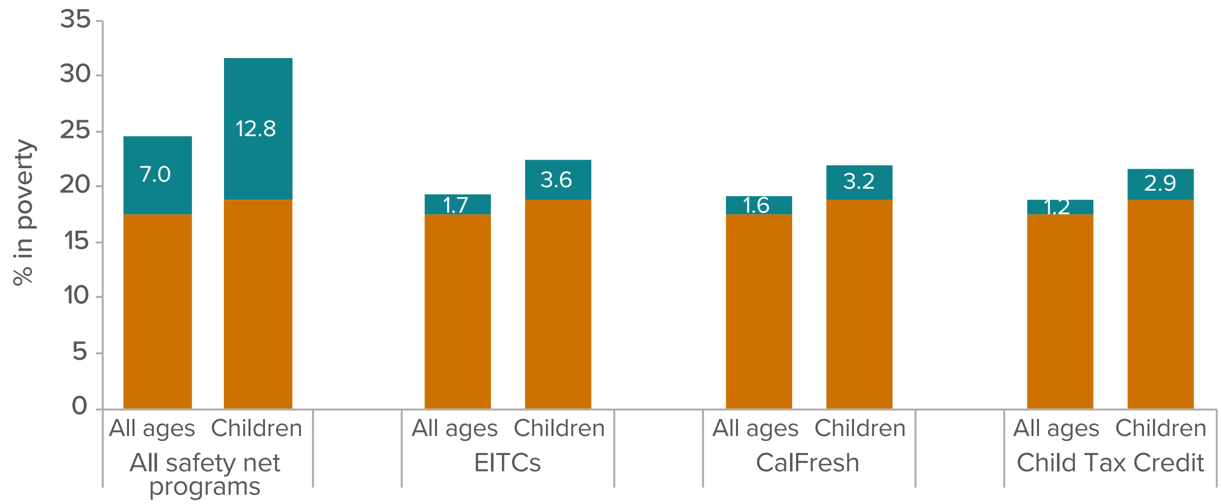


Figure 14. Poverty would be even higher in the absence of the social safety net, especially for children. Reproduced with permission from the Public Policy Institute of California.[49]

Supports, later in Part II, for more information.)

Most safety net programs are designed to prioritize children. Child poverty rates are high in California (18.8%), but would be even higher without the state's strong social safety net. Analyses by the Public Policy Institute of California demonstrate that California's social safety net kept an additional 12.8% of children out of poverty in 2018 (**Figure 14**).[49] California's largest social safety net programs for children continue to be the federal and state EITCs, which together lowered the child poverty rate by 3.6%; CalFresh, which lowered it by 3.2%; and the federal CTC, which lowered it by 2.9%.

Other primary prevention strategies are aimed at creating supportive and stable early living conditions through policies and programs that promote positive, nurturing relationships, environments, and communities. These additional strategies include:

- Enabling community opportunities for play and physical activity;
- Promoting parenting efficacy, resilience, attachment, and family bonds, including reducing family violence;
- Providing high-quality learning opportunities for children, including social-emotional learning, executive function skills, and responding to challenges; and
- Providing access to high-quality mental and physical healthcare, including enhancing access to family planning resources.

Public education

Policy- and systems-level efforts to prevent ACEs and toxic stress also depend on the awareness and engagement of the general public and governmental decision-makers. The "political will" to implement pro-child, pro-family policies and budgets is influenced by social norms about the status of children and the loci of responsibility for their well-being. The dominant public narrative about child abuse and neglect, for example, has been characterized by an individual focus on "bad" parents and government interference. Based on research findings, the FrameWorks Institute has created a social counter-narrative that can help engage the public in understanding early child development as it applies to child abuse and neglect prevention, understanding potential policy directions, and supporting solutions to pressing problems.[49]

Changing social norms is an important aspect of primary prevention for ACEs and toxic stress. Thus, the EfC initiative is promoting a social narrative grounded in shared values and a shared responsibility to enact proactive solutions that support safe, stable, nurturing relationships and environments for all parents and children. Educational efforts underway (primarily at the professional and practitioner level) are using ACE prevalence data to make the case for policy-level solutions such as expanded paid family leave, living wage policies, family-friendly business policies, access to home visitation services, and family resource centers.[1129] In partnership with First 5 California's educational campaign Talk. Read. Sing.®, the Office of the California Surgeon General is promoting public education messaging on concrete behavioral actions families can take to mitigate the effects of stress and adversity and enhance resilience.[1133,1134] The ACEs Connection movement has also played a central role in reframing the dominant social norms about risky behaviors (e.g., smoking, obesity, violence, substance use, and sexual assault) and AAHCs, among other chronic health outcomes.[1135]

However, broader-scale public education awareness campaigns to enhance understanding and shift public discourse around ACEs, toxic stress, and their impacts are needed to expand current state and local efforts and to create a resilient, trauma-informed state. Public health messaging and public education campaigns can be utilized to enhance public knowledge about ACEs, toxic stress, and their health impacts, and to bolster acquisition of concrete interventions and skills individuals can learn to regulate their stress responses, including improving sleep, nutrition, exercise, healthy relationships, access to nature, mindfulness practices, and when needed, mental healthcare, to build resilience.

Past public education campaigns have been effective at reducing the prevalence of health conditions and risk factors, such as smoking (see THE TRUTH INITIATIVE), lead poisoning, and motor vehicle deaths. These campaigns are most effective when partnered with concrete public policy efforts such as those limiting indoor use of tobacco products, restricting use of lead in industrial products, or requiring seat belt use.

THE TRUTH INITIATIVE

The 1998 Master Settlement Agreement between tobacco product manufacturers and states required the tobacco companies to pay billions of dollars to compensate states and territories for tax dollars that had gone to combat tobacco-related diseases. The agreement created the American Legacy Foundation, later renamed the Truth Initiative, as the first national public health organization dedicated to ending tobacco use among youth and young adults.[1136] In 2000, the Truth Initiative launched its first national public education campaign and brought information to teens at music and sports venues. The initiative also invested in state-level grants supporting youth empowerment, and targeted campaigns funding prevention and quitting projects among racial, ethnic, and lesbian, gay, bixesual, and transgender youth. The initiative also funded the 2007 report of the Institute of Medicine's *Ending the Tobacco Problem: A Blueprint for the Nation*, which offered recommendations for action by

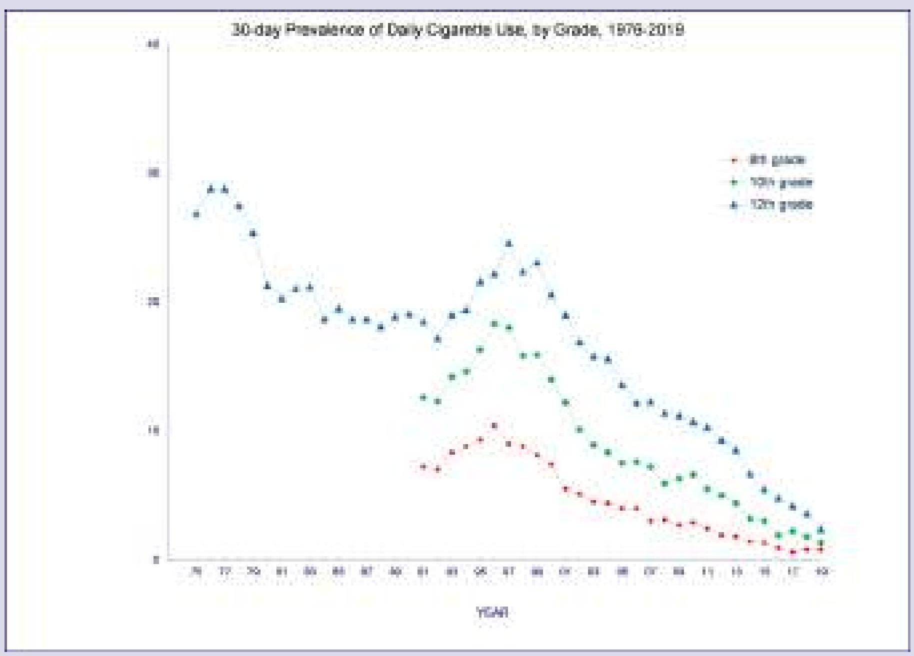


Figure 15. *Thirty-day prevalence of daily cigarette use, by grade, 1976-2019. Reproduced under an open license.*[1138]

THE TRUTH INITIATIVE

federal, state, local, non-profit, and for-profit entities.[1137] Over its two-decade history, the Truth Initiative has continued to launch multiple campaigns focused on refreshing messages for populations at the highest risk, such as those with mental illness, and for new generations of youth. The initiative has been credited as being a major driver of the decline in teen cigarette use from its peak of 25% in 1998 to just 3.6% in 2019 (**Figure 15**).[1138]

A critical part of interventions at all levels of prevention is providing widespread trauma-informed and ACEs-aware training for all child- and family-serving sectors, including all healthcare personnel, as well as all allied cross-sector workforces.[623,1133] The ACEs-informed lens can help providers and practitioners reframe the question from, "What is wrong with you?," to more root cause inquiry, instead asking "What happened to you?"[635] Prevention efforts also crucially depend on allied cross-sector initiatives and funding across systems that support children, families, other caregivers, and communities, including healthcare, behavioral health, public health, home visitation, supports for parenting, supports for adults living with toxic stress, trauma-informed social services, welfare, criminal justice, early care, immigration, insurance, first responders, and education.

SECONDARY PREVENTION STRATEGIES

Secondary prevention aims to reduce the impact of ACEs that have already occurred, before or early in the course of development of toxic stress and AAHCs. This is done by identifying ACEs as soon as possible and intervening to halt or slow the development of the toxic stress response, keeping it in the tolerable stress zone. The tolerable stress response is characterized by return to homeostasis and normal physiologic function as a result of adequate buffering care and other interventions.[6]

It also includes the use of surveillance of population-level indicators of exposure to ACEs and impacts of toxic stress to guide screening and secondary prevention strategies. For example, for heart disease and stroke prevention, the CDC conducts laboratory standardization, surveillance, and vital statistics activities, as well as more recently, public health program coordination and implementation.[1139]

Environmental solutions

Secondary prevention for common environmental exposures includes early screening and intervention for toxic exposures, as is done with lead among vulnerable populations (see LEAD EXPOSURE).

Asthma, an AAHC, remains a major public health concern in California, and the environmental remediation tactics employed by public health programs to address root causes for asthma are an example of public health-oriented secondary prevention strategies. Low-income Californians enrolled in Medi-Cal, the state's Medicaid program, have higher asthma severity, poorer asthma control, and higher

LEAD EXPOSURE

Both lead exposure and toxic stress can lead to life-long health risks by altering the developmental trajectory of neurological and biological circuits. Many of the actions of lead poisoning affect the same physiologic systems as toxic stress, with some symptoms and outcomes being shared between the two conditions. Both lead exposure and the toxic stress response are associated with changes to the structure and function of children's developing brains, especially the prefrontal cortex, and both may present clinically with executive functioning impairments, including inattention, irritability, learning impairments, and behavioral concerns.[1155,1156] Toxic stress and lead are both also associated with increased cellular oxidative stress and early cell death, [12,186,310,312-314,1156-1159] as well as increased risk for cardiovascular disease and impaired reproductive outcomes later in life.[2,429,430,443-446,457,1156,1160-1163] In the case of lead exposure, some mechanisms have only been established at higher exposure levels;[1158,1162] the impacts of early adversity on health are also known to be dose-dependent.[2] Thus, lead exposure and toxic stress may be synergistic in leading to negative health and developmental outcomes. In addition, they also share similar demographic profiles, disproportionately impacting low-income communities and communities of color.[30]

Many of the public health strategies to reduce or eliminate lead poisoning have been driven by scientific advances that demonstrate that there is no safe level of lead exposure. Lead leads to irreversible neurocognitive damage, so any exposure must be avoided, but the harms that result once exposure has occurred cannot be reversed.[1155]

Many important policies have strengthened primary prevention-related regulation of lead-based contaminants and exposures and have dramatically reduced lead exposure among children since 1971.[1155] After the ban of lead-based paint in 1971, lead in gasoline starting in 1973, lead in residential paint in 1978, and lead in plumbing in 1986 (all primary prevention efforts), the number of children who had blood lead levels of at least 10 µg/gL fell by about 80%.[1155] However, it is now recognized that no lead level is safe for children.

The California Environmental Health Tracking Program estimates that

LEAD EXPOSURE

eliminating lead exposure would result in $8–11 billion in additional lifetime earnings for all children born in California during a single year.[31] Experts recommend home lead abatement before a family with children moves in, using specific tools to sample house dust, soil, and water for lead, and removing its sources where possible.[1164]

Despite this progress and the growing body of evidence of independent and synergistic harm, childhood lead exposure in California remains common, and leads to poor behavioral and neurocognitive outcomes.[1155,1165,1166] Even with limited screening, in 2017, California identified around 10,000 children with blood lead levels above 4.5 µgm/dl, the California Department of Public Health's threshold for education and specific remediation interventions.[29] Sources of lead include lead-contaminated dust, soil, and water, lead-acid battery recycling, certain imported toys, foods, ceramics, and cosmetics.[1155,1166]

Secondary prevention strategies, after exposure has occurred, include testing public water sources, and these strategies involve case-finding after impacts have occurred, to prevent further exposure. Screening children for blood lead levels enables early detection and early intervention to prevent further lead exposure, as no

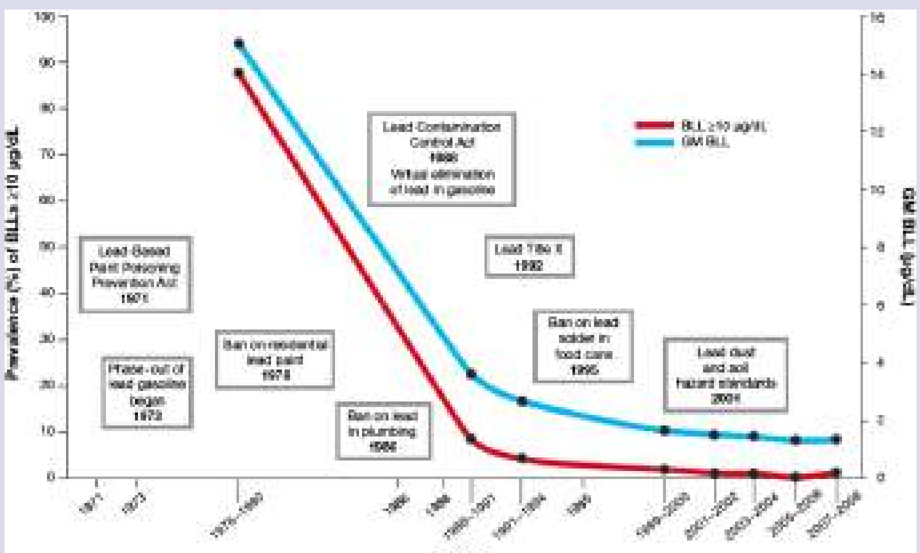


__Figure 16.__ A timeline of the prevalence of children's blood lead levels (BLLs) > 10 µg/dL, as various lead prevention policies were passed. Reproduced with permission from journal Pediatrics, volume 38 (1), page e20161493; copyright © 2016, by the American Academy of Pediatrics.[1155]

LEAD EXPOSURE

non-zero blood lead level is safe.

California has also enacted multiple laws to prevent and intervene on childhood lead poisoning and has established detailed requirements for implementing these laws, including establishing The Childhood Lead Poisoning Prevention Branch (CLPPB).[1167] The CLPPB prevention and lead abatement program offers home visitation, environmental home inspections, and nutritional assessments to families of children found to be severely lead-exposed, as part of a tertiary prevention approach. The CLPPB provides telephone contacts and educational materials to families of lead-poisoned and lead-exposed children. It also provides education to the general public, medical providers, and community-based organizations. There are local Childhood Lead Poisoning Prevention Programs in most California counties.

Efforts to support children with a history of lead exposure include many of the same interventions employed to buffer toxic stress,[1168] including high-quality child development interventions and enriched environments. Following the Flint water crisis, in which thousands of people were exposed to water contaminated with high levels of lead, a blend of government and philanthropic sources came together to support expanded mother–infant programs, universal home-based early intervention, high-quality early education, family and parenting support programs, early literacy and two-generation literacy initiatives, universal preschool, school health services, mindfulness programming, breastfeeding support, nutrition prescriptions, Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) co-location with primary care, mobile grocery stores, and trauma-informed care.[1169] Given the synergistic effects of lead poisoning and toxic stress, tertiary prevention strategies to mitigate the impacts of lead exposure should include education and efforts to prevent ACEs and reduce the risk of toxic stress.

rates of asthma emergency department visits and hospitalizations.[9] Although there is no cure, it can be controlled, including using remediating environmental interventions (item four below). The National Asthma Education and Prevention Program (NAEPP)'s best practice guidelines describe the four vital components of asthma management:

1. Assessment of disease severity and control;
2. Comprehensive pharmacologic therapy;
3. Patient education; and crucially,
4. Environmental control measures to avoid or eliminate factors that

contribute to asthma.[1140]

The Public Health Institute's Regional Asthma Management and Prevention program has reported that education and environmental remediation programs targeting high-risk children demonstrate returns on investment of between $7.69 and $11.67 for every $1 spent.[1141] Implementing these national guidelines to reduce the burden of asthma should also address the environmental and social inequities that perpetuate disparities in asthma symptoms.

The Office of Environmental Health Hazard Assessment, within the California Environmental Protection Agency, has developed and maintains the CalEnviroScreen, a mapping tool designed to help decision-makers identify California communities and vulnerable populations with high levels of exposure to the cumulative burden of multiple sources of pollution.[1144] The current version of the tool, CalEnviroScreen 3.0, uses 20 statewide indicators of pollution burden and population characteristics associated with increased vulnerability to pollution's health effects. For example, the tool includes data on air quality, drinking water quality, the presence of contaminated sites, and public health conditions such as low infant birth weight rates and asthma rates, as well as socioeconomic information such as poverty, educational attainment, and linguistic isolation. The data in CalEnviroScreen has been used to analyze the relationship between places with high cumulative pollution burdens and the racial/ethnic and age distribution of the community. Specifically, Latinx and Black individuals reside in highly impacted communities, while other groups reside disproportionately in less impacted communities. These inequities are especially stark in children, with one in three Latinx and Black children living in the most disadvantaged communities (that score in the highest 20% for cumulative exposures to pollution and community vulnerability characteristics) while the fraction is one in 14 for Whites, one in eight for Asians, and one in seven for Native Americans.

Public health efforts for secondary prevention of toxic stress should enable early detection and early intervention on both the individual and community levels. The first-in-the-nation ACEs Aware Initiative currently being implemented in California (see **The ACEs Aware Initiative** in Part III) is taking the lead in bringing to scale a comprehensive ACEs and toxic stress screening and intervention program by training healthcare providers throughout the state to facilitate routine screening among the California Medi-Cal population, coupled with thoughtful cross-sector linkages to intervene on risk of toxic stress.[1133]

The public health sector can support individuals identified by their health provider as being at intermediate or high risk for toxic stress and facilitate connections to resources to reduce the severity and prevent the transmission of toxic stress to subsequent generations (as discussed in the **Intergenerational Transmission of Adversity** in Part I). Additionally, public health efforts should target preventing or reducing environmental factors that worsen toxic stress physiology, such as exposure to lead and air pollution. Key components of secondary prevention include:

1. Assessment and monitoring of rates of ACEs and toxic stress (in the absence of clinical diagnostic criteria for toxic stress, clinical assessment of intermediate or high risk for toxic stress may be utilized).
2. Improvement of diagnostic criteria for toxic stress.
3. Support of networks of care for individuals identified as being at intermediate or high risk of toxic stress.
4. Patient education and public communication to raise awareness of effective interventions for those at intermediate or high risk of toxic stress.
5. Engagement of core public health functions, including surveillance, evaluation, research, and continuous quality improvement to improve outcomes, for individuals and communities impacted by ACEs and toxic stress.

TERTIARY PREVENTION STRATEGIES

Tertiary prevention aims to soften the long-term effects of ACEs and toxic stress across the life span, once their impacts are already underway, and includes interventions for homelessness, criminal justice involvement, and other sequelae of toxic stress (see HOMELESSNESS and **Primary, Secondary, and Tertiary Prevention Strategies in Justice** section later in Part II). Strategies to address childhood trauma and adversity include efforts to help people regulate toxic stress physiology, a root cause of longer-term, often complex health consequences (e.g. more severe or earlier onset AAHCs, more permanent impairments), in order to improve their ability to function, quality of life, and life expectancy.

Additionally, public health programming that seeks to address health or social conditions that are strongly associated with ACEs and toxic stress, such as asthma, obesity, diabetes, heart disease, homelessness, teen pregnancy, HIV/AIDS, and mental and behavioral health concerns (among others), should include training and competencies for providers, as well as education for patients or clients about the role of toxic stress as a driver of these conditions. In addition, these programs should work to incorporate strategies to mitigate the toxic stress response, including social supports, regular exercise, mindfulness interventions, sleep hygiene, nutrition, and mental or behavioral health interventions, as indicated (see the previous section, **Tertiary Prevention Strategies in Healthcare**, for details).

The use of population-level data collection and analysis to inform evidence-based screening, intervention, and evaluation of outcomes around ACEs, toxic stress, and AAHCs is also crucial. For example, in the National Program of Cancer Registries deploys data monitoring systems to aid in the systematic collection and analysis of data on cancer risk factors, incidence, and mortality, for the purposes of program monitoring, evaluation, and research.[1145] A thoughtful public health tertiary prevention approach also includes policy and programmatic investments in expansion of evidence-based interventions, such as the $9 million California Initiative to Advance Precision Medicine state investment to research precision medicine approaches to identifying and intervening on toxic stress.[337]

HOMELESSNESS

According to the US Department of Housing and Urban Development, in 2019, there were 151,278 homeless individuals in California, a nearly 17% increase over 2018. Over 108,000 of these individuals were unsheltered—living on the street or in a car.1146 There is a strong dose-response relationship between the number of ACE categories experienced and risk of housing insecurity, overcrowding, and homelessness.[1,1147,1148] In a large nationally representative survey, the National Epidemiologic Survey of Alcohol and Related Conditions (N = 34,653, 2001–2002 and 2004–2005), the lifetime homelessness risk that could be attributed to any given ACE was 45% in men and 60% in women, independent of any substance use disorder or mental health co-morbidities. Among men who were homeless, 85% had experienced at least one ACE; among women, 77% had experienced at least one ACE.[1] In another large population-based study (N = 2,323,340, of whom 5.6% were homeless) in Washington state, each cumulative ACE predicted a 40% increase in the probability of being homeless.[1149] In addition, very high rates of intergenerational transmission of ACEs have been documented among homeless families.[1150] In one study of 215 parents, an ACE score of 4 or more predicted homelessness in their children with an odds ratio of **10.4**.[1151]

Since taking office in 2019, Governor Newsom has directed the state to

HOMELESSNESS

invest more than $2 billion in new, direct aid as part of a comprehensive state response to homelessness, including the creation of the California Access to Housing and Services Fund ($750 million), Emergency Homelessness Aid, and availability of state land assets.[1152] These investments respond to the long-term impacts of toxic stress and should be paired with training and education about the role of toxic stress as a key driver of homelessness. As noted throughout this report, tertiary prevention of toxic stress in current or future parents is a key tool for primary prevention in the next generation. Investments to reduce homelessness, especially when paired with supportive services to mitigate the toxic stress response, can help to prevent the intergenerational transmission of ACE and toxic stress.

These new investments to combat homelessness represent a multi-pronged effort including early intervention: moving individuals and families off the streets; creating new temporary housing to effectively reduce street homelessness; and providing homeless individuals and families with needed services, including comprehensive care to address their health needs, including those related to toxic stress, such as targeted and coordinated treatment of AAHCs like heart disease, chronic obstructive pulmonary disease, cancer, depression, and substance use disorders, and comprehensives referrals and services to address any co-occurring social determinants of health. Programs and organizations who serve homeless individuals and families can refer clients to a healthcare provider trained in assessing for ACEs, identifying toxic stress and supporting patients with trauma-informed care through the ACEs Aware Provider Directory.[1153]

As part of the plan, Governor Newsom has also launched 100-day challenges for California cities and counties, replicating a successful national model to jumpstart action to fight homelessness. In direct response to the COVID-19 pandemic, the Project Roomkey initiative was launched to provide non-congregate shelter for people experiencing homelessness and for front-line healthcare workers. This initiative has been expanded through project Project Homekey, California's nation-leading $600 million program to purchase and rehabilitate housing—including hotels, motels, vacant apartment buildings and other properties—and convert it into permanent, long-term housing for people experiencing or at risk of experiencing homelessness.

Through these comprehensive efforts, state, and local partners are working together across systems to collaborate, innovate, and execute to create a coordinated community response to end homelessness, with special attention to specific populations for whom toxic stress poses special risks, including veterans, youth, and families with young children.

Primary, Secondary, and Tertiary Prevention Strategies in Social Services

In 1962, pediatrician C. Henry Kempe and colleagues published "The Battered-Child Syndrome" in the *Journal of the American Medical Association*, which recognized the prevalence and clinical manifestations of child abuse and called on physicians to report such findings to legal authorities.[1170] The report is widely credited with changing both medical and public views on child maltreatment, which was previously thought to be uncommon and not a significant medical or societal concern. The result was the recognition of child abuse as a public health concern and the transformation of medical and social service response.

The advancement of clinical recognition and response to child abuse prompted novel policy strategies for prevention and intervention. In 1974, the United States (US) Congress passed the Child Abuse Prevention and Treatment Act, which authorized federal funds for the development of Child Protective Services and hotlines for the prevention, identification, and treatment of child abuse and neglect and established the National Center on Child Abuse. Today, the child welfare system encompasses a broad array of interconnected systems and services that oversee four primary domains: child protection, family-centered support, foster care, and adoption.

Child abuse and neglect—also termed child maltreatment—constitute five of the 10 categories of Adverse Childhood Experiences (ACEs) included in the original ACE Study (physical, sexual, and emotional abuse, and physical and emotional neglect).[3-5] Estimates of substantiated child abuse or neglect (i.e., confirmed after child welfare investigation) demonstrate that child maltreatment will be confirmed for 1 in 8 (12.5%) US children by 18 years of age.[1171] The child welfare system has primary responsibility for identifying, investigating, and intervening to protect children who are referred to their agencies for abuse and/or neglect. The annual rates of reported allegations (i.e., referrals) of abuse and neglect have been relatively steady over the last decade in California, whereas the rates of substantiated incidents have decreased from 11.2 per 1,000 children in 2007 to 7.7 per 1,000 in 2019 (**Figure 17**).[1172] This represents nearly 70,000 California children

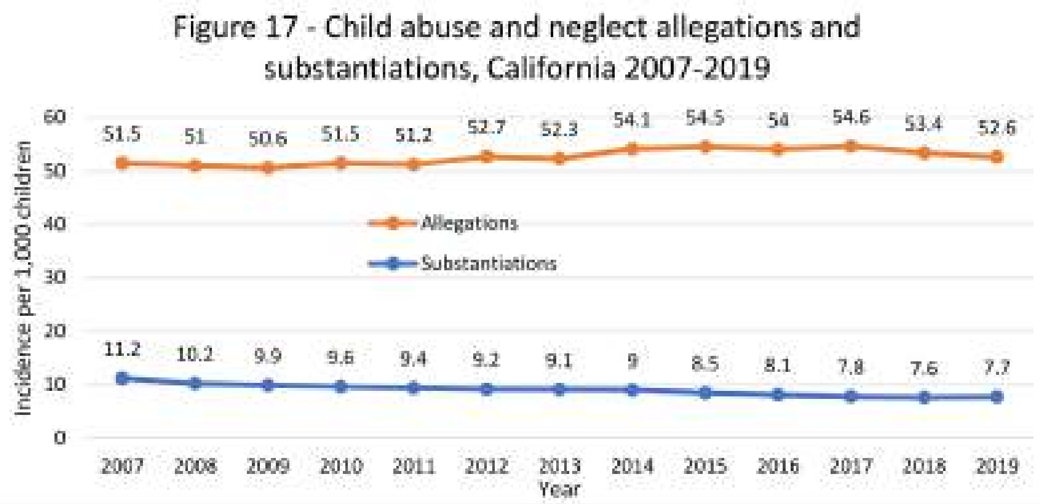


Figure 17. *California Child Welfare Indicators Project. Reproduced with permission.*[1172]

substantiated as abused and/or neglected in 2019, over three-quarters of which were for neglect. However, However, these rates probably dramatically understate the real children who are maltreated.[1171] National surveys have found that for the last two decades, approximately three times as many children are maltreated each year as are actually recorded by Child Protective Services (CPS) agencies.[1173]

Young children are the most likely to experience substantiated abuse and/or neglect.[1174] In California, nearly half (45%) of children who have experienced substantiated child abuse or neglect were five years of age or younger, and most of these (62%) were two years or younger.[1172] Between 70% and 80% of the 148 children officially determined to have died due to abuse in California in 2018 were under five.[1175]

Further, racial disparities occur throughout the full child welfare continuum of services, from reports of allegations through substantiations and removal from the home. For example, Black and Native American children in California have substantially higher rates of allegations and substantiations than other racial/ethnic groups (**Table 7**). Black children, who represent only 6% of California's child population, encompass 14% of children with abuse and neglect substantiations. Similarly, Native American children comprise less than 0.5% of the child population, but account for nearly 1% of the children with substantiated cases.[1172]

The other broad category of adversity in the original ACE Study is household challenges (household member mental illness, intimate partner violence, substance use, incarceration, and parental separation or divorce). Not only can these five ACEs activate the toxic stress response directly, but they are also risk factors

Race/Ethnicity	Allegations per 1,000 children	Substantiations per 1,000 children
Asian	16	1.9
Black	116	19.4
Latinx	50	8.3
Native American	96	16.3
White	42	6.1
Overall	53	7.7

Table 7. *Rates of child abuse and neglect allegations and substantiations in California, by race/ethnicity.*[1172]

for the other five ACEs: their presence can contribute to child abuse (physical, emotional, or sexual) and/or neglect (physical or emotional). For example, unaddressed mental health challenges of caregivers and active substance use can increase parental stress and reduce coping skills, and can be major drivers for a child's entry into the child welfare system. In fact, co-occurring mental health and substance use disorders are common among parents of children entering the child welfare system. In national figures, the percentage of children entering foster care for whom parent drug abuse was reported as a reason for removal increased from 30.7% in 2012 to 37.7% in 2017.[1176,1177] The most recent estimates of infants estimated to be prenatally exposed to alcohol and illicit drugs range from 8.7% to 11% for alcohol and from 5% to 6% for illicit drugs.[1178-1180] Parental incarceration as a reason for removal has also increased nearly 6% during this same period.[1176]

The intergenerational cycle of ACEs and toxic stress is demonstrable when analyzing these and other risk factors for entry into the child welfare system. Parents with substance use disorders often themselves have a history of trauma themselves, with 60%–90% of treatment participants experiencing one or more traumatic events.[1177,1180] In addition to the original ACEs, there are multiple other life stressors that can also reduce a caregiver's capacity to cope effectively with the typical day-to-day stresses of raising children. These include financial and social stressors, such as poverty or financial insecurity, unemployment, housing insecurity or homelessness, and community violence. Without sufficient buffering supports, these challenges can also lead to ACEs for their children through increasing child abuse, neglect, and/or household challenges, as well as potentially serving as additional risk factors for directly activating the toxic stress response.[1181,1182] The coronavirus disease 2019 (COVID-19) pandemic is a prime example of an acute stressor that is increasing ACEs and toxic stress (see **COVID-19 AND SOCIAL SERVICES**).

Children placed in foster care as a result of substantiated abuse or neglect represent a population at high risk for experiencing toxic stress and the neuro-endocrine-immune-metabolic dysregulation it produces. Together with the emotional, physical, and social disruptions that foster care can entail, the toxic stress response can take a heavy toll on the health and well-being of foster children throughout their lifetimes. Consistent with many other studies, the California Youth Transitions to Adulthood Study (CalYOUTH), which followed a cohort of foster youth during their transition to adulthood, found they were "faring poorly compared to their age peers across many measures of well-being, including their educational attainment, employment, economic self-sufficiency, physical and mental health, and involvement with the criminal justice system."[1183] For example, less than half of the participants rated their health as excellent or very good. In the second follow-up wave of the study, with 19-year-old adolescents, "More than 50% of CalYOUTH participants were found to have a positive diagnosis for one or more current mental and behavioral health disorders."[1184] Young people in the study were significantly more likely than those in a similar longitudinal study of a nationally representative cohort of adolescents (the National Longitudinal Study of Adolescent Health, or Add Health) to have received psychological or emotional counseling (22.0% vs. 7.9%, $F = 44.0$, $p < 0.001$) and treatment for a drug or substance abuse problem (6.5% vs. 3.2%, $F = 4.4$, $p < 0.05$) in the past year.[1183] Further, the foster youth were over three times as likely as youth in the Add Health study to have a health condition or disability that limited their daily activities—almost one-fifth of them did.[1183] CalYOUTH respondents were more likely than Add Health adolescents to have ever been diagnosed with ACE-Associated

COVID-19 AND SOCIAL SERVICES

Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic, child and family-facing service agencies have become concerned about the potential increased risk for child abuse and neglect during this time of crisis, grief, economic insecurity, and social isolation. With many school buildings shuttered and medical visits declined, children's lives have become more hidden behind closed doors. Reports to child abuse hotlines across the nation, including in California, have declined by as much as 50% during the pandemic. The drop began soon after California began its stay-at-home orders to prevent the spread of the coronavirus.[1211] On the other hand, child self-reports to the Childhelp National Child Abuse Hotline have increased; there were 31% more calls and messages in March 2020 than in March 2019.[1212]

When children are alone with caregivers for longer and more challenging times, including potentially being home-schooled, they are also more distant from non-family adults

COVID-19 AND SOCIAL SERVICES

in settings like daycare, schools, after-school programs, places of worship, and other public areas, where their safety and well-being can be assessed externally. There is a need for alternate ways to assess the safety and well-being of children and families during shelter-in-place. For example, Sacramento County has developed a tip sheet, "Supporting Safety and Well-Being of Children and Families during COVID-19," with guidance for teachers, social workers, counselors, day care providers, and others who work with children virtually.[1213] There is also a statewide guide, "Recognizing Child Abuse and Neglect through Distance Learning Recommendations for California's Educators."[1214] Both offer concrete suggestions for how to ask engaging, solutions-oriented questions that can help identify whether support is needed or a safety concern may be present.

However, although there are increased risks for children during the COVID-19 pandemic, it is important to avoid placing certain groups, such as families of color or low-income families, under heightened scrutiny and potential for child removal.[1215] Many families are dealing with growing food insecurity, lack of housing stability, inadequate income, and social isolation. The pandemic is also straining the availability of childcare. Poor families are becoming more impoverished. Families and communities of color are especially suffering in multiple ways, including disproportionate rates of the illness and death from COVID-19. As pointed out above, the majority of substantiated child maltreatment cases are for neglect, not physical abuse or exploitation, and neglect and the challenges related to poverty are strongly associated.

In April, 2020, Governor Gavin Newsom announced $42 million in funding for children who are at greater risk for abuse or neglect during the pandemic, including roughly $7 million for social worker overtime and additional outreach. "Without the structure and safety of school, children—who are already vulnerable to abuse and neglect at home—face a greater threat," said Newsom. "Similarly, we recognize that many parents who have lost jobs and income due to the COVID-19 pandemic may be feeling overwhelmed and strained." Funding for more resources and support for parents can reduce financial stress on parents, which will also reduce the chances of abuse.[1211]

From a trauma-informed perspective, all families have strengths and resiliency worthy of investment and care. The current crisis is an opportunity for the child welfare system to collaborate with and engage communities in efforts link families and children with needed supports and resources, including easing social isolation.

Health Conditions (AAHCs), including high blood pressure (10.3% vs 6.4%, $F=5.3$, $p < 0.05$), high cholesterol or high lipids (6.9% vs 3.7%, $F=6.4$, $p < 0.05$), diabetes or high blood sugar (4.8% vs 0.4%, $F=40.8$, $p < 0.001$), and asthma or reactive airways disease (26.6% vs 16.0%, $F=19.7$, $p < 0.001$).[1183]

In addition, CalYOUTH respondents were more likely than Add Health participants to have been hospitalized within in the prior three months (males 30.3% versus 3.1%; females 28.9% versus 15.4%). CalYOUTH participants were more likely to report they were hospitalized due to illness (males 30.2% versus 15.1%; females 30.9% versus 13.3%) or a substance abuse or mental health problem (males 36.7% versus 7.0%; females 11.7% versus 1.2%).[1183]

Child welfare involvement has also been consistently associated with poorer educational outcomes. Among 4,000 youth involved with California's foster care system enrolled in high school between 2002 and 2007, less than half (45%) had completed high school by 2010, compared to 79% of the general student population.[1185] Numerous studies have also documented former foster youth to have lower earnings and greater risk of unemployment, as well as greater risk of involvement in the criminal justice system.[1186-1192]

In summary, foster youth have been documented to have greater risk of the medical, behavioral, educational, and social consequences of toxic stress. These outcomes are not simply the result of foster care, but are also tied to the marginalized communities in which youth lived and their histories of trauma prior to entering care. Even when these challenging circumstances do not lead to entry into the child welfare system, children who face these types of childhood adversity are at high risk of experiencing significant short- and long-term health and social consequences.[8,23,817,1193-1197]

PRIMARY PREVENTION STRATEGIES

Historically, the national child welfare system has directed almost all its attention and resources to tertiary prevention efforts for children who have already experienced abuse and/or neglect (i.e., to prevent recurrence). In California, the Department of Social Services (CDSS) is the administrative agency that oversees the child welfare system. The Office of Child Abuse Prevention (OCAP) within CDSS has recently championed a more overt primary prevention focus (i.e., preventing abuse and neglect before they occur) by addressing the major drivers of child welfare involvement: poverty, unaddressed mental health challenges of caregivers, substance use, and a parental history of child abuse.[1198] OCAP receives the majority of its $60 million annual budget from federal sources. (These include the Child Abuse Prevention and Treatment Act; Community-Based Child Abuse Prevention;

Promoting Safe and Stable Families; and the Child Abuse Prevention, Intervention, and Treatment Act.)

OCAP's 2020–2025 Strategic Plan[1198] represents a forward-looking and strategic child welfare approach to incorporating a public health framework into its prevention efforts. With primary prevention of child abuse and neglect as a key priority, OCAP promotes not only trauma-informed services and responses, but also trauma-informed policies and systems. This requires a high level of state and local engagement and collaboration to foster safe, thriving families and communities. The overall goal is to establish an integrated statewide cross-sector system to support families and provide safe, stable, nurturing relationships and environments for all children, through training, grants, campaigns, county-level prevention, and evidence-based intervention efforts (for instance, see **THE CALIFORNIA EVIDENCE-BASED CLEARINGHOUSE FOR CHILD WELFARE**).[47]

Grounded in a public health framework, OCAP's primary prevention approach starts with acknowledging and addressing the foundational socioeconomic and environmental factors shaping the conditions in which families and children live their daily lives. The focus is on implementing systems of care that build community-protective factors and increase access to the resources that address the broader social determinants of health (economic supports, housing security, food security, and equity). Interventions at this level encompass cross-systems approaches to address poverty and other environmental conditions that impact child safety and wellness, and enhance equity. Key strategies include:[23,1198,1199]

- Reduce poverty and improve economic stability through increased access to safety net supports;
- Increase social connections through Family Resource Centers and community events;
- Improve neighborhood safety and play areas for children;

THE CALIFORNIA EVIDENCE-BASED CLEARINGHOUSE FOR CHILD WELFARE

The California Evidence-Based Clearinghouse for Child Welfare is an online resource for child welfare professionals, researchers, policymakers, staff of public and private organizations and academic institutions, and others working to improve outcomes for children and families. It allows user to identify, select, and implement "evidence-based child welfare practices that improve child safety, increase permanency, increase family and community stability, and promote child and family well-being."[977] The average number of visitors per month between July 2019 and March 2020 was 29,331.

- Improve access to high-quality child care to support school readiness;
- Improve access to high-quality healthcare;
- Increase family-friendly work environments (e.g., paid family leave and on-site child care); and
- Increase public awareness and support for a shared community responsibility for child well-being (i.e., investing in our future).

These strategies particularly address new parents, since children under five have the highest rates of reported and substantiated abuse and neglect. Efforts to raise the awareness of the general public, business leaders, educators, service providers, and decision-makers about the nature and scope of problems associated with abuse and neglect is also part of primary prevention.[1200,1201]

As documented above, racial inequities are evident across every part of the child welfare system impacting children and families. There are several initiatives underway in California to advance racial equity. For example, the California Strategic Growth Council supports the Capitol Collaborative on Race and Equity (CCORE), formerly the Government Alliance for Race and Equity (GARE) Capitol Cohort, which is a capacity-building program to embed racial equity approaches into institutional culture, policies, and practices for California state government entities, and a network that has been working together since 2018.[1202] As a network, CCORE is collectively elevating racial equity values, collaborating on strategies, creating leadership models for racial equity, developing customized Racial Equity Action Plans, and supporting transformational governance.

CDSS participated in the first GARE Capital Cohort. Implementation activities include workforce development to make the workforce more reflective of those who are being served, provision of learning opportunities for staff, and development of a racial equity tool to apply to policy development and program implementation. CDSS has a newly formed Office of Equity, whose mission is to: expand services for people with disabilities; provide services in multiple languages; review data to better understand who CDSS serves and how they are served; learn about racial equity; enforce our civil rights laws; support the work of Tribal, Immigrant, or Refugee programs; contract with providers to increase services to underserved populations; and work to diversify the workforce and create an inclusive environment that engages and partners with community. The Office of Equity houses immigration and legal services to serve mixed-immigration status households in seeking Deferred Action for Childhood Arrivals (DACA) status, avoiding inappropriate deportations, and proving other immigration remedies.[1203] It also houses the Office of Tribal Affairs, whose vision is to cultivate informed participation and trusting relationships with and among the tribes, CDSS, and counties to enhance the well-being of Native American children and families.[1204]

Although not totally new to the social services and child welfare field, there are currently widespread efforts to integrate trauma-informed policies and practices into all aspects of social services for families and children. Even with strengths-based approaches however, human service agencies need to understand the impact of traumatic experiences on client functioning and mitigate the potential re-traumatizing effects of their own service systems. Trauma-informed practices are both about what is being done, and how it is being done. Because implementing a trauma-informed systems approach involves considerable changes in policies and practice, agency leadership and middle management must be committed to the changes and actively engage in the process for it to be successful. As articulated by the National Child Traumatic Stress Network and others, trauma-informed policies and practices are of particular relevance in the social services sector for all levels of prevention.[1205,1206]

SECONDARY PREVENTION STRATEGIES

In the child welfare field, secondary prevention strategies are offered to populations that have one or more risk factors associated with child abuse and neglect, such as parental substance abuse, young parental age, parental mental health concerns, exposure to violence, and parent or child disabilities. These services and resources aim to strengthen protective factors to mitigate or eliminate risk based on the well-established Strengthening Families framework.[1207] Programs also seek to provide services and resources in communities with a high incidence of any or all of these risk factors. This assets-based approach supports families and communities to identify and build protective factors such as early parent–child attachment and nurturing, knowledge of parenting and child development, parental resiliency, concrete supports in times of need, social connections, and child social and emotional competence. In the child welfare sector, these secondary prevention strategies include:

- Differential response programs, as an alternative to formal CPS involvement, for families experiencing serious parental stress that use community resources to provide concrete services (e.g., crisis respite care or food and transportation assistance) and parenting guidance and education;
- Accessible Family Resource Centers that offer information, education, and referral services to meet concrete needs, as well as parenting supports to vulnerable families, such as peer mentoring and support groups, with a particular focus on teen parents, single parents, and families with young children;

- Home visiting programs that provide support and assistance to families at risk of experiencing abuse or neglect (see the next section, **Primary, Secondary, and Tertiary Prevention Strategies in Early Childhood Supports**);
- Respite care for families in crisis or with children with special needs; and
- Family-centered substance abuse treatment services.

In California, OCAP supports the implementation of these types of secondary prevention strategies by building the capacity and strengthening the sustainability of family-strengthening organizations to work effectively with diverse populations, particularly children and families in poverty, and to effectively implement evidence-informed prevention programs and practices through the dissemination of organizational best practices and workforce development opportunities.

TERTIARY PREVENTION STRATEGIES

Tertiary prevention strategies focus on families where child abuse or neglect has already occurred and seek to prevent its recurrence and reduce the negative consequences of the maltreatment. Traditional child welfare services provide supports and resources to families and children involved in the child welfare system to prevent recurrence and re-entry, including removal and foster care, traditional family reunification, and a range of wraparound support services. Specific tertiary prevention strategies include:

- Intensive family preservation services with trained mental health counselors that are available to families 24 hours per day for intensive bursts of time (e.g., six to eight weeks);
- Parent mentorship programs, with stable families providing support and acting as role models to families in crisis;
- Parent support groups that help transform harmful practices and beliefs into more positive parenting ones; and
- Healthcare services to address AAHCs in children and caregivers, support family-oriented therapeutic modalities, and strengthen resilience capacities for affected families. Some children in foster care are cared for by specialty child abuse pediatricians or a primary care clinic that specializes in the foster care community. Child welfare organizations can also connect children, youth, and families (via the online provider directory) to an ACEs Aware provider who is trained to recognize and respond to toxic stress.[1153]

These services may include trauma-informed clinical interventions to regulate the stress response, like mindfulness practices, improved nutrition, sleep, exercise, enhancing healthy relationships, access to nature, and if indicated, psychotherapy and other mental healthcare (see the earlier section, **Tertiary Prevention Strategies in Healthcare**, for more details).

Through this wide-ranging set of prevention programs at all three levels of prevention, OCAP plays a valuable and innovative role in encouraging and supporting cross-sector collaboration in statewide and community efforts to support all the children and families of California, and creating trauma-informed systems that includes primary, secondary, and tertiary prevention strategies (see EXAMPLES OF TRAUMA-INFORMED OCAP INTERVENTIONS AT ALL LEVELS OF PREVENTION).

EXAMPLES OF TRAUMA-INFORMED OCAP INTERVENTIONS AT ALL LEVELS OF PREVENTION

In 2020, the Chadwick Center for Children and Families at Rady Children's Hospital San Diego, a longtime OCAP partner, established a comprehensive, science-based professional education program to meet the needs of administrators and staff of Family Resource Centers, Child Abuse Prevention Councils, and other OCAP stakeholders in California. Curricula in multiple forms address the diverse needs of adult learners, ranging from five-minute micro-learning activities, to longer webinars or presentations, to multi-day, in-person trainings, followed by a series of consultations calls and booster sessions. Training topics include: Introduction to Trauma-Informed Care; Reflective Supervision; Trauma and Parenting; and Using the Wellness Recovery Action Plan as a Tool to Heal Trauma.

The Advancing California's Trauma-Informed Systems (ACTS) project supports the goal of providing trauma-informed care (TIC) throughout California. Based on the best research and expertise available, ACTS has created a menu of TIC training and technical assistance for county-level child-serving child systems (welfare, local community organizations, and schools) focusing on three core domains: the organizational environment, workforce development, and trauma-informed services.[1208] County systems implement these

EXAMPLES OF TRAUMA-INFORMED OCAP INTERVENTIONS AT ALL LEVELS OF PREVENTION

TIC improvements and continue the work of developing trauma-informed systems after training and technical assistance have ended. Counties served to date include: Calaveras, Los Angeles, Riverside, San Diego, Santa Barbara, Solano, Tehama, Tulare, and Tuolumne.

Lead4Tomorrow's Family Hui program[1209] is a peer-led parenting support group program. The Family Hui "Bloom" curriculum is trauma-informed and rooted in positive parenting principles, and includes information about ACEs, resiliency, and parenting skills. This program is intended to train parents to become leaders within communities and systems. It has had great success in reaching refugee and tribal communities, including the Afghan community. The Farsi language does not contain a word for child abuse, and the Family Hui program worked with translators to find an appropriate definition. Program materials have been translated into Farsi and Spanish, and a graphical representation has been created for those who do not read.

Celebrating Families funds a train-the-trainer model for a trauma-informed skill-building program for families with a parent with a substance addiction, through the Celebrating Families curriculum. Three organizations are being trained: SHIELDS for Families in Los Angeles; Para Los Niños in Los Angeles, and the Sherwood Valley Band of Pomo Indians in Mendocino County.

The **Innovative Partnership** grants provide funding for statewide regional collaborative networks between Child Abuse Prevention Councils and community stakeholders to strengthen families and prevent child abuse through increased availability of meaningful resources. Each regional and local network focuses on different strategies. Examples of innovative partnerships include outreach to families at risk of homelessness, mental health/ substance abuse, those affected by fires, tribal communities, and migrant families (Lake, Mendocino), and trainings on ACEs, poverty, substance abuse, and protective factors (Amador, Fresno, Kern, Placer, Sacramento, San Francisco, San Joaquin, San Louis Obispo, Santa Barbara, Ventura and Yolo Counties).[1210]

Primary, Secondary, and Tertiary Prevention Strategies in Early Childhood Supports

Scientific advances in the late 20th century led to dramatic progress in public understanding of how experiences and environments shape brain health and impact developmental trajectories.[23,1216] In 2000, a groundbreaking report from the National Academies Press, *From Neurons to Neighborhoods: The Science of Early Childhood Development*, summarized the emerging evidence.[1217] The report began by highlighting that

> "...an explosion of research in the neurobiological, behavioral, and social sciences has led to major advances in understanding the conditions that influence whether children get off to a promising or a worrisome start in life. These scientific gains have generated a much deeper appreciation of: (1) the importance of early life experiences, as well as the inseparable and highly interactive influences of genetics and environment, on the development of the brain and the unfolding of human behavior; (2) the central role of early relationships as a source of either support and adaptation or risk and dysfunction; (3) the powerful capabilities, complex emotions, and essential social skills that develop during the earliest years of life, and (4) the capacity to increase the odds of favorable developmental outcomes through planned interventions."

The report went on to highlight the role of chronic stress in shaping neurobiology, noting: "*Environmental factors that play a significant role in modulating prenatal and early postnatal brain development include substances and circumstances that are necessary for normal brain development, as well as exposures to chemicals, diseases, and **stressors that are toxic or disruptive** (emphasis added).*"[1217] Since the recent turn of the century, further research has highlighted the importance of early exposures in shaping not only neurodevelopmental trajectories, but also immunologic, endocrine, metabolic and genetic regulatory responses to stress.[12,39,299,1218-1220] Thus, the early childhood period represents a crucial time when primary, secondary, and tertiary prevention of Adverse Childhood Experiences (ACEs) and toxic stress are of outsized importance due to the increased malleability of developing systems, for both negative and positive outcomes.

PRIMARY PREVENTION STRATEGIES

Primary prevention of ACEs and toxic stress in the early childhood sector centers on preventing adverse experiences from occurring and strengthening buffering influences, typically through policies and programs that promote safe, stable, nurturing early relationships and environments.[23,1198] Universal programs may encourage positive parenting, amplify access to quality support services, and provide parent education and supports for healthy child development and relationships (for example, see **FIRST 5 CALIFORNIA**).[1221,1222] While vulnerable communities experience greater stressors and are therefore at higher risk, it is important to recognize that ACEs happen in every sociodemographic group, and that they are often under-recognized in upper-income and non-minority groups; therefore, universal approaches are necessary. Key stakeholders in primary prevention of ACEs and toxic stress for young children include child care professionals, community-based organizations, home visitors, healthcare providers, employers, preschool teachers and staff, social workers, policymakers, and, of course, caregivers and families themselves. Prevention strategies should align with the National Academies of Sciences, Engineering, and Medicine's (NASEM) 2019 framework on the contextual

FIRST 5 CALIFORNIA

Advances in scientific understanding of the role of early experiences and environments in shaping neurobiology have been applied to policies for the development of broad-scale interventions to support children and families. In 1998, Californians passed Proposition 10, a ballot initiative increasing the tax on cigarettes and other tobacco products to fund early childhood services. Proponents of Prop 10 cited the scientific research on early childhood development as a rationale to target early investment. The measure established the California Children and Families First Program (First 5), which created both state and local entities to promote and implement early childhood development priorities, partnerships, and initiatives.[1321]

First 5 California and the 58 local First 5 Commissions invested $345 million in fiscal year 2019–20[1322] toward programs and services that improve outcomes in early education, child care, child health and development, research, and community awareness. Over 60% of counties in the state currently offer home visiting programs through First 5, which provide nearly 100,000 services each year.[1323] To promote thriving parent-baby relationships, the Talk. Read. Sing. social marketing campaign was launched in 2014 to encourage positive, age-appropriate interactions that stimulate healthy brain development and build resilience against the harmful effects of stress.[785,1324] influences on life course health (**Figure 18**).[23]

Long-term outcomes of ACEs and toxic stress often put substantial pressures on state and national budgets.[1223] The pervasive, high prevalence of ACEs and the enormous costs of health, economic, criminal justice, and other downstream effects suggest a need for greater emphasis on preventive measures, especially during the earliest years of life, when impacts are most consequential and produce the highest return on public investment.[63,1224-1227] Shoring up supports for families is among the most effective strategies for preventing ACEs.[1225] Governor Gavin Newsom's inaugural Budget Act for 2019–20 put forth a robust parents' agenda that included over $2 billion in early childhood investments, among them strategic funding for California's child care and early learning systems, paid family leave, home visiting, developmental and trauma screenings, cash assistance to families with children, and child savings accounts.[1132] These strengthened channels of support build on California's existing framework, composed of evidence-based programs that lead to greater family financial stability, high-quality environments for young children, early detection of challenges, and timely responsiveness to families' and children's unique needs.[23,1102]

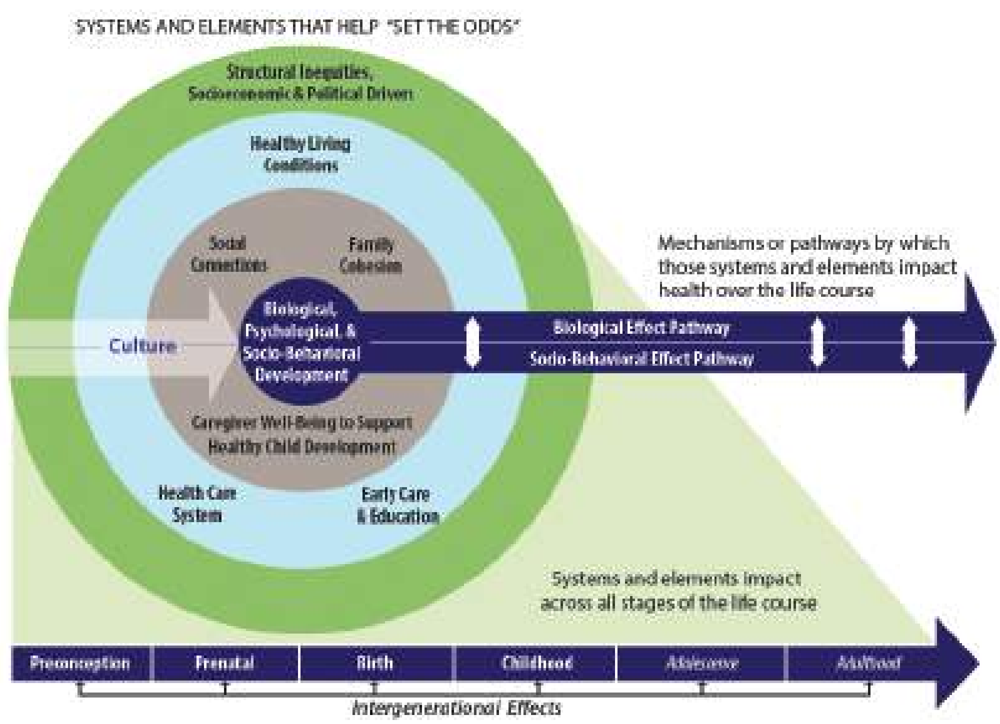


Figure 18. *Multi-layered structural and contextual factors that influence life course health. Reproduced with permission from the National Academies of Sciences, Engineering, and Medicine (2019), courtesy of the National Academies Press, Washington, D.C.*[23]

Figure 19. *The spectrum of services available to enhance early childhood development from ages 0-5 years.*

The Governor's budget reaffirmed a long-term commitment to children's well-being by establishing key infrastructure to ensure a comprehensive, sequenced policy approach. It included (**Figure 19**):

- Investment in a Master Plan for Early Learning and Care, a comprehensive roadmap to universal preschool and improved access to high-quality child care;[1228]
- Establishment of an Early Childhood Policy Council, composed of more than 20 cross-sector experts, practitioners, and parents and charged with advising the state on issues of early learning, child care, and child development;[1229] and
- Formation of a Paid Family Leave Task Force, composed of representatives from business, policy, research, and early learning communities and responsible for developing options for the state to expand the Paid Family Leave Program.[1230]

Child care

Improving the access of parents and caregivers to high-quality child care, and giving children opportunities to form relationships with nurturing child care providers and engage in a variety of socially and emotionally enriching activities, can help prevent ACEs and toxic stress.[7,1130,1231-1233] High-quality child care also benefits children's development, as measured by improvements in executive functioning, verbal skills, task persistence, school readiness, and general knowledge while also decreasing hostile behavior.[1234-1244] For example, the Study of Early Child Care by the National Institute of Child Health and Human Development assessed child care providers and children's behavioral and cognitive outcomes and found that for every additional recommended standard met by a child care provider, three-year-old children scored an average of 4.4% higher on school readiness and 2.4% higher on language comprehension evaluations.[1236] Long-term, high-quality child care is also associated with numerous other benefits, including higher rates of high school completion and lower risk of adult poverty.[1245,1246]

High-quality child care occurs in a range of settings, largely categorized as center- or home/family-based, and provides consistency, developmental enrichment, and emotional support.[1238] Voluntary accreditation from leading organizations offers detailed guidance for improving child care quality, accounting for safety, cleanliness, nutritional support, health consultation, staff-to-child ratios, and other parameters that extend beyond the minimum requirements for state licensing.[1247,1248] Staff training and retention are critical factors in child care, as forging relationships with nurturing adults beyond the immediate family is a strong protective buffer that can prevent and mitigate toxic stress.[7,78] When high-quality child care is available in a local community, subsidies may enhance families' access, leading to opportunities for children to learn and grow in safe and stable environments.[1249] Studies have tracked subsidy usage and found that subsidy recipients are 28% more likely to choose center-based care,[1250] 3% more likely to benefit from uninterrupted care, and 3% less likely to be cared for by more than one provider in a given month.[1251] Subsidies can also lower risk for ACEs by enhancing family economic stability, relieving parental stress, and suppressing rates of parental depression.[1217,1226,1252-1258] Researchers found that subsidies can lower the likelihood of child-care-related work challenges by 14–75%, including missing days of work, arriving late or leaving early from a job, or being unable to fulfill the requirements of a position.[1251,1259,1260] In addition, ratings of parental satisfaction with child care increase, on average, by 7%, compared to parents who do not receive subsidies.[1251]

The CalWORKs Child Care program is jointly administered by the California Department of Social Services (CDSS) and the California Department of Education (CDE). In fiscal year 2018–19, California allocated over $4.6 billion for child care programs.[1261] The purpose of the CalWORKS Child Care Program is to help a family transition from immediate, short-term child care needs when a parent starts working to more stable, long-term child care that allows the family to exit the program and remain off aid.[1262] Stage 1 is administered by CDSS through county welfare departments and provides child care subsidies until the family no longer needs them.[1261] Child care facilities include license-exempt child care centers, and family child care homes. In fiscal year 2017–18, over 38,000 children were served; 67% of the children were five or younger, and 54% were in full-time care programs.[1263] Stages 2 and 3 are administered by CDE. Child care programs are supported by federal funds: the Temporary Assistance for Needy Families Block Grant (administered by CDSS) and the Child Care and Development Block Grant (administered by CDE). The latter also supports expenditures for provider training, workforce development, and child care licensing.[1264]

Early education

Until a child attends kindergarten, learning takes place in the home, child care facilities, community, and preschool programs, collectively classified as early childhood education (ECE). Often, ECE programs are a prominent channel through which families often engage with the broader community, as services and supports are commonly provided by organizations or the government. Multigenerational ECE programs in particular, such as Early Head Start, Head Start, and other preschool enrichment programs with family engagement, can generate lifelong benefits by strengthening caring relationships and helping children meet developmental milestones.[1265-1273] Emerging evidence is beginning to shed light on the long-term health impacts of high-quality ECE, including modest but statistically significant reductions in rates of adolescent obesity and childhood chronic health problems that require specialized equipment, such as a brace, wheelchair, or breathing mask.[1274] ECE may also serve a vital role in providing a network of support and belonging for the whole family, which has been shown to be particularly impactful for immigrant, economically disadvantaged, and marginalized groups.[1130,1275] Beyond relational benefits, ECE advances children's learning and behavioral competencies, thereby reducing social risk factors of ACEs and other poor outcomes.[794,1241,1276] The evidence is clear that educational experiences cannot wait until kindergarten, as brain development is most rapid and consequential during the first few years, when the fundamentals of one's neural architecture are laid down to facilitate all future learning and development.[1277] Research on this topic has matured over the last century and, with modern data collection and analysis methods, continues to reveal and support long-term benefits from high-quality ECE.[60,1227,1245,1278-1282]

Fewer than half of the children living below the poverty line in the United States have the skills needed to do well when they enter kindergarten.

A seminal study, the Carolina Abecedarian Early Intervention project, provides a detailed look at how an ECE intervention can elevate academic and social achievement across the life course. In the 1970s, the project recruited four-month-old infants for the intensive intervention, which included on-site pediatricians and had four key components: language, conversational reading, enriched caregiving, and learning games.[1283] After only five years of the intervention during early childhood, former participants continued to log significant long-term benefits well into adulthood. At age 21, the experimental group demonstrated better reading skills (1.8 grade levels), better math skills (1.3 grade levels), and higher IQ scores (4.4 points), compared to the control group which received standard services during early childhood.[1227,1277,1284] Social outcomes were equally impressive: participants were 2.5 times as likely to be attending a four-year college and 1.7 times less likely to have become teenage parents. Benefits continued through age 30, as well. Recipients of the intervention exhibited a lower prevalence of risk factors for metabolic and cardiovascular diseases, were four times as likely to have a four-year college degree, six times less likely to have recently received public assistance, more than twice as likely to be consistently employed, and had delayed parenthood by almost two years, on average, compared to the control group.[1227,1285]

Fewer than half of the children living below the poverty line in the United States (US) have the skills needed to do well when they enter kindergarten. This sets the foundations for poorer educational outcomes and entrenched health and social disparities further along in life.[1286] As trusted professionals, pediatric, medicine-pediatric, and family practitioners can be effective partners in supporting ECE.[1287] Reach Out and Read is a national program that provides developmentally appropriate books to families when they visit their primary care practitioner and introduces caregivers to the concept of early reading and its benefits.[1288,1289] Data show that such efforts improve kindergarten readiness, as in one study that tracked improvements in high-quality home literacy environments and additionally found that kindergarten teachers rated 67% of program participants as above or far above average by the end of the year, compared to their grade-level peers.[1290] The program seems to improve health appointment adherence, as well. One study found that children who received books were twice as likely to attend the full panel of well-child visits recommended as a baseline standard by the American Academy of Pediatrics.[1291] Reading frequency at home improved as a result of program participation, between a half and a full day per week.[1292,1293] Participating children score 6.8–8.6 points higher in receptive language and up to 4.3 points higher in expressive language evaluations.[1293,1294] One study went further and suggested a dose-response effect to these impacts, linked to the number of exposures to the program.[1293]

SECONDARY PREVENTION STRATEGIES

Beyond the universal supports and services provided by primary prevention strategies, secondary prevention focuses on providing additional supports to those at risk for ACEs, in order to strengthen buffering influences that would prevent ACEs from leading to toxic stress.[1198] For example, children of parents with high ACE scores are themselves at greater risk of experiencing ACEs and toxic stress.[1150,1295,1296] Factors such as poverty and young parental age can also contribute to additional risk, though it should be recognized that all populations can experience ACEs and toxic stress.[42,1198] Secondary prevention in the early childhood sector for at-risk populations includes home visitation programs, economic supports, and educational opportunities for parents and early childhood professionals about ACEs and toxic stress, long-term health and developmental impacts, and strategies relating to parental self-care and positive, buffering interventions focused on preventing the transmission of adversity.

While screening for ACEs should be performed in the primary care setting, early childhood professionals should understand how to recognize the signs and symptoms of toxic stress and how to connect parents and families to the appropriate resources for support. Home visitors and other early childhood professionals can locate ACEs Aware health providers to whom they can connect families in need through the ACEs Aware provider directory.[1153]

Home visiting

Among the best-supported interventions for improving child and family outcomes are high-quality, voluntary home visiting programs for new parents to ensure they have the community support and services they need during a significant time of transition. Home visiting spans all levels of ACEs and toxic stress prevention, with some supports universally available to all pregnant and newly parenting individuals (primary prevention), most programs specialized for early detection and provision of buffering protective factors for at-risk children and families (secondary prevention), and additional services equipped to facilitate interventions and mitigation strategies for adversities that have already occurred (tertiary prevention). Trained professionals including teachers, nurses, public health professionals, and child development specialists conduct home visits during pregnancy and early childhood to provide a wide array of services, including pregnancy consultations, parenting skill-building, newborn health visits, and services for children.

To emphasize the value of home-based support, compared to other modalities of care, one study of 20 evidence-based interventions in pediatric healthcare for the prevention of toxic stress from ACEs and found that 95% incorporated home visiting plus parenting education and/or mental health counseling.[794] Many established programs have known benefits in preventing the incidence and intergenerational transmission of ACEs.[87,1297-1303] Projections of the Nurse-Family Partnership (NFP) on a national level anticipate that by 2031, services it provided from 1996 to 2013 will prevent 500 infant deaths, 42,000 child maltreatment incidents, 36,000 intimate partner violence incidents, 90,000 violent crimes by youth, 41,000 person-years of youth substance abuse, and 594,000 property and public-order crimes by youth.[1303] NFP has shown an overall 48% reduction in child abuse and neglect, improved parenting practices, lower rates of substance use in mothers and children, and reduced exposure to intimate partner violence, which are all ACEs.[690,691,693-695] A systematic review of 21 RCTs on home visiting concluded that prenatal initiation of home visiting most successfully prevented child abuse, especially when mothers enrolled at or before a gestational age of 24 weeks.[1304,1305] Another common risk factor for ACEs is untreated parental mental illness, which can also be alleviated to a certain extent by home visiting programs. One study found that depressed mothers experienced improved symptoms by 8.8%, were 12.7% more likely to be screened for depression, and had 23.9% higher usage of evidence-based services following a positive screen.[1297]

> By 2031, services the Nurse-Family Parnership provided from 1996 to 2013 will prevent 500 infant deaths, 42,000 child maltreatment incidents, 36,000 intimate partner violence incidents, 90,000 violent crimes by youth, 41,000 person-years of youth substance abuse, and 594,000 property and public-order crimes by youth.

Home visitation programs are inherently multi-generational and seek to address parental stress and readiness, identify needs and care directly for young children (typically up to two to five years old), and facilitate social support networks. In alignment with the Centers for Disease Control and Prevention's (CDC) Social-Ecological Model for violence prevention, home visiting professionals strengthen the parent-child relationship with specific tools and resources to secure a strong start in life.[1089] As they interact with children, professionals also model appropriate and constructive responses for the parents' benefit.[1306]

In addition to preventing ACEs, home visiting programs can also be effective at reducing manifestations of toxic stress physiology, such as poor health and behavioral outcomes and dysregulation of immune, endocrine, metabolic, and neurological systems.[87,1306] The NFP program has shown, in five randomized controlled trials (RCTs), improved maternal employment, maternal/child attachment, child cognitive and language development, gains in academic achievement, fewer behavioral problems, lower rates of substance use, fewer arrests, convictions, and parole violations by age 19, lower use of public assistance and food stamps, and reductions in subsequent family births.[31,690,692,1307,1308] In a systematic review of 21 RCTs, home visiting was associated with improved cognition and developmental outcomes, especially language skills, improved externalizing and internalizing behaviors, reduced incidence of low birth weight, increased appropriate weight gain for children, increased routine immunizations, and reduced incidence of illness, injuries, and feeding problems, many of which are ACE-Associated Health Conditions (AAHCs).[1304]

In one year, from 2018 to 2019, over 50,000 families had received home visiting services in California, and Governor Newsom's 2019–20 budget increased funding to further increase that number.[1309] The federal Maternal, Infant, and Early Childhood Home Visiting (MIECHV) Program is administered through the California Department of Public Health (CDPH) and a wide range of local First 5 Commissions. All of California's home visitation programs are held to high evidence-backed standards, build local capacity, and implement ongoing quality improvement measures that amplify trauma-informed policies and practices.

The California Home Visiting Program (CHVP) administers funds from the federal MIECHV grant.[1310,1311] During the 2018—19 federal fiscal year, CHVP funded 23 local home visiting programs implementing one of two approved evidence-based home visiting models—Healthy Families America (HFA) or NFP. The CHVP is designed for overburdened families who have a history of or are at risk of further ACEs, including any of the following factors: intimate partner violence, insufficient income, unstable housing, less than 12 years of education, substance abuse, and mental illness. The program is a voluntary preventive intervention that pairs trained home visitors (i.e., nurses or paraprofessionals) with pregnant and newly parenting women to promote positive parenting and improve child health and development by providing parents the tools and know-how to independently raise their children. HVPs can be augmented to specifically address intimate partner violence.[1312,1313]

When the CHVP began in 2010, CDPH conducted the California Statewide Home Visiting Needs Assessment to understand where resources would have the greatest impact across the state for optimal and fair allocation of resources.[1314] Following the collection of a swathe of county-level indicators of health, birth outcomes, economic activity, unemployment, public safety, child welfare, and other aspects of community well-being, the department was able to map out statewide needs and expand home visiting services into the regions that demonstrated the highest concentrations of risk factors.[1315] Federal funding for home visitation programs is contingent on a regular assessment schedule. An update is anticipated by the end of 2020 and will also include an analysis of the CHVP's impact thus far.

Another statewide home visiting initiative, called the CalWORKS Home Visiting Program, is supervised by CDSS and administered by California counties.[1316] New parents are provided guidance, services, and supports in prenatal, infant, and toddler care; infant and child nutrition; child developmental screening and assessments; parent education, parent and child interaction, child development, and child care; and job readiness and barrier removal. With over $150 million in funding, the long-term mission of this voluntary program is to expand future educational and economic opportunities to ultimately improve the likelihood that participants will rise out of poverty.[1317] All state-funded home visiting programs are evidence-based, as determined by an evaluation using criteria from the US Department of Health and Human Services or CDSS and listed in the California Evidence-Based Clearinghouse for Child Welfare.[977,1318] Nurses and other home visiting professionals provide guidance, coaching, and access to health and social services and have been trained on intercultural competence, trauma-informed care, and disproportionality.[1319,1320] Services were modified as appropriate during the coronavirus disease 2019 (COVID-19) pandemic (see ADAPTATIONS TO THE COVID-19 PANDEMIC).

Network of care

Early childhood professionals represent a critical part of the network of care for responding to ACEs and toxic stress. One primary avenue of reducing children's risk factors for poor outcomes is the support of parents. Successful interventions include support groups that focus on parents' everyday needs and responsibilities, expanded opportunities for parents to develop relationships with early childhood professionals, respite care for caretakers of children with developmental disabilities, informational and social events for parents, and Family Resource Centers that provide education and holistic, strengths-based services to families with young children.[1325,1326]

While providing resources to caregivers, early childhood professionals are well positioned to develop trusting relationships as a warm and attentive adult and deliver regular doses of nurturing care that, cumulatively, can help to directly buffer the toxic stress response in children. Positive or protective childhood experiences, like a close connection with a caring adult, can generate significant protective factors against toxic stress. For those who have experienced ACEs or risk factors for toxic stress, buffering care can elevate short- and long-term health by fostering secure attachments and emotional self-regulation, and regulating the stress response.[1327-1329] Early childhood professionals benefit from training in trauma-informed practices and supports for self-care as well.[1330-1333] Provider well-being is a fundamental component of sustainable systems of care.[1334-1338]

Parenting supports

When parents struggle to meet basic needs, negative outcomes can cascade.[37] Research has shown that children of low socioeconomic status experience higher rates of neglect (seven times as high), maltreatment (five times), and physical or sexual abuse (three times) than their peers in higher-income families.[1173] Similarly, the odds of an ACE score of three or more are doubled for children in families with incomes below 150% of the Official Poverty Measure ($34,575 for a family of four in 2012), compared to those in higher income brackets.[1102] Psychological stress arising from economic hardship can lead to parental distress and inter-partner conflict, which are associated with detached and abusive parenting and hindered cognitive and socioemotional development in children.[1339-1342]

Numerous public programs are administered by the California state government.

- Family-oriented economic supports include tax benefits like the Earned

ADAPTATIONS TO THE COVID-19 PANDEMIC

On March 17, 2020, at the beginning of the coronavirus disease 2019 (COVID-19) pandemic, the federal Health Resources and Services Administration approved the use of virtual home visits during the crisis.[1348,1349] Home visiting has truly been a lifeline to many families during the pandemic.[1350] Barely one month into the pandemic, approximately 44% of home visits were being conducted via video conferencing, 44% by phone, and 8% by text message; prior to that, all home visits had been in person.[1351] Home visiting programs are individually designed to be adaptable to the family's unique needs and have always included elements that are critical to strong responses to the pandemic, including nurse engagement, hygiene training, and resource access.

High-quality and affordable child care is likewise essential in this era.[1352] By law, the California State Emergency Plan includes a statewide child care disaster plan, which demonstrates how the agency will address the needs of children, such as safe child care, before, during, and after a state of emergency.[1353] It assists local officials in training early learning and child care providers on disaster preparedness, recovery, and connecting people to local Office of Emergency Services local personnel and procedures.

Income Tax Credit; safety net programs like CalWORKS, the Supplemental Nutrition Assistance Program, the Women, Infants and Children Supplemental Food Program, the Housing Choice Voucher Program, and the Supplemental Security Income Program; child care subsidies; minimum wage; affordable health insurance; and paid family and medical leave.[1102]

- The CDPH's Comprehensive Perinatal Services Program serves pregnant women on Medi-Cal, from conception through 60 days postpartum; in addition to standard obstetric services, women receive enhanced clinical services in nutrition and psychosocial and health education, funded by a Title V Maternal and Child Health Block Grant.[1343]
- Starting Early is a primary-care-based and family-centered program that focuses on preventing child obesity and enhancing nutrition, starting in the third trimester. Studies show increases in exclusive breastfeeding and reduction in complementary foods for three-month-old infants.[1344] Funds are provided by the US Department of Agriculture.
- Cal-Learn is administered by CDSS for pregnant and parenting teens in CalWORKS-supported families. The program provides resources to help teens graduate from school, become independent, and form healthy families. Services include child care, coverage of educational expenses, and transportation support. In fiscal year 2017–18, over 3,000 teens participated.[1263]

TERTIARY PREVENTION STRATEGIES

Many children receiving early care and education are experiencing ACEs, and supports are needed for children and families to help prevent or mitigate the toxic stress response.[1345] Tertiary prevention targets families where ACEs or other risk factors for toxic stress are already present, such as untreated parental mental health or substance use concerns, homelessness, domestic violence, or child maltreatment—along with evidence of toxic stress symptoms. The central aim of tertiary prevention activities is to reduce the magnitude of negative downstream consequences and halt any chance of recurrence.[1346]

In the healthcare sector, there is an important role for providers who are able to recognize and respond to the presence of symptoms of toxic stress, such as AAHCs—to treat these conditions in part by putting into place strategies to regulate the stress response and ameliorate related neuro-endocrine-immune-metabolic disruption. Evidence-based strategies in this vein include enhancing healthy relationships, sleep, exercise, nutrition, access to nature, mindfulness practices, and when needed, mental and behavioral healthcare (see the section **Tertiary Prevention Strategies in Healthcare** for more details).

In the early childhood sector, many programs provide services that braid primary, secondary, and tertiary prevention. For example, Family Resource Centers typically provide:[1347]

- Parent skill training
- Drop-in centers
- Home visiting
- Job training
- Substance abuse prevention
- Violence prevention
- Services for children with special needs
- Mental health or family counseling
- Child care
- Literacy
- Respite and crisis care services
- Assistance with basic economic needs
- Housing

Tertiary prevention programs may engage trained mental health counselors for intensive family preservation services (typically for up to two months), coordinate parent support groups to share best practices on positive parenting behaviors and attitudes, recruit parent mentors from stable, non-abusive families to serve as role models to families in crisis, and deploy mental health services to bolster effective communication and family cohesion.[1325] Especially when working with very young children, whose stress response systems are still developing, there is an enormous opportunity to mitigate long-term negative impacts. Promoting positive caretaking practices before individuals begin to develop significant toxic stress physiology and downstream consequences can slow or halt the progression of health sequelae while also educating parents to further diminish future incidents, addressing the root of the exposure and physiology, and bolstering opportunities for positive childhood experiences.[41]

CDSS administers the Family Stabilization Program, which is designed to provide a basic level of stability for families in crisis; it includes family crisis counseling, anger management services, and parenting classes. As of June 2018, nearly 3,500 cases were open. Family-oriented treatment programs for substance use that include parenting skill-building have also been shown to be effective. CDSS's CalWORKS Home Visiting Program also provides intimate partner violence and sexual assault, mental health, and substance abuse treatment, as needed.[1316]

RECOMMENDATIONS

- Networks for referral and treatment systems should be strengthened toward greater effectiveness, accountability, and ease of navigation for children, adults, and providers.
- Cross-departmental collaboration should be enhanced, including setting

mutual goals and outlining clear accountability for maintaining such partnerships.

- Data integration across programs and agencies should be facilitated to better serve the needs of the family and child.
- Universal messaging on the prevention of ACEs and toxic stress should be produced and disseminated, and systems should be aligned to support these needs.
- The early childhood sector workforce should receive regular training in trauma-informed approaches, and competence may be reinforced through the licensing and accreditation process.
- Emphasis should be placed on equity by tailoring services and supports to local contexts and cultures, promoting meaningful parent engagement.
- Further research to better individualize prevention and intervention options for optimal outcomes and cost-effective approaches is necessary.

All segments of society have a role in supporting families as they raise healthy children. Assuring the well-being of all families is the cornerstone of a healthy society and healthy future generations, and requires universal access to support programs and services.

Primary, Secondary, and Tertiary Prevention Strategies in Education

Among the most direct and profound effects of Adverse Childhood Experiences (ACEs) and toxic stress is their impact on learning and school success.[222,1056,1354-1357] The **toxic stress response** is defined by the National Academies of Science, Engineering, and Medicine (NASEM) 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"; it involves neuro-endocrine-immune-metabolic and genetic regulatory dysfunction, and occurs when severe or prolonged stress is experienced without sufficient buffering sources.[23]

The biological stress response has been characterized as falling into three types: positive, tolerable, and toxic.[6,78] Not all stress is bad. Some stress is a necessary and even essential part of growth and development; it can help us transiently mobilize energy and increase focus to perform better at the task at hand, such as an upcoming test, the big game, or a presentation at work. The **positive stress response** is characterized by brief elevations in stress hormones, heart rate, and blood pressure in response to a routine stressor.[6,78]

The **tolerable stress response** "activates the body's alert systems to a greater degree as a result of more severe, longer-lasting difficulties, such as the loss of a loved one, a natural disaster, or a frightening injury. If the activation is time-limited and buffered by relationships with adults who help the child adapt, the brain and other organs recover from what might otherwise be damaging effects."[674]

The biological embedding of the **toxic stress response** is key to understanding how ACEs can impact learning, relationships, and other aspects of school functioning. The toxic stress response can result in impairments to the brain's developing limbic system, including the amygdala and hippocampus, which are the areas of the brain responsible for learning, memory, threat detection, and emotional regulation, making these tasks more difficult.[147,1358] Furthermore, the toxic stress response inhibits higher-order decision-making in the prefrontal cortex, which is responsible for impulse control and executive functioning.[125,304,330,1359] The immune, metabolic, and inflammatory changes that result from the toxic stress response lead to increased risk of infections, asthma and other atopic conditions, poor dental health, and somatic complaints, such as headache and abdominal pain, which can contribute to school absenteeism and impair the ability to engage fully when present.[222,449,1357,1360,1361]

Extensive research has linked ACEs to several relational, educational, and learning difficulties. In school, effects of ACEs and toxic stress include trouble concentrating in class, lack of school engagement, not completing homework, school failure and noncompletion, learning disabilities, impaired executive and relational functioning, and increased need for special education.[37,696,703,1056,1354-1356,1362,1363] Robles and colleagues examined ACEs and school performance measures among over 65,000 children and reported that as the ACE score increased, the risk of repeating a grade, reporting lack of school engagement, and not completing homework increased in a graded manner (**Figure 20**).[696] Neuropsychiatric manifestations of toxic stress are associated with increased school-based victimization and perpetration of interpersonal violence, executive dysfunction, attention-deficit/hyperactivity disorder (ADHD), learning disabilities, and suicidality, which can

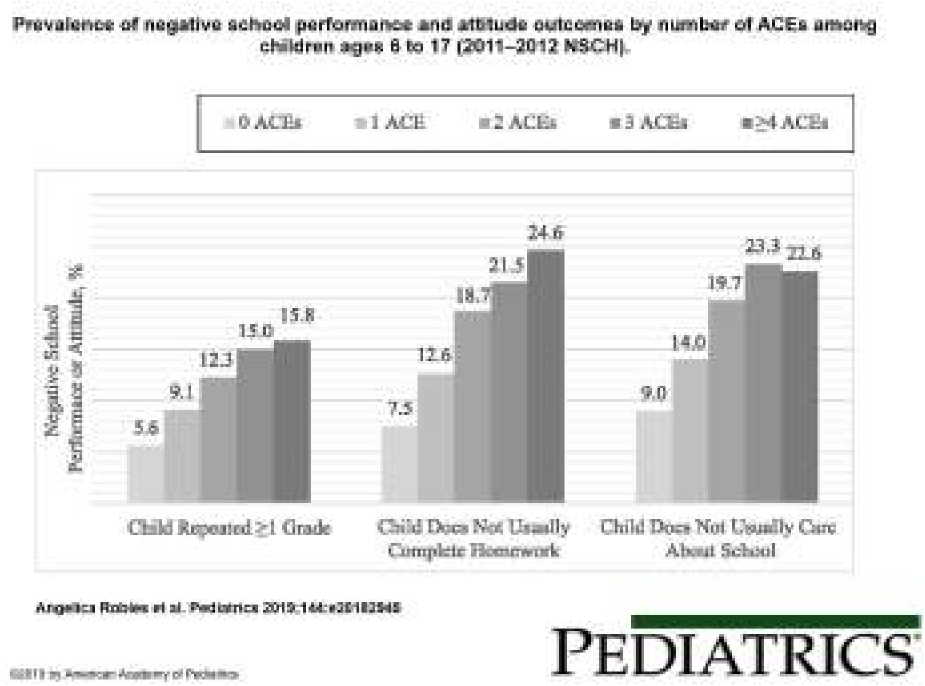


Figure 20. There is a graded (dose-response) impact of the number of ACE categories experienced on various school outcomes: the need to repeat a grade, not completing homework, and school disengagement. Reproduced with permission from the journal Pediatrics, Volume 144, page 4, ©2019, American Academy of Pediatrics.[696]

result in school absenteeism, suspensions, failure, repeating a grade, or the need for special education.[2,125,304,330,703,1359,1364] Burke and colleagues reported that compared to children with no ACEs, children with four or more ACEs are approximately 32 times more likely to experience learning and behavioral problems.[37] ACEs and toxic stress also increase the risk of poor self-regulation, suicidality, and excessive school absenteeism related to physical and mental health concerns, or behavioral difficulties.[37,696,703,1056,1354-1356,1362,1363]

ACEs and toxic stress can also affect later learning and success among those who attend two- or four-year higher educational institutions.[1365-1369] Late adolescence and early adulthood constitute an under-appreciated period when the biological consequences of toxic stress may lead to dropping out of college, depression, anxiety, or suicidal ideation, among many other health problems.[1366-1370] Adults who have experienced a greater number of ACEs and other adversities report lower levels of educational attainment.[1371,1372]

Education is about more than receiving a diploma; it includes learning, which is the process of acquiring skills that can help shape lifelong health through three interrelated pathways: 1) health knowledge and behaviors; 2) employment and income; and 3) psychosocial factors.[1373] Children spend the better part of their lives in K-12 school settings, making experiences in these settings instrumental in promoting not only learning, but also immediate and longer-term well-being. In California, compulsory-education laws require children between the ages of six and 18 years to attend school full-time; thus, a child spends more than 1,000 hours per year in school.[1374] Consistent school attendance is an evidence-based factor for academic success.[1375] Yet, chronic absenteeism is currently a critical national problem that puts school children and youth at risk for academic failure and dropping out of school,[1376] as well as worse longer-term health and social outcomes. Overall, the rate of chronic absenteeism in California, defined as being absent 10% or more of the school days in the school year,[1377] has steadily increased, from 10.8% in 2016–2017 to 12.1% in 2018–2019, a relative increase of 12%.[1378]

Subgroup analyses indicate that economically disadvantaged students, English learners, foster youth, and students with disabilities have experienced disproportionate increases in chronic absenteeism during the same period. Racial and ethnic disparities in absenteeism rates also exist, with Black (22%) and American Indian or Alaska Native (21%) students having substantially higher rates than White students (10%).[1378] The reasons for the increases in chronic absenteeism observed in California are complex and are still being elucidated, but family challenges and students' acute and chronic health problems requiring time away from the classroom contribute.[1379-1382]

Rates for overall school suspensions in California have slightly decreased from 2016 (36.5 per 1000) to 2019 (34.7 per 1000).[1383] Yet, as with chronic absenteeism, subgroup analysis of suspension rates indicate significantly greater rates among economically disadvantaged students, homeless youth, foster youth, and students with disabilities (**Table 8**).[1383] Suspension rates were between two to three times higher for economically disadvantaged students, homeless youth, foster youth, and students with disabilities. Racial and ethnic disparities in suspension rates also exist, with Black (92.2 per 1000) and American Indian or Alaska Native (73.1 per 1000) students having substantially higher rates than White students (29.8 per 1000).[1383]

PRIMARY PREVENTION STRATEGIES

The impact of ACEs on learning and education calls for school settings to build capacity to implement evidence-based interventions for the primary, secondary, and tertiary prevention of toxic stress in the educational sector. Primary prevention strategies use interventions that target the general population rather than a specific risk group, with the goal of reducing the total dose of adversity experienced and increasing the total dose of buffering factors. A consensus of scientific evidence demonstrates that adequate doses of safe, supportive, nurturing relationships and environments, and other interventions can prevent development of the toxic stress response and its physical and behavioral sequelae.[1385-1389] Within school settings, adults can proactively model behaviors of kindness, empathy, and compassion, which promote supportive, safe, and nurturing learning environments and buffering for toxic stress.[1390] This makes stressors more likely to be experienced

Category	Rate per 1,000
Foster youth	**151.7**
Non-foster youth	34.0
Students with disabilities	**66.0**
Students without disabilities	30.3
Homeless students	**59.6**
Non-homeless students	33.8
Socioeconomically disadvantaged	**44.5**
Non-socioeconomically disadvantaged	18.6

Table 8. *Subgroup analysis of California suspension rates, 2018-2019.*
Data source: kidsdata.org, California Department of Education suspension data (through December 2019)[1383]

as tolerable, rather than as toxic.[6] Models that enable universal positive school climates that emphasize safety, inclusiveness, and predictable rules and routines, are also very important for setting up trauma-informed and universal supports for all children.[1365]

Another integral component of primary prevention in schools is ensuring staff wellness through the use of evidence-based health-promotion interventions, such as exercise, mind-body practices, proper nutrition, and employee assistance programs.[922] The primary prevention of toxic stress for children in schools relies on ensuring the well-being of adult mentors and caregivers, including school personnel.[635,1391,1392] The ability of adults to proactively model kindness and empathy to promote supportive, safe, and nurturing learning environments is greatly reinforced by their understanding of the impacts of ACEs and toxic stress on school functioning, and also on their own resilience to vicarious trauma and burnout.

An integral component of primary prevention in schools is ensuring staff wellness through the use of evidence-based health-promotion interventions.

Well-integrated communication with and active inclusion of parents and caregivers in school activities in a proactive way is also vital, in order to knit together buffering sources at school and at home. Engaging parents and families to raise awareness of ACEs and their impact on learning, through health communication campaigns can foster increased understanding, and empower families to be instrumental in preventing and addressing ACEs and toxic stress and their impacts, including by partnering with healthcare providers.[1393] Important adaptations to all these features have had to be made in the context of the coronavirus disease 2019 (COVID-19) pandemic (see **COVID-19 PANDEMIC IMPACTS ON EDUCATION**).

In general, there is substantial evidence that even before children enter the formal school system, access to high-quality early education and care is an important primary prevention tactic.[23,31] Early education and care for children from birth to five years also counts as primary prevention of ACEs and toxic stress because it targets a particularly critical period for healthy development and lays the foundation for long-term preventive health and education benefits.[1227,1245,1278-1280,1394,1395]

The Carolina Abecedarian intervention is one of the oldest and best studied early childhood programs.[1227] This childhood educational intervention includes on-site pediatricians, and four key components: language, conversational reading,

COVID-19 PANDEMIC IMPACTS ON EDUCATION

The abrupt and sustained school closures and transition to remote learning due to the coronavirus disease 2019 (COVID-19) pandemic is exacerbating challenging conditions for many students and families and creating new situations that place more children at risk of ACEs and toxic stress.[354,355,1421] Federal data show that in 2018, 20.5% of reports of suspected child abuse nationwide came from education personnel.[1422] In March 2020, during the first week of school closures in San Diego County, the child abuse hotline received nearly 60% fewer calls than average.[1423] The decrease is most likely not indicative of fewer cases of abuse or neglect, but of the diminishment of educators' time with children and ability to detect signs of abuse and neglect.

Schools recognize their roles beyond academic education, such as providing meals and counseling, but have so far struggled to continue these critical services as remote instruction supplants the classroom. Guidance from the CDE, "Stronger Together: A guidebook for the safe reopening of California's public schools," addresses the physical, emotional, health, and financial strains from the pandemic, which can cloud student and staff experiences and hinder academic and social achievement. In partnership with communities, local educational agencies are tasked with addressing social-emotional well-being more than ever, while also handling logistical requirements. For example, the necessary move to remote learning has shone a light on the digital divide: not all families can access the technology needed to fluidly shift children to virtual learning spaces. When approximately one in five students and half of all low-income families in California are unable to participate in online lessons due to lack of a device or high-speed internet, achievement gaps and educational disparities are likely to grow.[1424]

For many children, the school is a bedrock of community belonging. The pandemic has not only disrupted children's academic opportunities and connections with their peers and educators, it has also surfaced new and difficult experiences in the home: fear, anxiety, financial distress, food and housing insecurity, and countless other challenges. Economic uncertainty is associated with increases in harsh parenting, which increases risk for child abuse and neglect, and the loss of friends and family through illness and isolation can also increase the total dose of acute stress and adversity and reduce the dose of buffering supports available from caregivers, educators, and other adults.[356]

Educators are faced with an unprecedented test to adapt trauma-informed practices to distanced settings, especially since learners are separated from person-to-person instruction. As outlined in the *Vibrant and Healthy Kids* report from the National Academies of Sciences,

COVID-19 PANDEMIC IMPACTS ON EDUCATION

Engineering, and Medicine, children need to feel safe, both physically and psychologically.[23] Whereas the classroom provides a controlled environment characterized by routine, encouragement, and safety, home settings introduce a host of variables that may be less conducive to learning. For students who are in home settings that are less than optimal—where caregivers are under extreme stress, for example—supporting both student and caregiver becomes a core trauma-sensitive practice. To build and maintain a trusting relationship, educators must amplify culturally responsive teaching practices by valuing and respecting students and their families, purposefully escalate opportunities for Positive Childhood Experiences and other protective factors, and model healthy emotional regulation and coping strategies for both students and caregivers.[41] With children learning from a distance during a pandemic, educators may need to prioritize social-emotional resilience over the academic goals stated in a typical year's curriculum. Such trauma-informed elements of an online learning program can help students return to school feeling connected, supported, and ready to reengage with academic learning.

enriched caregiving, and learning games. Campbell and colleagues found that among adults 30 years and older who received the intervention, the Framingham 10-year risk score for total coronary heart disease (stable and unstable angina; myocardial infarction; coronary heart disease death) was 2.15 ($p < 0.05$) lower for treated men and 0.34 ($p < 0.05$) lower for women, compared to the control group, who did not receive the intensive interventions. Also, for men, a mean difference of 13.5 for diastolic blood pressure and 17.5 for systolic blood pressure was reported, compared to the control group.[1227] In the High/Scope Perry Preschool Program, in the 1960s, at-risk Michigan children were randomly assigned to receive this intensive preschool intervention. Nores and colleagues examined data available for participants aged 40 years, which included educational attainment, criminal activity, earnings, and welfare receipt. The treatment group had higher lifetime earnings, by +$111,719 for men and $132,406 for women. They also report that costs due to criminal activity were reduced, by $732,894 for men and $23,985 for women. For every dollar invested, the program repays $12.90, when a 3% discount rate is applied.[1395]

In addition to the long-term health and societal benefits, sufficient evidence exists that high-quality early childhood education provides a strong start to educational success across the life span.[1396,1397] Using the Early Development Instrument, Duncan and colleagues[1396] longitudinally studied 3,000 children in seven school districts in Orange County, California. They saw a 100% to 300% increase in proficiency in third-grade mathematics and language arts in at-risk children.[1396] In the Fast Track study, Jones and colleagues examined associations between social competence, including pro-social behaviors in kindergarten, and on-time high school completion, completing a college degree, stable employment, and full-time employment 13–19 years later. Kindergarten social competence predicted a 54% higher probability of graduating from high school, 100% higher of completing a college degree, 66% higher of having stable employment, and 46% higher of full-time employment.[1398]

SECONDARY PREVENTION STRATEGIES

Secondary prevention strategies utilize selective interventions that target groups of individuals who are at higher-than-average risk for toxic stress, due to prior exposure to ACEs or other risk factors, and who are potentially showing early signs of toxic stress impacts on learning, relationships, or health in school (such as absenteeism and behavioral or learning difficulties). These can include small-group or one-on-one mentorship or supports, close family engagement, or coordination with community-based resources, such as those that provide supports to families experiencing challenges such as poverty, addiction, intimate partner violence, housing insecurity, or mental illness.[1384] These supportive strategies are best levied in consultation and coordination with the student's primary pediatric provider.

Access to natural environments such as school playgrounds and other outdoor spaces can also improve outcomes associated with toxic stress.

As mentioned earlier under Primary Prevention, buffering sources include adults who can provide compassion, safety, nurturance, and support, and can turn the experience of a stressor into tolerable stress, rather than toxic stress. Additionally, exercise, nutrition, mindfulness, interacting with nature, and sleep are associated with reduced stress reactivity, reduced inflammation, and enhanced neuroplasticity.[817,927,928,962,1399] These strategies can be employed in the school setting and at home, in coordination with families and healthcare providers.

Enhancing sleep hygiene and quality is effective in buffering toxic stress, which is also critical for effective learning. Children and adolescents who do not get sufficient or high-quality sleep are at greater risk for attention and behavioral problems, which are known to contribute to poor academic outcomes in school.[1400] Improving sleep requires a consistent bedtime routine and is associated with better child mood, emotional behavioral regulation, mother's self-reported mood, school readiness, and literacy outcomes (especially when reading is part of the bedtime routine).[805,813,814] Bedtime routines can include feeding (for infants and children), bath, massage, reading books, rocking, prayer, singing, and listening to music.

Physical activity is associated with improved memory and attention, cognition, academic achievement, and psychosocial functioning; however, studies are not uniform in the type, intensity, or frequency of exercise needed to achieve these outcomes.[581,754] Exercise training increases hippocampal perfusion and hippocampal volume, specifically the anterior, left, and right hippocampus.[864-866] Physical activity increases hippocampal white matter volume, new neuron growth (neurogenesis), positive changes in the connections between neurons (synaptic plasticity), and blood flow.[581] Physical activity may also help metabolize the increased energy associated with anxiety or perceived (but not actual) threats. For example, a child who has experienced ACEs and is hyper-aroused and hypervigilant at school may be more activated by perceived threats and have trouble sitting still. Brief physical activity breaks may help the child release the excess energy and regulate the threat-response system.[880] In one study, team sports participation during grade 7-12 (involving strong coach and peer relationships and exercise) among 9,668 adolescents exposed to ACEs was associated with lower odds of adulthood (at ages 24-32 years) depression (aOR 0.76, 95% CI 0.59-0.97) among men and anxiety (aOR 0.70, 95% CI 0.56-0.89 among men and women.[880]

Mindfulness is increasingly being utilized in schools as an intervention to decrease arousal and promote coping and resilience. The known impacts of mindfulness includes adaptive alterations in brain function, such as increased blood flow and brain activity in regions such as the prefrontal cortex and hippocampus.[1401,1402]

Diets with greater fruit, vegetables, fish, and whole grains have also been associated with decreased inflammation and improved health.[843,850] National school nutrition programs include the School Breakfast Program, the National School Lunch Program, and the Special Milk Program. The first two are federally assisted meal programs operating in public and nonprofit private schools and residential childcare institutions. It provides nutritious, low-cost or no-cost breakfasts and lunches on each school day. The Special Milk Program provides milk to children in half-day pre-kindergarten and kindergarten programs without access to the school meal programs.[1403]

There is sufficient evidence to demonstrate that recess and play time during school benefits students' memory, attention, and concentration and reduces disruptive behavior in the classroom, while improving social-emotional development.[1404,1405] Attention and learning are best optimized with breaks, since the brain has difficulty maintaining attention for extended periods and requires new stimuli to regain focus.[1406] Recess and play can take place inside or outside, but are enhanced in the presence of nature.

Importantly, access to natural environments such as school playgrounds and other outdoor spaces can also improve outcomes associated with toxic stress. Interacting with nature is associated with decreased diabetes, depression,[947] heart rate and blood pressure,[948] heart disease,[949] and mortality.[948,950-952] Adding green spaces in low-resourced communities has been associated with reduced crime and violence, improved perception of safety, increased social connections, and reduced depressive symptoms.[947,956,957] By contrast, losing trees has been associated with increased crime and worse health, including increased cardiovascular and respiratory deaths.[952,957,958] Nature most likely improves health for children and adults with toxic stress by directly calming the stress response system, as well as by increasing healthy behaviors such as physical activity, mindfulness, and relational health. Parks and exposure to nature have been shown to increase play and physical activity, as well as to decrease screen time.[959] Nature may also increase opportunities for relationship and connection and improve sleep.[757,758] Studies also document improvement in family functioning and attachment,[757,960] and increased social ties.[758]

After-school programs can also play an important role in the secondary (and tertiary) prevention of toxic stress by providing focused skill-building activities and important mentorship with peers and adults for students. In 2019–20, the Governor's budget included $50 million for after-school and safety programs.[1131] All of these efforts support building school capacity for students exposed to ACEs to learn in a safe, supportive environment with the promotion of nurturing relationships both inside and outside school.

TERTIARY PREVENTION STRATEGIES

Tertiary prevention targets those students who are already exhibiting signs of toxic stress—such as ACE-Associated Health Conditions (AAHCs), high-risk learning or relational behaviors, and/or other downstream sequelae of toxic stress—and require specific therapeutics to address and prevent worsening health problems, chronic behavioral or learning difficulties, school suspension, expulsion, or dropping out. Such interventions enact tertiary prevention or seek to minimize future risks in those who already have signs and symptoms that suggest they are experiencing significant toxic stress physiology.[6-10,704] The interventions outlined for primary and secondary prevention apply to the tertiary prevention of AAHCs and children exhibiting signs of toxic stress. School-based health services can also provide students focused healthcare interventions. In many cases, such services may not be available; in these scenarios, school personnel should work closely with the child's family and healthcare provider to ensure that all aspects of school and health are well coordinated with the child's primary medical provider. Needed resources may include therapeutic counseling and wraparound services that include healthcare, social services, and trauma-specific therapy.

Restorative justice techniques that emphasize redirection and de-escalation tactics, and prioritize time in the classroom, can minimize re-traumatization and mistrust and better support students' long-term growth.

Disciplinary strategies that are not overly harsh or punitive, but instead, are restorative, emphasizing de-escalation and redirection when disruptive behaviors occur, are also vital to prevent retraumatization and escalation of acute behavioral and/or other disruption. This can help prevent the "school-to-prison pipeline."[1407-1410] This phrase refers to children having their first encounters with the criminal justice system while still in school, often after punitive disciplinary actions are taken, including suspensions that take them out of school. Children of color are disproportionately affected.[1408-1410] Between 2005–2006 and 2017–2018, there was a 47% relative increase in the number of public schools nationwide with one or more security staff with the authority to arrest students.[1411] When public schools increasingly rely on school resource officers to discipline students at school, school-based arrests go up.[1412] Combating these systems using restorative justice techniques that emphasize redirection and de-escalation tactics, and prioritize time in the classroom, can minimize re-traumatization and mistrust and better support students' long-term physical, social-emotional, and cognitive growth.[1408-1410]

Sometimes targeted health and mental health interventions are needed, including ones that involve family-based treatment. In some cases, these can happen in school settings (when there are trauma-trained health professional staff), and in others, schools may recommend that students and families seek such treatment in healthcare contexts. Ideally, schools and child-serving health providers such a pediatricians and family practitioners would closely coordinate on any school-based and external health resources for students displaying toxic stress symptoms. For example, coordination of a student's Individualized Education Program (IEP) for a health condition such as asthma, ADHD, a learning difficulty or disability, depression, or anxiety, is one example. School personnel may connect families in need with a local healthcare provider trained in ACE screening, identifying signs and symptoms of toxic stress and trauma-informed care through the ACEs Aware provider directory.[1153]

The introduction of the federal Handle with Care Act of 2018 was intended to strengthen the infrastructure to promote trauma-informed schools and prevent repeated traumatization impacts. It illustrates the important opportunity to bridge between the justice system and the education system.[1413] The proposed act is based on a pilot program in West Virginia that supports coordination between law enforcement and educational professionals to provide additional supports to students present at the site of a traumatic event. Law enforcement personnel who are called to the scene and observe that a child is present are trained to gather information about where the child goes to school in a trauma-informed manner and send a notification to the school, without revealing any confidential information. For example, when law enforcement is called to a home for an episode of intimate partner violence, the school of any affected child is notified that the child should be "handled with care" so that school personnel can be prepared to respond by providing extra precautions in promoting safety and nurturance for the student in the days to come.[1413] West Virginia first piloted Handle with Care in 2013, and to date, 527 notices involving 959 students have been provided.[1414] School interventions have helped up to 90% of the identified children, and about 130 children received counseling service on-site at school. In addition, observed relationships between education and law enforcement have shown improvements.[1414]

Another example of an allied tertiary prevention approach between justice and education is an after-school program for juvenile offenders called Project Back-on-Track, which included a comprehensive multi-modal treatment program emphasizing family and group interventions for youth violent offenders; the control group received a community intervention. The Back-on-Track intervention group had a 90% non-arrest rate after 12 months following enrollment, compared with 69% of the community control group.[1415]

CASE STUDIES

Project Cal-Well of the California Department of Education (CDE)[1416] and the Healthy Environment and Response to Trauma in Schools (HEARTS) program of the University of California, San Francisco (UCSF),[1417] are two case studies in California that are presented to provide a snapshot of how primary, secondary, and tertiary prevention of toxic have been translated into school settings.

Both programs utilize the Multi-Tiered System of Supports (MTSS) model, which operationalize a three-level prevention and intervention approach (**Figure 21**). More specifically, CDE's Project Cal-Well uses RtI[2] (Response to Intervention and Instruction) to help prevent students from falling behind by using data-driven decisions that support a team-based problem-solving approach to meet California's Common Core State Standards. The UCSF HEARTS framework is a prevention and

Figure 21. Examples of primary, secondary, and tertiary prevention strategies to address toxic stress employed in the education sector. Reproduced with permission of Corwin, from Romero, Robertson, and Warner, Building Resilience in Students Impacted by Adverse Childhood Experiences: A Whole-Staff Approach (Thousand Oaks, CA: Corwin, 2018); permission conveyed through Copyright Clearance Center, Inc.[1384]

intervention approach that utilizes the MTSS framework to address adversity at the student, staff, and school organizational levels.

Project Cal–Well

Project Cal-Well: Primary prevention of ACEs and toxic stress

Since 2014, the CDE has been involved in Project Cal-Well, a federally funded project to promote mental health awareness and wellness among California's K-12 students. The CDE received two, five-year grants from the Substance Abuse and Mental Health Services Administration to implement Project Cal-Well in two cohorts. In Cohort 1 (2014–19), Project Cal-Well was a consortium of the CDE, ABC Unified School District, Garden Grove Unified School District, and San Diego County Office of Education. **Figure 22** provides an overview of the project's three-component model. Component 1 utilizes primary prevention to promote and improve school climate across the full population. The ultimate goal is to increase school connectedness over time. To accomplish this, Project Cal-Well utilizes intervention strategies such as Positive Behavioral Interventions and Supports (PBIS), trauma-informed care, Restorative Practices in Schools, Youth Mental Health First Aid, and suicide prevention policies and trainings. To increase student engagement and reduce problematic behaviors, PBIS uses evidence-

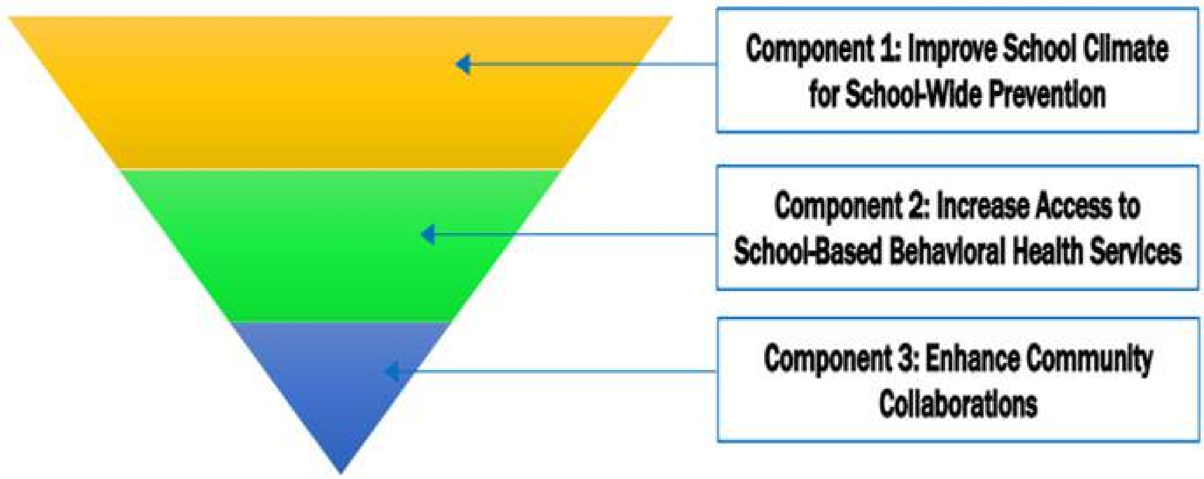


Figure 22. Project Cal-Well employs a primary prevention approach to enhance school environments and success for all children, and targeted and interventions for at-risk and high-risk youth. Reproduced with permission from Project Cal-Well.[1419]

based behavioral interventions like reward and positive reinforcement to promote desired behaviors and positive outcomes for all students.[1418]

Project Cal-Well: Secondary and tertiary prevention of ACEs and toxic stress

Component 2 aims to provide targeted school-based health services to students who show symptoms that suggest risk for or early toxic stress physiology, despite universal intervention practices and thus enacts secondary prevention of toxic stress. School-based health services include individual and group counseling to support such students, in addition to physical health services for AAHCs such as asthma and somatic complaints like headaches or digestive concerns, which contribute to school absenteeism.[6,703,1420] Project Cal-Well schools successfully increased access to school-based mental health services in two ways: by hiring a variety of on-site mental health professionals, and through training to increase staff awareness of students' mental and physical health needs and how to refer students to needed health services. As a result, the proportion of school staff reporting that they referred students to school-based mental health professionals in the past 12 months increased from 75% in 2013-2014 to 85% in 2018-2019. In addition, 6,754 students were provided school-based mental health services in 2018-2019, compared to 2,664 students in 2013-2014, which was a relative increase of 154%.[1416]

Component 3 of Project Cal-Well, which enacts tertiary prevention of toxic stress, focuses on providing intensive mental health interventions to students with identified mental or behavioral health needs through strong community collaborations. Schools liaise closely with community-based behavioral health and other organizations to develop referral pathways to ensure students receive needed interventions.

By the end of 2019, Project Cal-Well had improved access to and availability of mental health services in the three Cal-Well local educational agencies and had trained almost 6,000 educators, school staff, and parents in Youth Mental Health First Aid throughout the State (**Figures 23** and **24**). Additionally, among 9th graders, Garden Grove Unified School District saw a 6% decrease in suicidal ideation and a 5% increase in school connectedness. In the San Diego County Office of Education, there was a 30% increase in 9th and 11th graders reporting there was a caring adult in their lives, and an 11% increase in school connectedness.[1416]

HEARTS

HEARTS: Primary prevention of ACEs and toxic stress

HEARTS is largely aimed at supporting school climate and culture change by building capacity of school personnel. A key focus is training personnel on the effects of complex trauma and trauma-informed practices. Building school capacity also includes promoting staff wellness by addressing stress, burnout, and vicarious trauma. For staff to effectively implement trauma-informed practices, procedures, and policies, they must have the competency and skills to respond to behavioral, health, relational, and learning difficulties. School leadership and a team of key school staff meet regularly (e.g., coordinated care teams), along with the rest of the school community (e.g., administrators, credentialed and classified staff, students and their caregivers) to implement these supports and systems. Systems change in this model typically requires between two and five years, depending on a school body's level of need and the intensity of services provided.

Primary prevention goals of the HEARTS program include:[1365,1417]

1. Increasing student wellness, engagement, and success in school;
2. Building school system capacities to support trauma-affected students by increasing knowledge and practice of trauma-informed strategies; and
3. Promoting staff wellness through addressing burnout and vicarious trauma.
4. HEARTS services that aid in these goals can include:
    a. Professional development training and consultation for school personnel and community partners, and
    b. Workshops for parents/caregivers.

HEARTS can be implemented as a full, site-based program or as the HEARTS Flex.

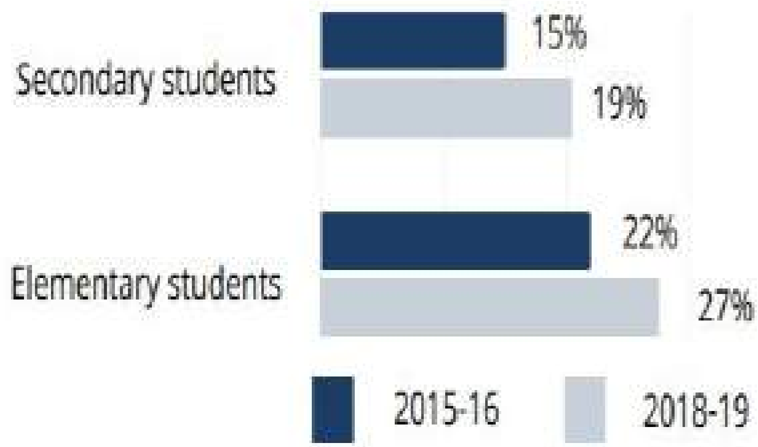


Figure 23. From 2015 to 2019, overall changes in the percentage of students reporting that they would seek help from a counselor, doctor, or therapist if scared, stressed, or depressed. Reproduced with permission from Project Cal-Well.[1416]

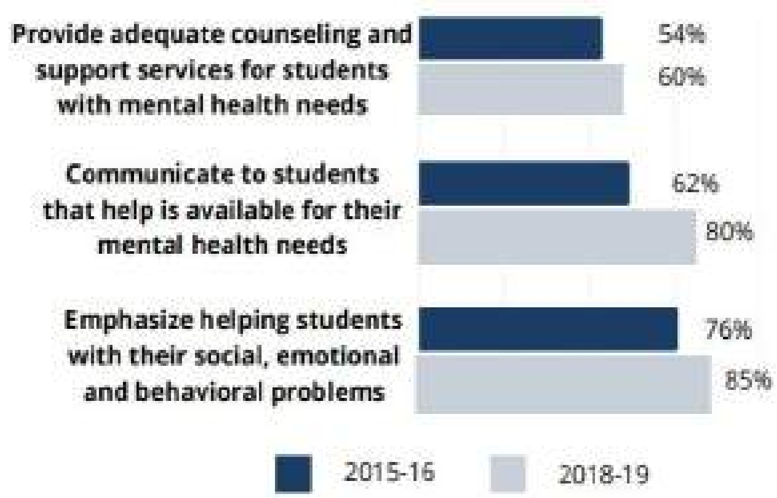


Figure 24. From 2015 to 2019, changes in the percentage of ABC Unified School District staff reporting that their schools were meeting the emotional and mental health needs of their students. Reproduced with permission from Project Cal-Well.[1416]`

The full, site-based program includes a HEARTS consultant on-site at a school three to five days per week, who collaborates with school leadership and staff to provide the full range of support and services across all three MTSS tiers (**Figure 25**). In the Flex format, HEARTS implementation focuses on primary prevention (tier 1) and early/secondary prevention (tier 2), without direct therapeutic services

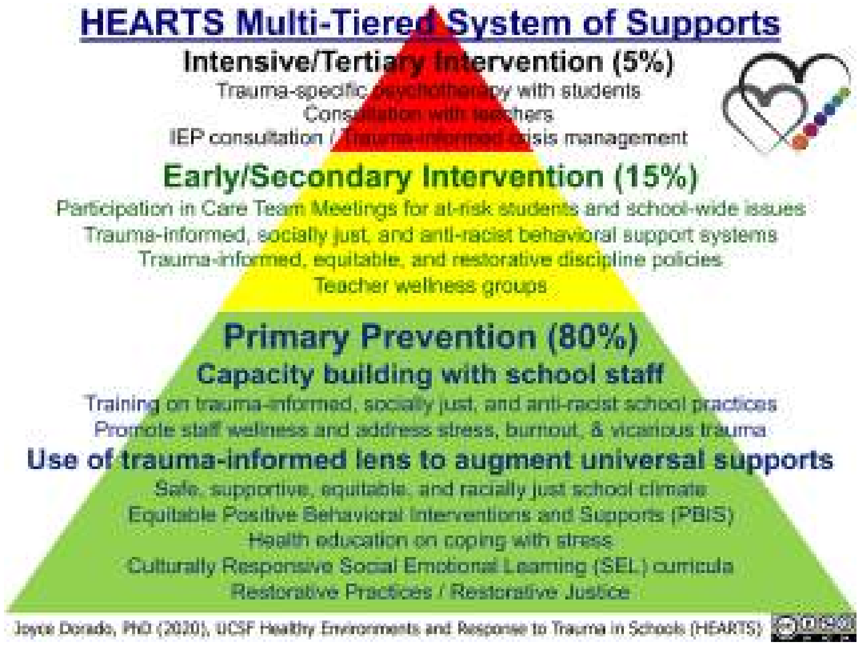


Figure 25. *Three-level prevention framework for UCSF's HEARTS (Healthy Environments and Response to Trauma in Schools). Reproduced with permission from Joyce Dorado, PhD (2020), "HEARTS Multi-Tiered System of Supports", Healthy Environments and Response to Trauma in Schools (HEARTS). Retrieved from* https://hearts.ucsf.edu/program-overview[1417]

for students.

HEARTS: Secondary and tertiary prevention of ACEs and toxic stress

Secondary and tertiary prevention of ACEs and toxic stress include training and consultation for school and district staff, and on-site health services like psychotherapy for students with toxic stress. Frequency of training and consultation depends on needs and resources of a school site or district.

An important aspect of HEARTS is a focus on using restorative justice principles to prevent the "school-to-prison pipeline,"[1408-1410] and particularly, on reducing racial disparities in disciplinary office referrals, suspensions, and expulsions. The HEARTS site-based program aims to increase instructional time and decrease time spent on disciplinary actions.

After the full program had been implemented for two or more years, school personnel reported significant increases in understanding trauma, their use of trauma-sensitive practices, and in students' ability to learn, time on task, and school attendance. At one school, after the first year of HEARTS, total disciplinary office referral incidents had dropped by 32%, and incidents involving physical aggression reduced by 43%.[1417] After the fifth year of HEARTS, there was an 87% reduction in total incidents, an 86% reduction in incidents involving physical aggression, and a 95% decrease in out-of-school suspensions.[1365] A nurturing school climate with more intensive services for at-risk and high-risk students promotes improved student learning, health, and relational success.

IMPLICATIONS AND FUTURE DIRECTIONS

Using multi-tiered, school-based interventions that incorporate assessment and response to toxic stress, California has witnessed greater school connectedness among students, reductions in suicidality, increased reports of caring adults, and reduced levels of aggression in school systems. These findings are promising.

Case Study

A Middle School Program in Antioch

At a middle school in Antioch, staff struggled to control student behavioral disruptions. Teacher morale was plummeting. In 2015, 19.2% of the student population had been suspended. The principal and staff took advantage of a trauma-informed program that Contra Costa County was implementing called the Sanctuary Model to essentially replace a "What's wrong with you?" approach to dealing with kids who are having trouble with "What happened to you?" and then providing them with the evidence-based interventions that can help them.[1425]

Using tools from the training, one teacher was able to make new inroads in building trust. "I have a student in class. When she's angry, she will burst out cussing. She will walk out of class." The student was also frequently tardy.

After talking with her, her teacher discovered that her anger stemmed from not being able to live with her mother, who struggled with drug use. The teacher acknowledged the student's anger, but gently impressed upon her that she had to find another way to deal with it, prompting a discussion: "What's your plan when you're angry? Because you can't be cussing like that in the middle of a classroom, in a library, in a courtroom, or anywhere. It doesn't work." The girl came up with a plan that if she was triggered, she would step outside the classroom until she calmed down. Not long after, a classmate said something that angered the student. "She looked at me. I looked at her," the teacher recalled. "She left the classroom and came back a few minutes later when she felt calmed down."

By integrating this trauma-informed approach into all parts of the school and rebuilding many of its practices from the inside out, suspensions dropped more than 50% in 2017. The method transitioned organizational culture from one that stigmatized students and increased stress to one that buffers stress and builds skills for resilience. The model has been implemented by hundreds of organizations and communities across the United States, including public and private schools, health organizations, residential treatment centers, domestic violence shelters, and drug and alcohol treatment centers.

Case Study
Middle School Program in Antioch

Similar to HEARTS (Healthy Environments and Response to Trauma in Schools) and other methods, the program embraces a whole-school primary prevention approach based on the science of ACEs and toxic stress. Part of the staff training, for example, highlighted how ACEs can lead to toxic stress, damaging the structure and function of kids' developing brains, and can cause them to be on high alert for danger, easily triggered into a state of fight, flight, or freeze, and less capable of rational thought in triggered moments.

The Sanctuary Model puts as much emphasis on teacher and staff self-care as on caring for students. Sometimes teachers need to step away. A buddy system allows teachers to ask one another to briefly take over their class, for example. Students and teachers are able to pay attention to what triggers them and pause and reflect. It has been made easier by a rich array of new practices—including mindfulness meditation, a staffed wellness center, individual student check-ins, restorative meetings after tangles between students, or between students and teachers, teacher safety plans, and yoga—that have been embedded in school to help both students and teachers.

The many students who need more than mindful moments can visit the wellness room housed in a modular structure, for up to 10 minutes, which is helpful for secondary and tertiary prevention—regulation of the toxic stress response. The room features a "talk" area and a "chill out" area with comfortable black armchairs, separated by dividers, and an open area for yoga poses. The room is staffed by a wellness counselor and a marriage and family therapy and school-counseling intern, who see students individually and in support groups. There, they can curl up under a weighted blanket or cuddle a weighted stuffed animal, listen to mindfulness music, squeeze stress balls, focus on iridescent water-filled wands, or just sit quietly and take deep breaths. If they need more time with a counselor or psychologist, the counselor can set up a longer appointment.

Administrators collected data on the use of the wellness room and found that 823 students made use of it in a single quarter. The next year, for the same time period, that number decreased to 710 visits. The data are still being analyzed, but educators are convinced that more suspensions would have occurred had those hundreds of visits not taken place. Many

Case Study
Middle School Program in Antioch

students also report using mindfulness at home and teaching the methods to their families, further amplifying primary, secondary, and tertiary prevention of toxic stress for multiple members of student households, especially those at risk of ACEs and toxic stress, and those already living with their consequences.

Case Study

An Elementary School Program in Suisun City

Three years after an elementary school in Suisun City began a trauma-informed training program called Collaborative Learning for Educational Achievement and Resilience (CLEAR), its suspension rate dropped from 18.5 percent to zero.[1426] Data from the California Department of Education's School Dashboard showed additional improvements, like a 5.5-point increase in English language arts testing from the previous academic year.[1427]

The transition began when every staff member—custodians, front office staff, cafeteria workers, teachers, and the principal—began participating in a program that integrated the science of ACEs and toxic stress into their work and lives. This approach describes how childhood adversity can easily trigger a child's brain into fight-flight-or-freeze mode, stimulating the sympathetic nervous system; how recognizing triggers and creating safe spaces for students in the grip of an outburst can minimize interruptions in learning; and how building positive relationships between adults and children impacted by adversity can buffer long-term health, learning, and relational effects and build resilience. Instead of punishing students for outbursts and disruptions, teachers and staff learned to implement trauma-informed practices to spot and intervene with students when they're about to have a meltdown or other difficulty. The training explained to staff why a triggered child was physiologically unable to talk or learn. Teachers learned how to be proactive in preventing and responding to students' triggers. For a student who freaks out every time she gets a paper cut, for example, one could place a stack of Band-aids on her desk. Another example is awareness that if a kid is hungry, they may be more easily triggered, so teachers can keep snacks on hand in their classrooms.

In a corner of one classroom, a first-grader kneels on the carpet in an area known as a regulation station, repurposed from "time out" areas when the school moved to a strengths-focused model, using tenets from Positive Behavioral Interventions and Supports (PBIS), a federally funded program.[1418] Regulation stations are in every classroom and

Case Study
Elementary School Program in Suisun City

feature kinetic sand, puzzles, pencils, paper, books, and Rubik's cubes, all tools that students can use to soothe and calm themselves. Other examples of that shift to PBIS are "welcome" cards instead of "tardy" cards for students to present to their teachers, to remove the sense of shame about being late.

A CLEAR consultant made monthly visits to the school, observed classes, answered questions, and helped reinforce the idea of looking at what drives the behavior of a student who is triggered. The consultant taught staff about self-regulation and co-regulation (how teachers can regulate themselves when they are stressed, and how to model regulation for their students); strategies to help students regulate when they are struggling with big emotions and behaviors; how to have empathy and compassion while holding kids accountable; how to increase safety, predictability and consistency across environments; what self-care is and how to integrate it; and how to understand triggers for children and adults. The consultant also showed staff how to help students restore their relationships with teachers or other students.

Other schoolwide practices were implemented to help keep students on an even keel, like morning meditation for second and third graders, from a mindfulness program known as Inner Explorer.[1428] After the meditation and time for journaling, the students assemble in a circle on the floor for what is called their morning meeting. The teacher leads them through an exercise where each child is prompted to mention someone they admire and why they admire them.

And while all these measures may help the majority of kids as part of primary and secondary prevention strategies, some will need more assistance when they've hit a rough spot in their day, especially those who live with ACEs and other adversities. In other words, they need strategies for the tertiary prevention of toxic stress. That's where a behavioral technician may come in. For a student whose parents are both incarcerated, living with his grandma means living under strict discipline. When the behavioral technician learns that firmness makes the student shut down, he is intentional about using a tone of caring and concern to stimulate the parasympathetic nervous system to prompt calmness and emotional regulation.

Primary, Secondary, and Tertiary Prevention Strategies in Justice

Adverse Childhood Experiences (ACEs) are very common and highly consequential for health and well-being.[3-5] There are deep connections between ACEs and the justice system, given that family member incarceration is one of the ACE criteria that increases risk of developing toxic stress in children, and that many symptoms of the toxic stress response (such as impairment of impulse control or mental health disturbances) significantly increase risk of justice involvement. Thus, the justice system plays an essential role in primary, secondary, and tertiary prevention of ACEs and toxic stress and is a key partner in a public health response.

Recent estimates suggest that **62%** of California adults have experienced at least one ACE, and **16%** have experienced four or more ACEs (2011–2017 data).[27] A key mechanism by which ACEs increase risk for negative health, behavioral, and social outcomes is through biological changes known as the **toxic stress response**, which is defined by the National Academies of Sciences, Engineering, and Medicine (NASEM) 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."[23] In a dose–response fashion, ACEs can lead to serious health risks, including heart disease, stroke, cancer, dementia, mental health and substance use disorders, and premature mortality, including by suicide.[2-5,13,16,28-30,63,64]

While most individuals with significant ACEs do not encounter the criminal justice system, exposure to ACEs is a well-documented risk factor for justice involvement, which may be an important indicator of severe and untreated toxic stress. This increased risk is mediated through a complex interaction of biological and social factors, including biological susceptibility, family and social supports, income, race, education and access to treatment services.

The neurobiological impact of trauma begins before birth and contributes to what is known as the "cradle-to-prison pipeline."[1429] As discussed in **The Biology of Toxic Stress** in Part I, children repeatedly exposed to adversity are at increased risk of developing the toxic stress response, which involves disruption of the neurobiological systems responsible for learning, memory, impulse control, attention, and emotional regulation, and of endocrine, immune, metabolic, and genetic regulatory domains.[6,125,330,1359,1430] Without the protective effect of adequate supportive environments and other interventions, impairments in these areas can lead to poor health and social outcomes.

And as discussed in the **Intergenerational Transmission of Adversity** section in Part I, the toxic stress response not only affects the life course of an individual, but acting through biological pathways, including genetic and genetic regulatory mechanisms, it may influence the health and social outcomes of succeeding generations. For example, a person with dysregulation of the biological stress response may pass on epigenetic markers associated with increased stress reactivity and poorer modulation of the stress response, glucose and lipid metabolism, and the regulation of telomere length (a part of the chromosome whose shorter length is associated with cellular aging), and increased health risks throughout life, including psychiatric and neurodevelopmental disorders.[302,303,351,413,414,433,468,472-481] Of note, animal and human studies suggests that these genetic regulatory markers are malleable from generation to generation in response to environments. And research suggests that an individual born with markers of stress reactivity, but raised in a highly nurturant environment, may be more likely to pass on markers of stress tolerance and self-regulation.[492,41,306,544,545,551]

> The same populations that are disproportionately impacted by ACEs also are more likely to interact with the justice system.

Cumulative adversity is also associated with poorer educational and social outcomes, including learning, developmental, and behavior problems, high school noncompletion, unemployment, low life satisfaction, and poverty—many of which increase risk of incarceration and also serve to transmit adversity to the next generation.[2,16,17,34-38] Many ACE-Associated Health Conditions (AAHCs), including substance dependence, school failure, and mental illness, predispose for exposure to the justice system and higher risk of incarceration.[1431-1433] Undertreated substance dependence, depression, anxiety, and other mental health disorders are not only risk factors for justice involvement, but also represent ACEs for the next generation.[1434,1435] For those who have faced early adversity, because of the dose–response relationship between ACEs, these AAHCs, and the known biological impacts of toxic stress, entry into the justice system can lead to a difficult-to-break cycle of further trauma, impaired judgment and decision-making, and health and relational problems.[6,125,330,1359,1430]

The same populations that are disproportionately impacted by ACEs also are more likely to interact with the justice system.[1436,1437] Social and structural inequities disproportionately concentrate ACEs, toxic stress, their precursors, and their consequences in racially, socially, and economically marginalized communities. Studies have found a higher prevalence of ACEs among groups who are racially marginalized (Black, Latinx, Native American, or multiracial), high school nongraduates, unemployed or unable to work, in lower income brackets, uninsured or underinsured, involved in the justice system, women, and/or identify as lesbian, gay, bisexual, or transgender.[10,13-22,1051] At the same time, there exist significant disparities by race and ethnicity in likelihood of disciplinary action, arrest, and incarceration for youth and adults. Between 1972 and 2000, the annual percentage of White students suspended for more than one day increased from 3.1% to 5.1%. In that same time period, the percentage for Black students increased from 6.0% to 13.2%.[1438] In a 2017 sample of United States (US) adults, Black and Latinx adults were 5.7 and 3.0 times as likely to be incarcerated as White adults, respectively.[1439] In addition, some estimates suggest that as many as 40% of those in the juvenile justice system identify as lesbian, gay, or bisexual, compared to only 12% in the general population.[1440] As such, sociodemographic disparities in exposure to childhood adversity are compounded by disparities in rates of referral to the criminal justice system to give rise to a chicken-egg cycle of trauma and harm in vulnerable communities.

Sociodemographic disparities in exposure to childhood adversity are compounded by disparities in rates of referral to the criminal justice system to give rise to a chicken–egg cycle of trauma and harm in vulnerable communities.

Thus, research reveals a very high prevalence of ACEs among incarcerated populations, demonstrating dose–response relationships between ACEs and juvenile and adulthood arrest, felony charges, and incarceration.[34,35,38] One study found that half of incarcerated youth had experienced four or more ACEs,[1441] while data from the United States and Wales suggest that greater than 90% of incarcerated adults have experienced at least one ACE, and almost 50% have experienced four or more.[1442-1444]

One aspect of toxic stress physiology that is of particular relevance to the justice system is the notion of stress sensitization. Individuals with a dysregulated stress response may be more sensitive to subsequent stressors in terms of risk of manifesting the neuro-endocrine-immune-metabolic consequences of cumulative adversity. Once inside the justice system, those with a history of childhood trauma may have increased risk of AAHCs, which are as much as twice as prevalent among state and federal inmates as in the general population. Rates of hypertension, cardiovascular problems, stroke, diabetes, depression, and post-traumatic stress disorder (PTSD) that are higher among those who are incarcerated.[1445-1452] In addition, behavioral health needs associated with compromised impulse control and emotional dysregulation among those with a history of ACEs may lead greater conflict with other inmates and law enforcement officers.[1453] For this reason, it is important for criminal and juvenile justice systems to have the necessary resources and infrastructure to address the health and mental health needs of those with ACEs, especially in ways that are trauma-informed.[1454]

Individuals exiting the justice system face significant challenges accessing the educational, employment, housing, and financial resources necessary to support well-being and prevent transmission of ACEs to the next generation.[1455-1457] Together, the significant challenges faced by individuals with ACEs within the justice system may place this vulnerable population at greater risk of re-traumatization and recidivism, perpetuating the cycle of trauma and adversity for disadvantaged communities.[1458]

Given these greater impacts among those with histories of ACEs and toxic stress, justice systems have an important role in accounting for or seeking to prevent the effects of ACEs and toxic stress.[1429,1459-1462] Factors that underlie connections between victimization or trauma and later criminal justice involvement provide a window into areas for primary and secondary intervention strategies—reducing exposure to adversity and identifying those individuals with risk factors.

In implementing policies and practices to appropriately address ACEs and associated disparities among justice-involved youth and adults, the justice system has an important opportunity to help break the multigenerational cycle of ACEs and toxic stress. The rest of this section outlines primary, secondary, and tertiary prevention methods for reducing ACE-associated risks within the justice system.

PRIMARY PREVENTION STRATEGIES

As defined in previous sections, *primary prevention* generally refers to efforts to prevent harmful exposures from ever occurring. This concept is particularly relevant in the juvenile justice system, where the opportunity is to prevent cumulative adversity among youth. Encounters with law enforcement and the justice system are intrinsically stressful and potentially traumatic, especially for at-risk populations such as youth who have had ACEs,[1463] and may disrupt supportive relationships, increasing risk of developing a toxic stress response. Though not everyone entering the justice system has had ACEs, given the greater than 90% prevalence of ACEs in youth and adult carceral populations, primary prevention in this context aims to identify individuals who have had ACEs (and are likely manifesting symptoms of toxic stress) and offer evidence-based supportive interventions in order to prevent any exposure to the justice system.

Often cited in criminological research, the "school-to-prison pipeline" largely focuses on "zero-tolerance policies" implemented by school districts to delineate specific punishments for specified violations. Weapons and drugs on campus were the original target of these regulations, but they were later expanded to include behaviors like fighting, bulling, and noncompliance with school personnel.[1464,1465] These policies often lead to academic failure, suspension, and eventual school dropout.[1408,1409,1464,1466] Research has shown, however, that problems at school often start before a student faces these zero-tolerance policies, including having experienced ACEs and other traumas.[1409,1464,1467]

Coordination between healthcare and education to ensure that students are screened for ACEs in the healthcare setting and receive the appropriate supportive interventions helps ensure that toxic stress does not take hold.[1441,1467] Collaboration between the justice system, schools, and local communities can work to reduce risk factors and enhance protective factors, but also empower youth to address the impact that trauma has on communities at large. A study by McNeely and colleagues found that school connectedness—or the feeling of being part of a community or cared for while at school—was linked to lower levels of substance use, violence, suicide attempts, and emotional distress.[1468] Improving school connectedness and resiliency helps to empower youth who have had ACEs and trauma by reducing risk factors and enhancing protective factors.[1409,1441] Youth centers, such as the RYSE Center in Richmond, California, help to create safe spaces for youth to increase social connectedness, and can also improve access to primary care and mental health services.[1469] As important, the RYSE Center has programs that help youth build leadership skills in order to advocate for the services they believe are necessary to thrive.

Empowering youth not only increases their resiliency when addressing their own trauma, but also encourages them to advocate for systemic changes. The Center at Sierra Health Foundation's Positive Youth Justice Initiative, for example, partners with 11 nonprofit organizations to promote youth well-being by treating trauma, providing wraparound services, and promoting systemic changes such as:

- Preventing children from entering adult criminal courts;
- Ending mandatory minimum sentences;

- Increasing the age of "youth offender parole";
- Increasing police accountability;
- Ensuring youth access to counsel; and
- Increasing opportunities for people re-entering the community following interaction with the criminal justice system.

Just as in the education sector, a more trauma-informed justice system requires that the professionals interacting with youth and adults receive training on how ACEs and toxic stress impact health and behavior. Virginia's recently passed HB 744 exemplifies systems-level change by requiring "the court, when sentencing a juvenile as an adult, to consider the juvenile's exposure to adverse childhood experiences, early childhood trauma, or any child welfare agency and the differences between juvenile and adult offenders."[1470] This policy helps judges to make trauma-informed sentencing decisions and allows them to consider childhood adversity as a mitigating factor when sentencing a child as an adult. This policy change can be adopted and expanded to incorporate considerations about ACEs and toxic stress into all sentencing decisions, allowing juveniles and adults to receive restorative care and prevent further trauma from incarceration. Training in trauma-informed justice practices requires ongoing education on the effects of trauma on development and behavior, de-escalation techniques, and restorative justice strategies.

Fostering the health and well-being of staff who are charged with the care of those involved in the justice system is a critical component of trauma-informed justice practices, as many workers have had their own ACEs and also have high levels of stress in their jobs. This is especially true among justice-sector employees like police officers, social workers, and probation officers, who experience trauma, vicarious trauma, and burnout at very high rates. One in nine report suicidal ideation (compared to one in 33 in the general population), and 27% of correctional officers have PTSD symptoms (compared to 6% of the general population).[1471-1478] Providing staff with sufficient training before and after potentially traumatic experiences can mitigate negative impacts on their health and well-being and reduce empathy fatigue; see programs such as Desert Waters.[1479] Training on trauma-informed approaches for everyone working in the justice system—from first responders and court employees to peace officers and probation officers—may mitigate stress, trauma, and re-traumatization. The Gather, Assess, Integrate, Network, and Stimulate (GAINS) Center of the Substance Abuse and Mental Health Services Administration (SAMHSA) provides resources for education and specific training of criminal justice professionals.[1480]

SECONDARY PREVENTION STRATEGIES

For individuals with a history of ACEs and symptoms of toxic stress who end up being justice-involved, secondary prevention aims to minimize additional stress-response dysregulation and to prevent further involvement with the justice system.[1481] Minimizing encounters with the justice system and ensuring the least restrictive environment promotes the most positive outcomes for both youth and adult offenders.[1482]

Alternatives to traditional justice proceedings and incarceration are commonly available for individuals who commit non-violent offenses. One alternative to traditional criminal court proceedings is restorative justice, which is defined as an approach to justice that emphasizes repairing the harms caused by a crime, and often involves victim–offender mediation. Restorative justice programs aim to prevent additional traumas and maintain community supports and buffering, and have shown effectiveness in reducing recidivism.[1440,1483] A meta-analysis on the effects of restorative justice programs found that victim–offender mediation reduced juvenile recidivism by 34%.[1484]

Neighborhood Courts, which utilize a restorative justice approach to case resolution, involve the District Attorney's Office referring misdemeanor cases to settings in which residents and volunteers are trained in restorative justice and problem-solving. Volunteers hear from both the offender and the victim to discuss the case and its impact on the community. Directives such as community service or restitution are used to resolve each individual case. By participating in a Neighborhood Court, the individual not only bypasses traditional criminal court proceedings, but also avoids further trauma and exposure to the justice system, such as incarceration. Participants who completed the program between 2013 and 2015 had, on average, only an 8% recidivism rate.[1485]

Because of the eligibility requirements, not all individuals can take part in alternatives like Neighborhood Courts. California has taken steps to expand on alternatives to incarceration by finding alternatives to pretrial detention, increasing pretrial diversions, increasing use of alternative sentencing options such as home monitoring, and expanding early release of low-risk offenders. Alternatives to traditional criminal court proceedings, such as drug courts and mental health courts, focus on connecting individuals to needed services rather than incarceration. Mental health courts, for example, are a collaborative, treatment-focused alternative to traditional courts that refer participants to rehabilitative services and support networks rather than prison. In one study of a San Francisco "mental health court" program, the intervention led to a 26% reduction in new charges and a 55% reduction in new violent charges among participants over 18 months, compared to a control group.[1486]

Pretrial diversion programs offer valuable avenues to avoid the additional traumas associated with incarceration. In 2005, San Francisco launched the Back on Track program, which allowed which allowed pretrial low-level offenders to be referred by charging attorneys. During the 12-to-18-month program, individuals received job training, mental health services, parenting support, intensive case management, and educational opportunities, among other services. The program had a less than 10% reoffending rate over two years, compared to a rate of 53% among those who did not take part in the program.[1487]

These alternatives help prevent the further accumulation of adversity that may result from further exposures to the justice system, removal of youth and adults from their communities, and disconnection from support systems.[1441,1488-1491] It is estimated that there are 48,000 individuals, or two-third of California's jail population, awaiting sentence. This number includes individuals that are eligible for cash bail, but cannot afford it.[1492] In California, Senate Bill 10[1493] made changes to pretrial release by shifting the pretrial release of an individual from a monetary-based system to a system that is based on risk—essentially eliminating cash bail or bail bonds.

In California, all local juvenile detention facilities are required to include trauma-informed approaches as part of their policies and procedures.

For individuals who are placed in and remain in custody, implementation of systemic trauma-informed justice practices can further reduce trauma and mitigate toxic stress symptomatology. Multiple groups, including the US Department of Justice, SAMHSA, the National Association of State Mental Health Program Directors, and others, have recommended changes to make the justice system more trauma-informed.[1494-1500] Trauma-informed practice in the justice sector relies on the integration of a deep understanding of the consequences of trauma and toxic stress into all interventions, services, and organizational structure and functioning. Extending these principles to all sectors of the justice system may reduce individuals' overall dose of adversity and trauma and promote better outcomes by maintaining support systems, decreasing stress, and providing evidence-based treatment interventions.[1501]

In California, all local juvenile detention facilities are required to include trauma-informed approaches as part of their policies and procedures (Cal. Code Regs., tit. 15, §§ 1302, 1322, 1324, 1329, 1350, 1354, 1358.5, 1370, & 1391). In addition, any person hired into an entry-level corrections position must complete a core course of training, prescribed by the Board of State and Community Corrections (Cal. Code Regs., tit. 15, §§ 169-185). As part of this core training, juvenile corrections officers receive 24 hours, and adult corrections officers 21 hours, of training in behavioral health, which includes topics such as: foundation and definitions of behavioral health, signs and symptoms of substance abuse, trauma, and suicide prevention. Corrections officers are trained in identifying the specific behaviors associated with behavioral health issues, as well as recognizing how the behaviors and actions of officers may inflict trauma on individuals in custody. Ways in which these practices had been adapted for the coronavirus disease 2019 (COVID-19) pandemic are presented below (**TRAUMA-INFORMED JUSTICE PRACTICES IN THE TIME OF COVID-19**).

TRAUMA-INFORMED JUSTICE PRACTICES IN THE TIME OF COVID-19

The coronavirus disease 2019 (COVID-19) outbreak has put a strain on the justice system and required rapid adaptation to maintain people's health and well-being. During this time, trauma-informed justice practices are more difficult to provide but more important than ever. Nationwide, COVID-19 infection rates are higher in prisons than in the general population; 86% of correctional and detention facility jurisdictions nationally reported at least one COVID-19 case.[1503] Furthermore, the age-adjusted death rate from COVID-19 among prisoners is three times higher than in the general US population.[1504] The difficulty of maintaining health in congregate facilities during this time increases stress and prevents many forms of in-person buffering supports (like family visitation) and treatment. This may trigger or worsen toxic stress.

Rapid adaptation is necessary to ensure that people involved in the justice system receive sufficient care and support during this pandemic. These adaptations include increasing access to technology that facilitates digital contact with family and healthcare providers. Parole, probation, home visitation, drug testing, and other systems have been adjusted to maintain safe, stable, and secure monitoring. The Division of Juvenile Justice has implemented virtual visitation at all of its sites to maintain contact between youth and their support systems. The Division has also converted youth discharge consideration hearings to videoconference and works with counties to arrange videoconferencing for local reentry hearings when requested. Between March and June 2020, the California Department of Corrections and Rehabilitation reduced the prison population by almost 10,000, mainly by early release of inmates who met certain criteria (including serving time for a nonviolent crime, not being a registered sex offender, and not being categorized as at high risk for violence).

A program in Manchester, NH, known as the Adverse Childhood Experience Response Team (ACERT) exemplifies the impact of trauma-informed training and evidence-based interventions by first responders in preventing further adversity and/or toxic stress.[1502] When children are seen to witness violence in the form of ACEs or other traumatic exposures, such as at the scene of an intimate partner violence episode or a drug overdose to which law enforcement is called, a trained multidisciplinary team consisting of a family advocate, a crisis advocate, and a plain-clothes detective perform a home visit immediately after the incident and provide education on ACEs and linkages to necessary health and support services. In the first three and a half years, 1,454 children, ages 0-17 years, from 994 families were contacted by the program, and 1,048 total referrals were made.[1502]

TERTIARY PREVENTION STRATEGIES

Tertiary prevention in the justice system aims to lessen the effects of toxic stress in people under the care of the justice system who are showing signs and symptoms consistent with toxic stress, and to ensure continuing supports following release. Improving the quality of life for justice-involved individuals and those re-entering society is the focus.[1505-1507] This includes properly assessing not only their health and mental health needs prior to release, but also other considerations, such as family reunification, housing, and employment. Providing proper preventive and treatment-oriented physical and mental healthcare while an individual is justice-involved or incarcerated results in lower rates of delinquency and recidivism, higher employment, better social functioning, and other positive outcomes.[1415,1508-1514]

Assessing unmet mental health and physical health needs in addition to past adversity is vital to preparing an individual for their release back into the community. Screening for ACEs and other adversities may aid in identifying and intervening on toxic stress for justice-involved individuals, especially youth. Currently, the California Department of Juvenile Justice uses the Trauma Symptom Inventory and the ACE inventory to assess for exposure to trauma, track treatment progress, and inform clinical decision-making.[21] The American Bar Association and the California Department of Justice have also released guidance on identifying trauma and victimization in justice-involved youth, as well as recommendations for addressing the needs of children exposed to violence.[1501,1515,1516]

Screenings and assessments help link justice-involved individuals with programs that address their unmet needs. Programs that are comprehensive and consider the medical, educational, vocational, and psychosocial needs of individuals and their families upon release encourage rehabilitation and recovery.[1441] Interventions such as multisystemic therapy, cognitive-behavioral therapy, and family-based therapies, such as functional family therapy, have succeeded in improving mental and behavioral health in justice-involved individuals and also in reducing rates of recidivism.[1441,1517-1520]

Family connection and reunification upon release is vital for the maintenance of physical and mental health while incarcerated, and has been shown to improve successful reintegration and reduce recidivism among both youth and adults.[1508,1521-1525] Social support is associated with lower blood pressure and a decreased risk for cardiovascular disease,[764] decreased asthma symptoms, and improved immune responses, including inhibiting inflammation, providing protection against infection, and promoting wound healing.[668-672] Healthcare providers caring for formerly or currently incarcerated individuals should be skilled at assessing for signs and symptoms of toxic stress, and should be familiar with evidence-based interventions, including leveraging optimal sleep, healthy relationships, nutrition, exercise, access to nature, mindfulness practices, and when needed, mental and behavioral healthcare (see **Tertiary Prevention Strategies in Healthcare**, earlier in Part II). Additionally, cross-system collaboration between the justice system, the health system, the child welfare and other social service systems, the educational system, and community resources is key for maintaining youths' physical and mental health during and after release from custody.[1498]

Programs that facilitate re-entry can improve reintegration, decrease recidivism, and increase future employment by providing care, expanding community partnerships, and bringing in positive role models with lived experiences to mentor at-risk youths. Programs may also take place in custody and aim to prepare incarcerated individuals for a successful re-entry into the community. These programs support restorative justice principles, healing from trauma, educational opportunities, vocational opportunities, and transition programming. Recently, as part of its Innovative Programming Grants, the California Department of Corrections and Rehabilitation's Division of Rehabilitative Programs selected nonprofit recipients of the California Reentry and Enrichment grant awards.[1526] These nonprofit organizations provide restorative justice programs that seek to address resiliency, reducing the impacts of toxic stress and trauma, and increase empathy and mindfulness, among other positive outcomes. Project Rebound, administered through San Francisco State University, is a program that supports incarcerated individuals in furthering their education. The project provides enrollment guidance, educational and logistical support, financial support, and career guidance following graduation. The Division of Rehabilitative Programs also offers In Prison Programs, including Career Technical Education, which aims to train and certify incarcerated individuals in six different career sectors, including building trade, construction, and energy and utilities.

Once returning individuals are in the community, re-entry programs aim to help them in their transition back into society by providing comprehensive care that addresses past trauma and aim to support successful reintegration.[1441] One such organization is Homeboy Industries (see **HOMEBOY INDUSTRIES**), which offers formerly incarcerated individuals multiple services and care, including education and workforce training, mental health resources, and housing and food assistance. Similar to referral networks in clinical settings, individuals should be provided access to services and community resources. Data systems that function across sectors are necessary to track referrals and services, facilitate follow-up to ensure that each individual receives the necessary care, and assess outcomes. The California Department of Rehabilitation facilitates several such programs. Likewise, the San Francisco Department of Public health has begun to pilot the Shared Youth Database Initiative to construct a shared data early warning system for at-risk youth.

In sum, these strategies represent an important step towards dismantling the long-standing links between childhood adversity, toxic stress, related health outcomes, and involvement in the justice system. Prevention of these associations, and especially of their intergenerational transmission is the ultimate goal—with a particular focus on healing the families, neighborhoods, and communities who face disproportionate impacts from all of these outcomes.

HOMEBOY INDUSTRIES

Established in 1988 in East Los Angeles, Homeboy Industries[1527] was originally created to improve the lives of former gang members. It has since expanded beyond gang intervention to help formerly incarcerated individuals heal and successfully re-enter society. Homeboy Industries connects men and women with a wide variety of services, including trauma-informed mental health services, workforce development, educational services, case management, tattoo removal, and parenting classes, among many others. At the center is a focus on five key outcomes: reducing recidivism, reducing substance abuse, improving social connectedness, improving housing safety and stability, and reunifying families. Their advocacy and work in the community has been nationally recognized.

PART III

California's Response to Adverse Childhood Experiences and Toxic Stress

Roadmap for Resilience:
The California Surgeon General's Report on
Adverse Childhood Experiences, Toxic Stress, and Health

State Tools and Strategies for Responding to ACEs and Toxic Stress

Many states now collect data on the prevalence of Adverse Childhood Experiences (ACEs) as part of the Behavioral Risk Factor Surveillance System overseen by the United States (US) Centers for Disease Control and Prevention (CDC). In 2018, the National Conference on State Legislatures issued a report, ***Preventing and Mitigating Adverse Childhood Experiences***, detailing strategies that lawmakers may utilize to reduce ACEs and toxic stress.[1223] The report highlighted that between January and May of 2018, at least 68 legislative proposals in 25 states incorporated ACEs. State-specific policy responses targeting ACEs can be found in the Injury Prevention Legislation Database of the National Conference of State Legislatures,[1528] and on the ACEs Connection website under "Map the Movement."[1529]

A key aspect of California's strategy for reducing ACEs and toxic stress by half in a generation is recognition of the toxic stress response as a health condition that is amenable to treatment. While not every individual who has experienced ACEs and other risk factors for toxic stress will develop a toxic stress response, improvements in our ability to characterize and, ultimately, confirmatively diagnose and treat toxic stress have enormous potential to improve health and quality of life, as well as to enhance the effectiveness of programs to support individuals and families living with the legacies of intergenerational adversity and trauma. This rigorous scientific framework also provides a strong foundation for policy action to support a cross-sector, systems-level approach.

This rigorous scientific framework also provides a strong foundation for policy action to support a cross-sector, systems-level approach.

California has both learned from the successful efforts of other states and been a pioneer in assembling a suite of policy tools for combating ACEs and toxic stress. Central to coordinating and aligning efforts for primary, secondary and tertiary prevention of ACEs and toxic stress is training and capacity-building for the healthcare sector to enable early detection, evidence-based interventions and engagement of a network of clinical and community resources to support healing. Key tools and strategies that California has successfully implemented are described below.

TOOLS

Executive Order creating the Office of the California Surgeon General

On January 7, 2019, Governor Gavin Newsom issued Executive Order N-02-19,[1530] creating the Office of the California Surgeon General (CA-OSG). The office was established to advise the Governor, address Californians on matters of public health, and marshal the insights and energy of medical professionals, scientists, public servants, and everyday Californians to find solutions to our most pressing public health challenges. In creating the role of state Surgeon General, Governor Newsom charged and empowered the Surgeon General specifically to tackle "the upstream factors that eventually become chronic and acute conditions that are far more difficult and expensive to treat."[1530] In doing so, the Governor explicitly highlighted the consensus of scientific evidence pointing to toxic stress as a root cause of many of the most harmful and persistent health challenges facing Californians.

The Governor appointed Nadine Burke Harris, MD, MPH, a pediatrician and expert in the science of ACEs and toxic stress, as California's first Surgeon General, and together, they established early childhood, health equity, and ACEs and toxic stress as key priorities for her tenure. Dr. Burke Harris set the bold goal of cutting ACEs and toxic stress in California in half in one generation, and the blueprint presented in these pages lays out the coordinated, statewide approach that will achieve that vision.

Dr. Burke Harris's strategies are guided by evidence disseminated by our nation's leading scientific bodies, including the National Academies of Sciences, Engineering and Medicine (NASEM) and the CDC. The 2019 NASEM consensus report, *Vibrant and Healthy Kids: Aligning Science, Practice and Policy to Advance Health Equity*, highlighted several key recommendations for preventing and mitigating the effects of toxic stress and advancing health equity, including:[23]

> "**Recommendation 8-2:** Adopt and implement screening for trauma and adversities early in life to increase the likelihood of early detection. This should include creating rapid response and referral systems that can quickly bring protective resources to bear when early-life adversities are detected, through the coordination of cross-sector expertise.
>
> **Recommendation 8-3:** Adopt best practices and implement training for trauma-informed care and

> service delivery. Sector leadership should implement trauma-informed systems that are structured to minimize implicit bias and stigma and prevent retraumatization. Standards for trauma-informed practice exist in a variety of service sectors, including health care and social services; those standards should be replicated and implemented across systems."

Statutory framework supporting screening and provider training

Assembly Bill 340 (Arambula, Chapter 700, Statutes of 2017) established a Trauma Screening Advisory Group to provide recommendations on specific trauma screening tools which could be utilized by Medi-Cal (California's Medicaid program, see **Appendix B**).[1531] The group, composed of staff from the legislature and state departments, as well as experts and stakeholders from pediatrics, mental health, managed care plans, behavioral health, and child welfare, submitted its recommendations in January 2019. It recommended that Medi-Cal providers screen for ACEs, given the extensive evidence for ACEs influencing health over the life course (see **Establishing Causality between ACEs and Poor Health Outcomes**, in Part I, for details). In March 2019, The California Department of Health Care Services (DHCS) selected the Pediatric ACEs and Related Life-Events Screener (PEARLS) tool for children and the ACE Assessment for adults.[738]

KEY OBJECTIVES OF THE ACEs AWARE INITIATIVE

1. To inform and empower primary care clinicians with the latest evidence on how to recognize, address, and prevent ACEs and toxic stress.
2. To incentivize early detection and early intervention for toxic stress by reimbursing providers for screening for ACEs, which includes 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.
3. To increase awareness and utilization of cross-sectoral, evidence-based and promising clinical and community interventions for preventing and addressing the toxic stress response.
4. To build clinical capacity for screening for—and clinical and cross-sector community capacity for response—to ACEs and toxic stress by investing in clinical quality improvement and community networks for response.
5. To improve clinical outcomes and health equity by enhancing the quality and specificity of healthcare provided to individuals exposed to ACEs and/or at risk for toxic stress, through rigorous, evidence-informed methods.

Figure 26. The spectrum of implementation strategies needed to achieve prevention, practice transformation, and research and innovation in addressing toxic stress. Reproduced with permission from the Center for Youth Wellness.[1532]

Conceptual framework establishing the ACEs Aware initiative

Governor Newsom, in partnership with the California legislature, allocated approximately $143.1 million over two fiscal years (2019–20 and 2020–21) to support routine ACE screening in primary care through Medi-Cal. Of this amount, approximately $64.7 million was allocated to reimburse providers for performing ACE screening of children and adults (up to age 65) in Medi-Cal. Beginning January 1, 2020, eligible Medi-Cal providers could receive a supplemental payment of $29 for each eligible screening. Approximately $78.4 million was allocated to train Medi-Cal providers on how to screen for ACEs in order to assess for risk of toxic stress, and respond with trauma-informed care and evidence-based interventions for toxic stress.

This budget investment effectively created the ACEs Aware initiative, an evidence-guided approach to screening and response in Medi-Cal. This novel clinical and public health effort is jointly administered by CA-OSG and DHCS. The initiative utilizes training and key partnerships to build clinical and cross-sector capacity to identify and respond to ACEs and toxic stress. It aims to empower Medi-Cal primary care providers, leading to practice change, and ultimately, to improve health outcomes by advancing the quality and efficiency of care provided to individuals exposed to ACEs or at risk for toxic stress (**Figure 26**). Beginning in December 2019, the ACEs Aware Initiative offered providers a free, two-hour online training on how to integrate these steps into clinical care. Providers are able to receive free Continuing Medical Education (CME) and Maintenance of Certification (MOC) credits for this training. (For more information, please see the next section, **The ACEs Aware Initiative**.)

Framework for a cross-sector budgetary approach

Central to a national, statewide, or regional approach to reducing ACEs and toxic stress is the integration and coordination of efforts for primary, secondary, and tertiary prevention. The conceptual framework from the *Vibrant and Healthy Kids* consensus report (**Figure 27**) indicates the systems and elements that "set the odds" of adverse or enhanced health and developmental trajectories for individuals and families. A public health approach to preventing and responding to ACEs and toxic stress involves intervention at all levels of prevention and the implementation of several key principles, including:[23]

- Intervene early;
- Support caregivers;
- Reform healthcare systems to promote healthy development while ensuring access, quality, and coordination;
- Create stable and supportive early living conditions;

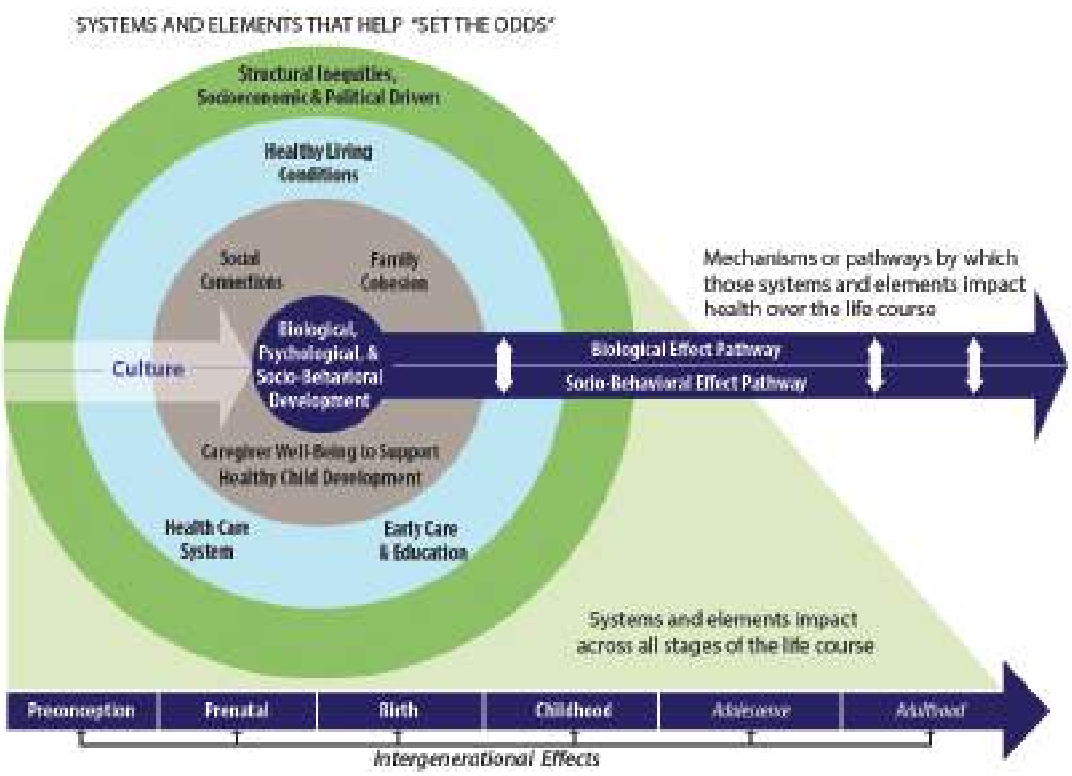


Figure 27. Multi-layered structural and contextual factors that influence life course health. Reproduced with permission from the National Academies of Sciences, Engineering, and Medicine (NASEM, 2019), courtesy of the National Academies Press, Washington, D.C.[23]

- Reduce child poverty, food insecurity, and economic insecurity;
- Provide safe and stable housing;
- Eliminate exposure to environmental toxicants;
- Maximize the potential of early care and education to promote healthy outcomes;
- Implement cross-system, trauma-informed initiatives to support children, caregivers, and communities and build a diverse and supported workforce;
- Support cross-sector collaboration and alignment; and
- Integrate and coordinate aligned cross-sector efforts, such as in education, social services, early childhood, justice, public health, and healthcare.

Additionally, the CDC's 2019 report, *Preventing ACEs: Leveraging the Best Available Evidence*, notes the importance of a cross-sector approach to implement the evidence-based strategies for preventing ACEs from occurring and mitigating subsequent harm (**Table 9**).[31]

Preventing ACEs

Strategy	Approach
Strengthen economic supports to families	• Strengthening household financial security • Family-friendly work policies
Promote social norms that protect against violence and adversity	• Public education campaigns • Legislative approaches to reduce corporal punishment • Bystander approaches • Men and boys as allies in prevention
Ensure a strong start for children	• Early childhood home visitation • High-quality child care • Preschool enrichment with family engagement
Teach skills	• Social-emotional learning • Safe dating and healthy relationship skill programs • Parenting skills and family relationship approaches
Connect youth to caring adults and activities	• Mentoring programs • After-school programs
Intervene to lessen immediate and long-term harms	• Enhanced primary care • Victim-centered services • Treatment to lessen the harms of ACEs • Treatment to prevent problem behavior and future involvement in violence • Family-centered treatment for substance use disorders

Table 9. *Strategies and approaches to preventing ACEs. Reproduced under public domain from the CDC.*[31]

Specific budgetary investments in allied cross–sector work

California has made several key budget investments in cross-sector work that have strengthened supports for children and families, helped them become more resilient, and prevented the incidence and intergenerational transmission of ACEs and toxic stress. These budgetary investments align with several of the NASEM and CDC principles mentioned.[23,31]

Strengthening economic supports for families

California has strengthened economic supports for children and families through significant state investments and through leveraging federal programs. California increased the Maximum Aid Payment available through the CalWORKs program, a public assistance program that provides cash aid for housing, food, utilities, clothing, or medical services to eligible families with children, including families with caregiver absence, death, or disability.[1131] The CalWORKS Child Care Program also provides childcare subsidies to help families transition from immediate, short-term child care needs to stable, long-term child care.[1262] Federally funded food assistance programs such as the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC), and CalFRESH (California's Supplemental Nutrition Assistance Program), provide valuable educational and supportive services as well as direct assistance purchasing food. The federal and state Earned Income Tax Credits and the federal Child Tax Credit provide critical economic assistance to families with children. California has also continued to expand the reach of its Paid Family Leave Program, which provides economic support to eligible working families through partial wage replacement benefits.

Supporting parents and children

Home visiting programs offer parents a wide variety of support and services during pregnancy and early childhood. Over the last several years, California has further strengthened these programs by expanding their funding in the 2019 and 2020 Budget Acts, by expanding eligibility beyond first-time parents, and by implementing a wider range of home visiting models.[1131,1132] California has also expanded the Black Infant Health Program, which provides case-management services to improve Black infant and maternal health (see the section on **Primary, Secondary**, and **Tertiary Prevention Strategies in Early Childhood**, in Part II, for more details).[1131]

Investments in early learning and care

One way California is strengthening early care and education is by creating the Master Plan for Early Learning and Care and convening the Early Childhood Policy Council. The Master Plan is a long-term strategic plan to provide a series of reports to inform the advancement of comprehensive, high-quality, and affordable child care and preschool for children from birth through age 12 years, with a particular focus on universal preschool, the workforce, quality, and facilities.[1131] The Early Childhood Policy Council is an advisory body that includes providers, parents, and state administrative agencies, to provide recommendations to the legislature and the administration on state early learning and care policy.[1131] The council is chaired by Surgeon General Burke Harris, who is well positioned to ensure that the plan will serve as a critical component of the cross-sector approach to addressing ACEs and toxic stress.

Expansions in healthcare coverage

In addition to embracing the healthcare coverage under the Affordable Care Act, California has further expanded Medi-Cal by expanding the duration of coverage for eligible pregnant women diagnosed with a maternal mental health condition and expanding full-scope Medi-Cal coverage to undocumented young adults age 19 through 25.[1131,1132]

Research and biomedical advances

Mitigating the harm from existing ACEs and toxic stress is a critical component of treating ACE-Associated Health Conditions and breaking the intergenerational cycle of adversity (see The ACEs Aware Initiative for more details). In 2020, the California Initiative to Advance Precision Medicine issued an request for proposals to provide $9 million in grants to support precision medicine approaches to advance the assessment and treatment of ACEs and toxic stress.[337]

Integration of cross–sector efforts

In addition to the above investments, Part II of this report outlines how the healthcare, public health, social services, early childhood, education, and justice sectors can all contribute to each level of public health prevention, as well as how each of these sectors can advance equity in outcomes. However, in order for these efforts to sum to a whole that is greater than its parts, coordination and alignment are required. Cross-sector coordination requires shared language, shared metrics, role clarity, and clear lines of accountability.

> **Cross–sector coordination requires shared language, shared metrics, role clarity, and clear lines of accountability.**

California's investments in the ACEs Aware initiative serve to apply the advancing science of ACEs and toxic stress to leverage the current multi-billion dollar statewide investments in primary, secondary, and tertiary prevention for greater precision and effectiveness. Training for primary care providers to screen and intervene on ACEs and toxic stress provides a necessary foundation to undergird an infrastructure for effective cross-sector coordination, enabling several critical milestones.

- Training primary care providers enables early detection of toxic stress, at a time when interventions are less intensive, less expensive, and more likely to be effective. This allows providers to diagnose and treat patients based on an evidence-based assessment of risk—rather than waiting for patients to manifest the health, mental health, and behavioral consequences of toxic stress, when they are more difficult and more expensive to treat. This early intervention also helps prevent the intergenerational transmission of toxic stress.
- Additionally, increasing the familiarity of clinicians and researchers with ACEs and toxic stress can serve to enlist greater numbers of scientific professionals to develop more effective science-based treatments and interventions for toxic stress and to rigorously evaluate their efficacy, thereby directly advancing the science and clinical management of ACEs and toxic stress.
- Training of healthcare providers is also a critical complement to public education efforts, ensuring that when people learn about ACEs, they can access a provider trained to recognize and respond to the sequelae of ACEs and toxic stress.
- Engaging the healthcare workforce includes deploying practices, tools, and technologies to enable cross-sector coordination through referrals and other interventions.
- Appropriately recognizing toxic stress as a health condition allows all sectors to understand and frame its consequences through that lens. This allows for the adoption of aligned legal, policy, and regulatory frameworks in response. (See PETER P. VERSUS COMPTON UNIFIED SCHOOL DISTRICT.)

STRATEGIES

Engaging cross-sectoral leadership inside and outside of state government

Engaging with leaders both within and outside state government is a critical component of California's broader approach to ACEs. Surgeon General Burke Harris convened an ACEs Reduction Leadership Team with directors of key departments in the Health and Human Services Agency, the California Department of Corrections and Rehabilitation, the California Department of Education, and the Governor's Office, among others. The team's meetings provided a venue to educate departmental leadership on impacts of ACEs and coordinate existing and new departmental efforts that could reduce or address ACEs and toxic stress.

Dr. Burke Harris also convened the Trauma-Informed Primary Care Implementation Advisory Committee (TIPC), which is composed of representatives of major healthcare plans, health systems, philanthropic associations, nonprofits, local government associations, professional provider associations, and subject matter experts. The TIPC advises on promising models, best practices, evolving science, clinical expertise, and strategies for the implementation of trauma-informed care systems in California. In addition to the full committee, several key subcommittees were created to provide specific guidance on training, clinical implementation, networks of care, and provider engagement efforts.

Assessment and expansion of best practices in trauma-informed, toxic stress-responsive work across sectors

The CA-OSG, the California Department of Public Health, the Strategic Growth Council, and DHCS have implemented two coordinated environmental scans to assess the status of current State and County efforts to prevent and address ACEs and toxic stress across all sectors, and to identify opportunities for future expansion and collaborations. (See **Approach to Environmental Scans of Statewide Trauma-Informed Work**, later in Part III, for more details.)

Trauma-informed, toxic-stress-responsive training enables all front-line providers, such as educators and law enforcement officers, to recognize the symptoms

PETER P. VERSUS COMPTON UNIFIED SCHOOL DISTRICT

Peter P. was a 17-year-old student at Dominguez High School in the Compton Unified School District. According to court filings,[1533] in the early years of Peter's life, his biological mother abused drugs, and he was repeatedly physically and sexually abused by his mother's boyfriends. He also witnessed the physical abuse of his siblings and mother. He reported having flashbacks and often experienced an instinct to be aggressive when approached by a male. When Peter was roughly five years old, he and his siblings were removed from the home of their biological mother and entered the foster care system. Peter was initially separated from most of his siblings and moved in and out of a series of foster homes. Peter was occasionally sent back to live with his biological mother for several weeks before being removed from her home again. When Peter was roughly 10 years old, the rights of his biological mother were terminated, and he and several of his

PETER P. VERSUS COMPTON UNIFIED SCHOOL DISTRICT

siblings were adopted. When he was 16, Peter's adoptive mother's health worsened, and he became a caretaker for her and his younger siblings. Peter reported that in middle school, he witnessed his best friend be shot and killed. In 2014, he received stab wounds and required stitches after throwing himself in front of a friend whose relative was attacking her with a knife. Peter reported that he had witnessed more than 20 people get shot. Peter's two older brothers were incarcerated. The man who was living with Peter's mother and serving as a caretaker for him and his siblings when they entered the foster system was also incarcerated for murder. Peter was homeless for two months in March and April 2015. During that period, he slept on the roof of the Dominguez High School cafeteria. According to the court filing, he was never offered support or services. Instead, he was suspended. Although some school personnel were aware of his circumstances, Peter's attempts to return to school were denied, and he was threatened with law enforcement involvement if he persisted in attempting to return.

Peter is one of three student plaintiffs and three teachers represented by Public Counsel, a pro bono law firm, in a lawsuit against Compton Unified School District in Los Angeles, California, filed on May 18, 2015. The lawsuit alleged that the repeated traumatic events experienced by the plaintiffs and other class members had resulted in health conditions that fit the Americans with Disabilities Act's definition of "individuals with disabilities." Therefore, the plaintiffs argued, the school district was required to provide meaningful access to services, programs, and other benefits to enable to the students to learn. The central point in the case rested on the scientific research connecting significant childhood adversity to increased risk for negative health outcomes. The plaintiffs sought to compel the district to employ trauma-informed practices that are research-backed, and proven to help educators support traumatized children and better enable them to learn. On September 29, 2015, the court denied the defendants' motion to dismiss the case, acknowledging that the "allegations that exposure to traumatic events might cause physical or mental impairments that could be cognizable as disabilities under the two Acts" (the Americans with Disabilities Act and the Rehabilitation Act).[1533] Subsequently, the plaintiff's lawyers and Compton Unified School District officials have met to discuss settling the lawsuit. The lawsuit has been on hold since 2016. But since then, the district has reportedly worked with the plaintiffs' lawyers to address trauma in schools. According to news reports, teachers now get training on trauma-informed practices, and the district has agreed to set up wellness centers in secondary schools to provide mental and physical healthcare to students.

> **Progress towards incorporating trauma–informed training has been made in various sectors in California state government.**

of a dysregulated stress response due to toxic stress so that they can respond with trauma-informed, evidence-based principles, rather than escalate the encounter, for instance, through harsh punitive measures. Such training also benefits the front-line providers themselves, by enabling them to recognize signs of their own stress responses being activated and to regulate those responses through practicing evidence-based interventions. Progress towards incorporating trauma-informed training has been made in various sectors in California state government, including the Department of Social Services, the Department of Public Health, the Department of Education, and the Commission on Peace Officer Standards and Training. However, these trainings may not use standardized language, definitions, or guidelines. CA-OSG continues to look for opportunities to engage leading experts to incorporate the latest evidence, enabling further coordination and standardization of training, as well as expansion of existing efforts.

Increasing public awareness

Increasing public awareness and understanding of ACEs and toxic stress is a critical means to provide all sectors and the general public shared language, validate individuals' experiences, and promote resilience-building or toxic stress buffering interventions. Past public education campaigns have been effective at reducing the prevalence of health conditions and risk factors, including smoking, lead poisoning, and motor vehicle deaths (see **Primary, Secondary, and Tertiary Prevention Strategies in Public Health**, in Part II, for details). Public health campaigns are most effective when partnered with public policy efforts such as those limiting indoor use of tobacco products, restricting use of lead in industrial products, or requiring seat belt use. The World Health Organization outlines six major principles for effective communications: they should be accessible, actionable, credible, relevant, timely, and understandable.[1534] Under this framework, knowledge of the audience, incorporation of feedback from that audience, and tailoring the message appropriately, are critical. A public education campaign on ACEs and toxic stress should:

1. Explain what ACEs and toxic stress are, how common they are, and how they impact health and well-being;
2. Highlight the structural and systemic conditions that can make ACEs and toxic stress more or less likely to occur; and
3. Offer strong messages of hope, including practical strategies for buffering

factors and scaffolding protective factors that can improve outcomes for a child or adult at risk for or experiencing toxic stress, to prevent further harm, and how to break the intergenerational cycle of adversity.

Paid media and earned media, including social media, and engaging champions, trusted messengers, and spokespersons to raise the awareness of ACEs and toxic stress and how to heal from them are all strategies that can be deployed.

The ACEs Aware Initiative

ACEs AWARE PHASE I: TRAINING PROVIDERS

In January 2020, the Office of the California Surgeon General (CA-OSG) and the California Department of Health Care Services (DHCS) launched the ACEs Aware initiative as a key lever in achieving the California Surgeon General's bold vision to cut Adverse Childhood Experiences (ACEs) and toxic stress in half in one generation.

ACEs Aware Phase I aims to train providers on screening for ACEs and on recognizing and responding to toxic stress. This is an important mechanism for reducing the population-level burden of ACEs and toxic stress for several reasons.

1. **ACEs are common, so a routine, population-based approach is needed.** Among Californians on Medi-Cal, 69% report one ACE, and 23% report four or more ACEs.[27] Given the significant prevalence, health consequences, and costs of ACEs and toxic stress, a routine (universal) and population-based approach to screening is warranted.[2,15,16,30] As outlined in the section, **Primary and Secondary Prevention Strategies in Healthcare** (in Part II), ACE screening 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.[699]
2. **Screening provides an opportunity for early intervention and prevention.** The toxic stress response often involves a latency between exposure (such as to ACEs) and negative health outcomes. Latency between exposure and outcome is one of the key World Health Organization (Wilson and Jungner) criteria for selecting optimal screening efforts (see **Primary and Secondary Prevention Strategies in Healthcare**, in Part II, for more details). This latency enables targeted interventions against toxic stress to be deployed prior to onset or early in the disease course, when they are most effective and economical. Screening for ACEs and toxic stress meets all World Health Organization screening criteria.[724]
3. **Early intervention improves outcomes.** Cumulative ACE exposure is

known to cause toxic stress and, consequently, a multitude of adverse clinical and social outcomes.[6,60] The physiological response to stress can be either positive, tolerable, or toxic.[6,7] In the positive and tolerable stress responses, there is a return to homeostasis with adequate buffering interventions. The tolerable stress response is a period during which opportunity for early identification and intervention is optimal. Scientific consensus demonstrates that early intervention to address exposure to childhood adversity can improve physical and mental health outcomes through regulating the toxic stress response.[23,603,704]

4. **Screening facilitates the recognition of possible toxic stress physiology and tailored interventions that can reduce causes of disease and death.** While strong evidence links ACEs to leading causes of death, including cardiovascular disease, stroke, chronic obstructive pulmonary disease, Alzheimer's disease, and diabetes, the association between toxic stress and non-neuropsychiatric conditions is under-recognized in medicine. Patients who present with significant toxic stress and non-neuropsychiatric conditions often receive care that does not adequately address the role that toxic stress physiology plays in their disease process(es).[1535,1536] Also, screening for ACEs in order to identify toxic stress

KEY OBJECTIVES OF THE ACEs AWARE INITIATIVE

1. To inform and empower primary care clinicians with the latest evidence on how to recognize, address, and prevent ACEs and toxic stress.
2. To incentivize early detection and early intervention for toxic stress by reimbursing providers for screening for ACEs, which includes 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.
3. To increase awareness and utilization of cross-sectoral, evidence-based and promising clinical and community interventions for preventing and addressing the toxic stress response.
4. To build clinical capacity for screening for—and clinical and cross-sector community capacity for response—to ACEs and toxic stress by investing in clinical quality improvement and community networks for response.
5. To improve clinical outcomes and health equity by enhancing the quality and specificity of healthcare provided to individuals exposed to ACEs and/or at risk for toxic stress, through rigorous, evidence-informed methods.

risk allows for educating patients about the links between early adversity and long-term health, and the evidence on how to intervene, which can empower individuals and families to attend to toxic stress to address their own health and also break the intergenerational cycle of adversity.[53]

Training and resources for providers

To help providers recognize and respond to ACEs and toxic stress, ACEs Aware includes a thoughtful approach to clinical training and seeks regular guidance from key stakeholders and global experts through multiple advisory committees.

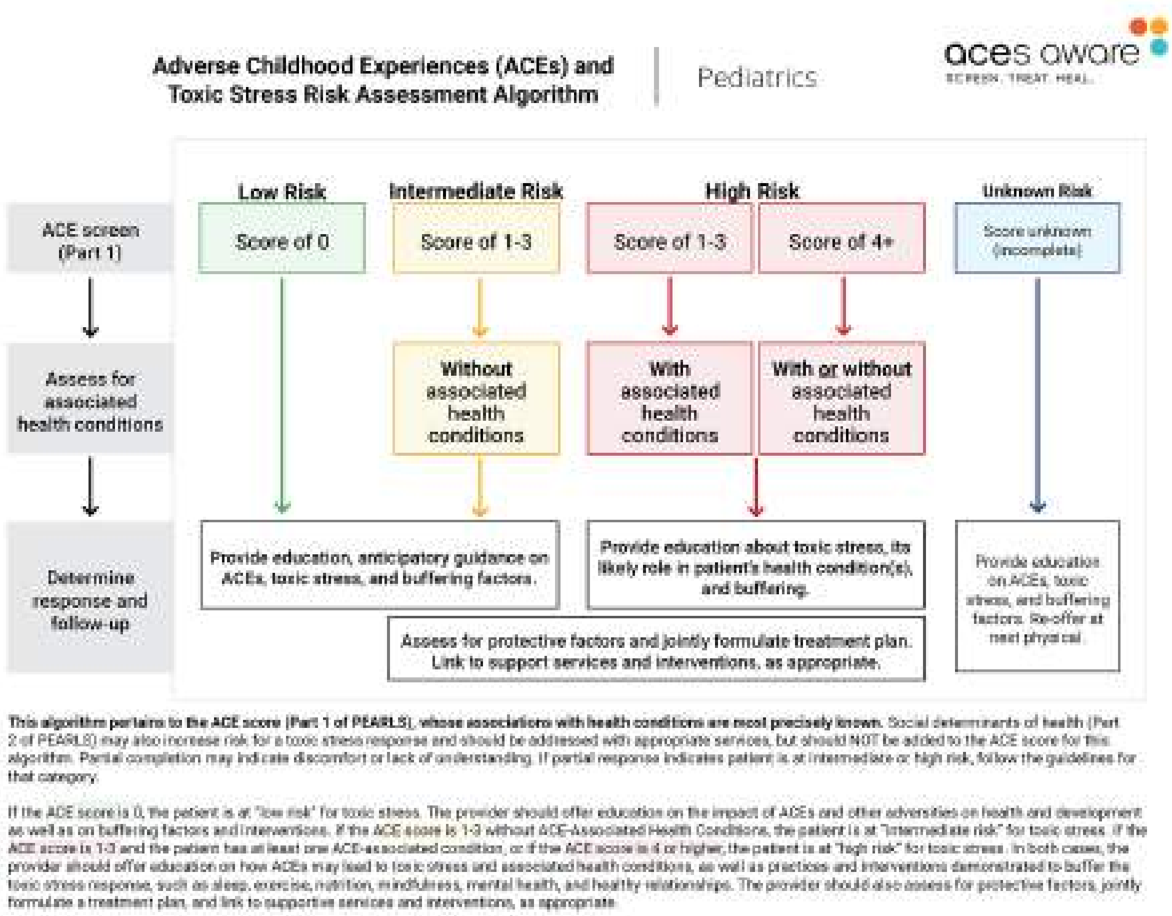


Figure 28a. *ACEs and toxic stress risk assessment algorithm for pediatrics. Of note, this was the algorithm as it existed at the time of publication; its most recent version can be found at ACEsAware.org. Reproduced with permission from ACEs Aware.*[86]

The California Surgeon General's Clinical Advisory Subcommittee (CAS), which is composed of medical, behavioral health, and public health experts, adapted and added evidence-based content to a case-based curriculum originally developed by the Office of Women's Health of the United States Department of Health and Human Services. The two-hour training, ***Becoming ACEs Aware in California***, which includes 11 common pediatric and adult primary care case studies, is available free to any provider online at ACEsAware.org, with free Continuing Medical Education (CME) and Maintenance of Certification (MOC) credits.[1537] It covers the impacts of ACEs and toxic stress on health and social outcomes, clinical scripts for introducing these concepts, a clinical algorithm to assess for risk of toxic stress (**Figures 28a** and **28b**), and steps to create an appropriately tailored, strengths-oriented, and evidence-based treatment and follow-up plan.

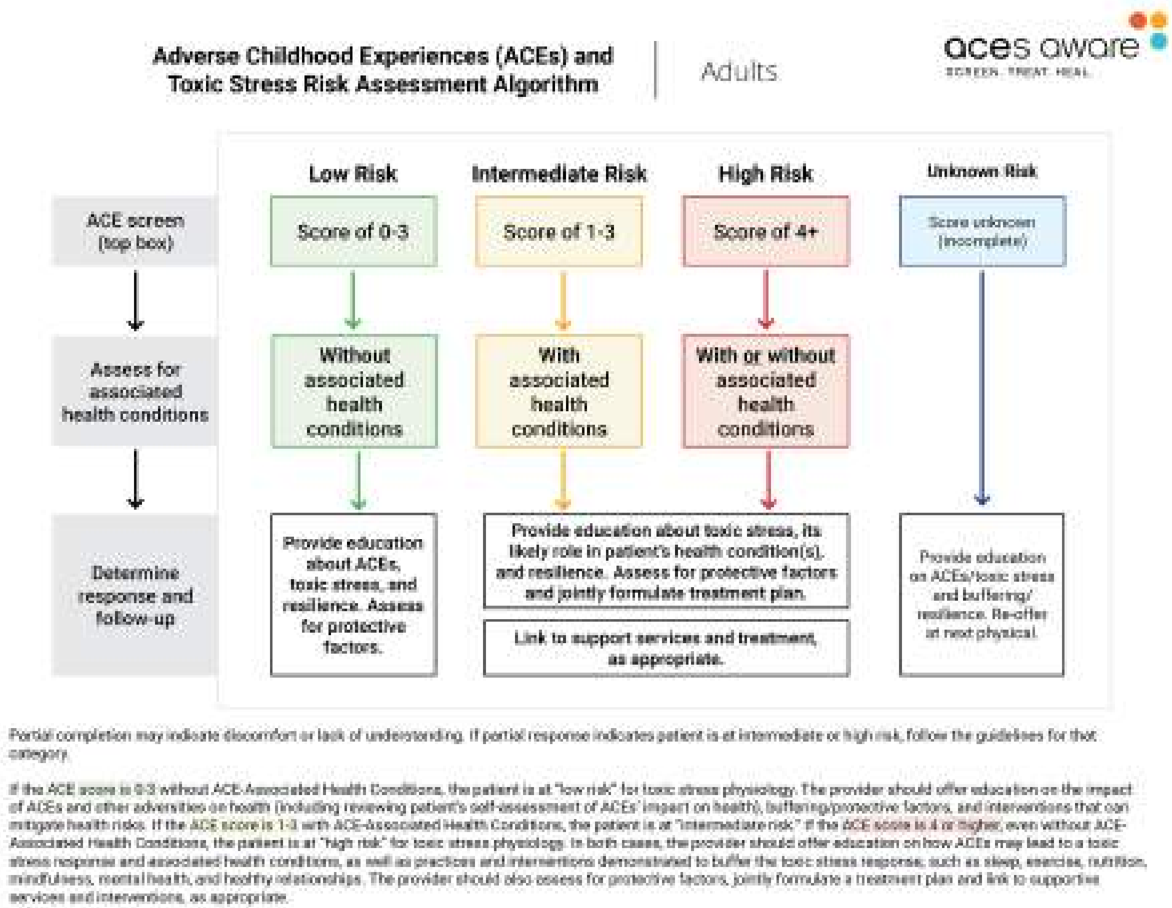


Figure 28b. *ACEs and toxic stress risk assessment algorithm for adults. Of note, this was the algorithm as it existed at the time of publication; its most recent version can be found at ACEsAware.org. Reproduced with permission from ACEs Aware.*[86]

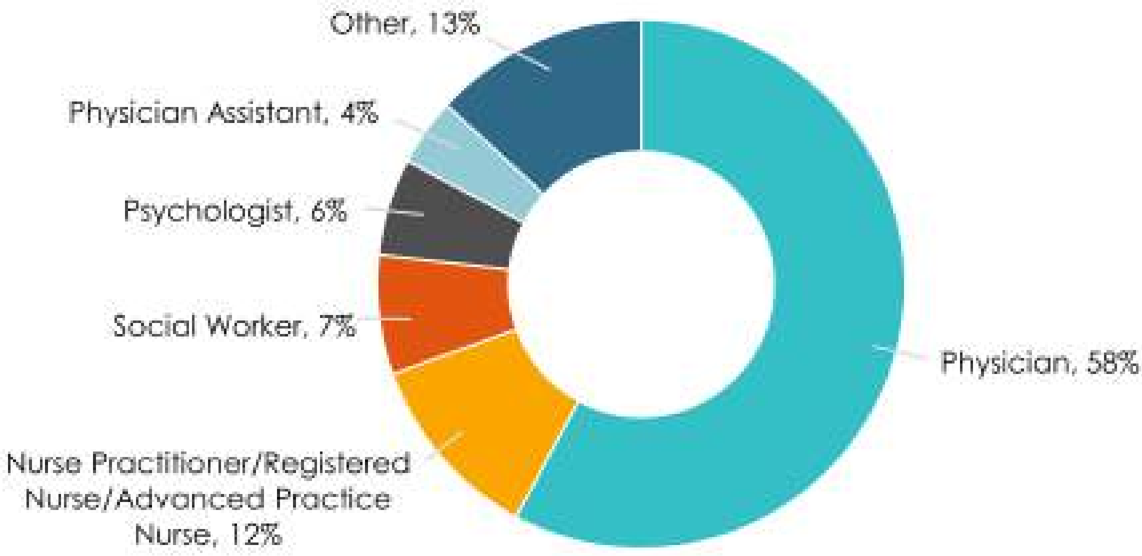


Figure 29. *Trained providers by occupation/provider type.*

Since January 1, 2020, eligible Medi-Cal providers have been able to receive an incentive payment when they screen Medi-Cal patients for ACEs.[1538] As of July 1, 2020, Medi-Cal providers are required to self-attest to completing a Certified Core Training to continue receiving this Medi-Cal payment for ACE screenings.[1538] At the time of this publication, the two-hour online Becoming ACEs Aware in California was the only Core Training available, though several others are under development.

Becoming ACEs Aware in California online training data

In the first nine months of the project (December 4, 2019 through August 31, 2020), nearly 14,000 healthcare providers completed the Becoming ACEs Aware in California two-hour online training.[1153] Physicians make up 58% of those who have completed the training to date (**Figure 29**). Of all the healthcare providers who completed the training, 49% specialize in pediatric or family medicine (**Figure 30**). Of users who provided a National Provider Identifier, 86% are Medi-Cal providers. A provider directory can be found on the ACEs Aware website that represents the subset of the Medi-Cal providers who have attested to completing the training, and have opted in to being added to the public-facing directory. As of August 31, 2020, approximately 8,300 Medi-Cal providers have attested to training completion overall, and about half of them are listed in the directory.[1153]

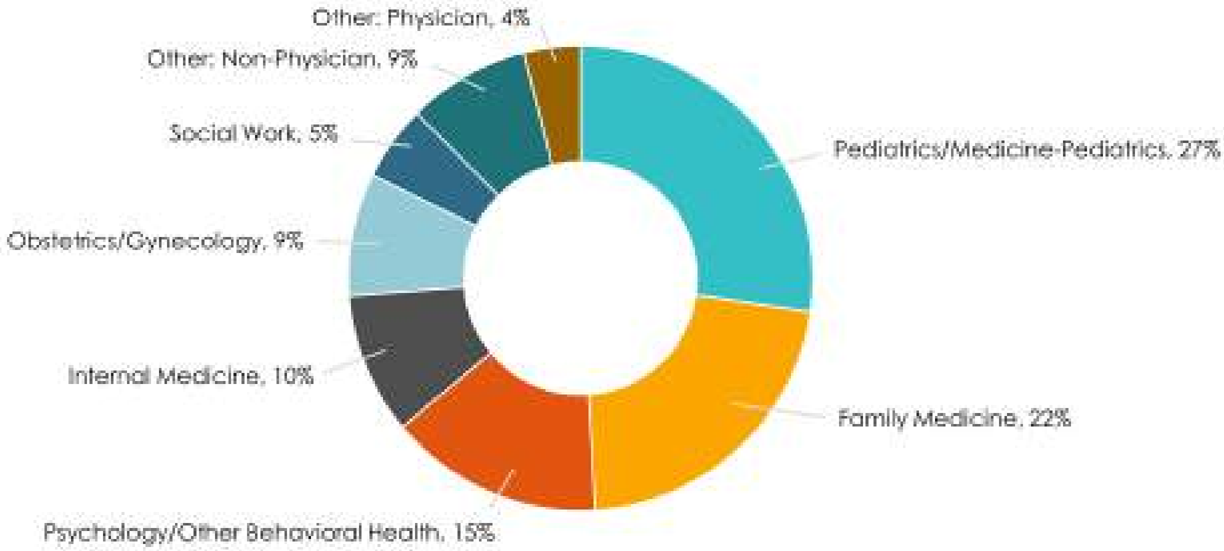


Figure 30. *Trained providers by clinical specialty.*

Nearly one-third (32%) of providers who completed the training are part of a managed care organization or health maintenance organization (HMO) provider network (**Figure 31**).

Before taking the training,

- 7% of providers reported screening all patients for ACEs;
- 64% reported they had been screening fewer than 25% of their patients for ACEs; and
- 35% reported they did not screen any patients for ACEs.

After taking the training,

- 97% reported that they planned to implement changes in their practice to address ACEs (**Figure 32**) or that their current practice was reinforced by the information presented—only 3% said they need more information before they would change their practice;
- 91% of providers reported confidence that they would be able to make practice changes;
- 54% reported that they planned to conduct routine ACE screenings for children adults; and

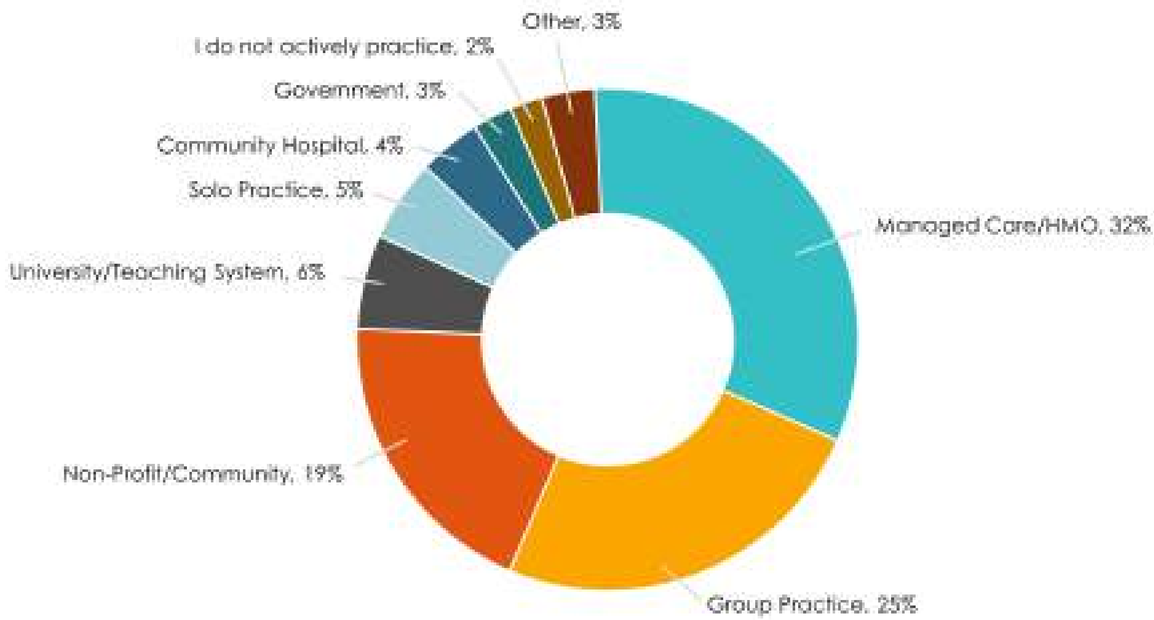


Figure 31. *Trained providers by primary practice setting.*

- 51% reported that they planned to conduct routine ACE screenings for adults.
- Of those who were not previously screening patients for ACEs, 81% indicated that they intended to implement routine ACE screening for children and/or adults.
- The most common anticipated barriers to implementing change included time constraints (71% of participants), systems constraints (32%), and patient compliance (30%).

Screening tools

Compared to the substantial volume of published scientific literature on ACE exposure and the role of toxic stress in creating acute and long-term risk for poor health outcomes, fewer scientific works have been produced regarding specific screening tools, clinical methods and treatment algorithms;[53,1539,1540] therefore, the California Surgeon General convened the CAS team of subject matter experts and clinicians experienced in ACE screening to review the literature and develop recommendations in these domains. Their consensus recommendations for optimal screening tools, clinical workflows, and ACEs and toxic stress risk assessment algorithms provide the foundation for clinical guidance in the ACEs

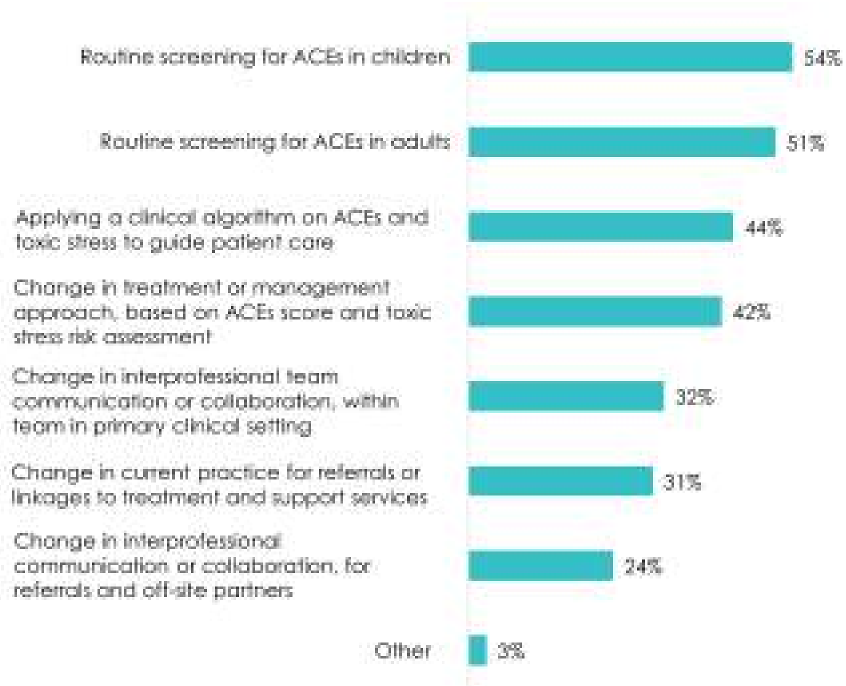


Figure 32. *Types of intended practice change.*

Aware initiative.[737]

For pediatric ACE screening, the Trauma Screening Advisory Group submitted its recommendations in January 2019, including the Whole Child Assessment and the Pediatric ACEs and Related Life-Events Screener (PEARLS).[1541] For pediatrics, the DHCS and the CAS ultimately recommended the PEARLS, developed by the Bay Area Research Consortium on Toxic Stress and Health (BARC),[1083] as part of a randomized controlled trial evaluating the clinical utility of ACE screening, association of ACE scores with biomarkers of neuro-endocrine-immune-metabolic and genetic regulatory dysregulation, and treatment efficacy. This tool was selected because of the rigorous research framework under which it was developed and because it allows patients' answers to be de-identified, meaning that respondents can disclose the total number of ACE categories that apply rather than specifying which ones. According to early data from one large pediatric FQHC, randomization to a de-identified versus identified screen was associated with greater patient disclosure and comfort.[1542]

PEARLS includes age-appropriate questions on the 10 ACEs and seven to nine additional social determinants of health (SDOH), including community violence, food and housing insecurity, bullying, discrimination, and a caregiver's physical illness or death, which may be risk factors for toxic stress. (As noted in the ACEs and toxic stress risk assessment algorithm, the SDOH questions should be addressed with appropriate services, but are not used in calculating a child's ACE score because the strengths of association between these SDOH and health outcomes have not been standardized in the ways that ACEs have been.) The PEARLS tool's initial development, face validation, and concurrent validation with a limited set of health outcomes are published;[56,703] more extensive validation and outcomes evaluation[703] are currently underway.

For adult patients, the CAS updated the original 10 ACE questions. As with PEARLS, both identified and de-identified formats are available in multiple languages on ACEsAware.org. Data on patient disclosure, and patient and provider preference for adult ACE screening tools is more mixed than in pediatrics.[678,734] These screening tools, the ACEs and toxic stress risk assessment algorithms, as well as patient education materials, are available for free at ACEsAware.org.[743]

Training healthcare providers on ACE screening is just a first step in addressing ACEs and toxic stress. Subsequent phases of the ACEs Aware initiative, discussed below, include more in-depth engagement of provider networks, promoting innovation, and iterating upon and spreading data-driven best practices.

ACEs AWARE PHASE II: STRENGTHENING PROVIDER ENGAGEMENT AND CAPACITY

ACEs Aware Phase II focuses on key objectives 1, 3, 4, and 5. Phase II aims to support providers and build capacity to extend the reach and impact of the ACEs Aware initiative. This robust effort includes funding **ACEs Aware grants** for organizations to expand access to ACEs training, provider engagement, and communications opportunities; **monthly webinars** for deeper provider training and education; and **external stakeholder engagement** to elicit information on promising models, best practices, evolving science, clinical expertise, and strategies for the implementation of coordinated trauma-informed care systems in California.

Provider engagement—ACEs Aware grants

Early detection and intervention for ACEs and toxic stress among all patients is critical to preventing and mitigating the negative health effects of the toxic stress response. Because this broad clinical approach is relatively new for many healthcare organizations, it is critical to offer grants to support providers and build their capacity to assess for and respond to toxic stress, using a clinical assessment that combines the ACE score with the presence and extent of AAHCs and protective factors.

In January 2020, ACEs Aware sent out a request for proposals for **grants** to fund organizations to support awareness and capacity building to respond to ACEs and toxic stress. Funding was offered in three key areas: **provider training**, **provider engagement**, and **communications**, as described below. Overall, 274 proposals were submitted, and $14.3 million was awarded in the form of 150 ACEs Aware grants to 100 organizations. (ACEs Aware also initially intended to provide convenings grants to foster collaboration across healthcare systems and community organizations to build local networks of care, but these grants were eliminated or repurposed due to physical distancing requirements imposed to address the coronavirus disease 2019, COVID-19, pandemic.)

Organizations were given preference for funding awards if they had a history of working with providers that serve Medi-Cal beneficiaries, demonstrated organizational readiness to leverage those partnerships in promoting the importance of ACE screening and response, and had plans for reaching communities with higher prevalence of ACEs. The selection process also accounted for the prevalence of ACEs and proportion of Medi-Cal beneficiaries among the populations served by the applicants in order to effectively target funding. Reviewers ensured that grantees represented a diverse range of approaches, organizations, populations served, and geographic regions. Organizations were strongly encouraged to collaborate and develop joint grant applications. The ACEs Aware website features the full list of grantees.[1543]

Throughout the grant period—from July 2020 through June 2021—ACEs Aware grantees will work individually and collectively to advance the goals of the ACEs Aware initiative. Grantees meet regularly (virtually) in large and small groups, focused on particular areas of interest, sharing strategies and best practices, and troubleshooting when necessary. Grantees are required to submit quarterly reports, including quantitative data on their activities and progress, as well as a midpoint and a final narrative report highlighting successes and lessons learned.

Finally, ACEs Aware has engaged the Frameworks Institute, an internationally renowned organization with experience in using the science of framing to develop effective communication to spark change for a wide range of social issues.[1544] The Institute is charged to work with all ACEs Aware grantees to build capacity, offer technical support, and develop consistent and effective messaging on ACEs and toxic stress that is grounded in the latest science.

Provider training grants

ACEs Aware awarded 31 grants to help educate Medi-Cal providers on using ACE screening (including assessment for the presence of AAHCs and protective factors) as a component of toxic stress risk assessment, providing trauma-informed care, and delivering evidence-based treatment plans to aim to mitigate the toxic stress response. These trainings seek to build upon the original ACEs Aware training by providing further guidance for specific provider types, contexts, and/or in a variety of modalities.

- Five grants are supporting organizations to adapt existing or develop new trainings to meet ACEs Aware Core Training Certification criteria (**Table 10**). (Completing a Core Training certifies providers to receive the Medi-Cal payment for screening beneficiaries for ACEs.)
- Twenty-six organizations received grants to support the development of "Supplemental" trainings on key topics that augment the information provided through the Core Trainings. While these trainings do not qualify participants for Medi-Cal payment for ACE screening, they are designed to provide additional support to providers in promoting practice change. Supplemental training grants include resources for training members of the care team other than the primary care provider, such as social workers, mental health professionals, community health workers, or home visitors, and for addressing ACEs in specific patient populations, such as lesbian, gay, bisexual, transgender, and queer individuals, tribal communities, and communities of color.

Training topics required in core training curricula
Trauma-informed care principles
Information on ACEs and toxic stress physiology
Clinical algorithms to address the role of toxic stress in ACE-Associated Health Conditions
Guidance for tailoring treatment and follow-up for specific kinds of conditions or symptoms
Tools and interventions to promote resilience
Preventing, recognizing, and responding to vicarious trauma and burnout among staff
Information on how providers can participate in ACEs Aware
Guidance on how trauma-informed approaches can mitigate health inequities

Table 10. *Training topics required in core training curricula.*

Provider engagement grants

Eighty-three grants have been awarded to supplement and promote provider engagement. These grants feature opportunities for providers and other stakeholders to share lessons learned and best practices that are tailored to specific geographic areas, patient populations, provider types, and practice settings.

- 22 organizations will conduct provider engagement to build appropriate clinical response networks of care in preventing and/or responding to toxic stress;
- 25 organizations will develop peer-to-peer learning strategies;
- 24 organizations will enable broad-based provider engagement; and
- 22 organizations will develop practice papers highlighting best practices, lessons learned, and promising implementation strategies around screening for ACEs as a component of toxic stress risk assessment, and trauma-informed systems of care.

Communications grants

ACEs Aware has awarded 36 grants to support strategic communications efforts and to promote the work of fellow grantees. These grantees are working to disseminate information on provider training and engagement opportunities, and to increase awareness about the mission and scope of the overall initiative. Organizations will use a wide range of communication approaches to share ACEs Aware information, as well as their own content tailored to their audiences.

Network of Care grants

On December 1, 2020, ACEs Aware announced availability of a second round of grant funds of up to $30 million intended to build on and grow a robust system—a Network of Care—to support Medi-Cal providers and their communities in effectively responding to ACEs and implementing protocols for interrupting the toxic stress response in children and adults. The objective of these "Network of Care" grants is to create, augment, and sustain formal connections between Medi-Cal providers, social service systems, and community partners to effectively address toxic stress in children and adults through clinical and community interventions following an ACE screening, to prevent future ACEs, toxic stress, and intergenerational transmission, and prevent or assist in treating AAHCs.

Two types of grants will be provided:

- Network of Care Planning Grants (up to $300,000 per grant)
- Network of Care Implementation Grants (up to $3,000,000 per grant).

Provider engagement—monthly webinars

Beginning in December 2019, ACEs Aware has hosted monthly webinars to promote ongoing practice improvement and clinical implementation learnings among California providers (with a focus on those serving Medi-Cal patients) around adopting ACE screenings as a tool for assessing and intervening on risk of toxic stress and providing trauma-informed, evidence-based care.[1545] The webinars feature clinicians with deep expertise in these topics who share practical information with rich implementation lessons, often drawing on clinical experience and case studies. Topics have included:

- *Taking Care of Our Patients, Our Teams, and Ourselves: Trauma-Informed Practices to Address Stress Related to COVID-19*
- *Building Trauma-Informed Connections via Telehealth during COVID-19*
- *Primary Care & Telehealth Strategies for Addressing the Secondary Health Effects of COVID-19*
- *Fundamentals of ACE Screening & Response in Pediatrics*
- *Fundamentals of ACE Screening & Response in Adult Medicine*
- *Regulating the Stress Response for Kids: Practical Tips for Primary Care Providers*
- *Assessing Readiness & Building Resilience in the Clinical Workforce: A Foundation for ACE Screening Integration*
- *Supporting Patients during Pregnancy: ACEs and Maternal Health*

Information on upcoming topics and registration can be found on the ACEs Aware website.[1545] CME credit is now offered for the webinars.

Provider engagement—external stakeholder engagement

The ACEs Aware initiative considers strategic engagement with external stakeholders and leaders a key guiding framework for its work.

The Trauma-Informed Primary Care Implementation Advisory Committee (TIPC)

The **TIPC** advises ACEs Aware on promising models, best practices, clinical-, systems-, and policy- expertise, strategic insights, and the latest science, for optimal implementation of toxic stress-responsive and trauma-informed systems in California. The TIPC is comprised of field-leading experts, including representatives of major healthcare plans, health systems, philanthropic associations, nonprofits, local government associations, professional provider associations, and subject matter experts (see TIPC MEMBER ORGANIZATIONS). The TIPC advises on promising models, best practices, evolving science, clinical expertise, and strategy for the implementation of trauma-informed care systems in California.

The TIPC met in June of 2019 and set 10 short-term goals:

1. Develop and implement a robust training plan for a broad group of healthcare providers and staff that includes the standardization and attainment of Continuing Medical Education (CME).
2. Identify the process for including CME in provider trainings and establish a subcommittee with key stakeholders and members to oversee the implementation of this training plan.
3. Collaborate with healthcare professional organizations to leverage existing resources to offer and disseminate provider trainings.
4. Identify and disseminate strategies, protocols, and best practices to support ACEs screening. Share assessments with stakeholders in order to

TIPC MEMBER ORGANIZATIONS

- American Academy of Pediatrics
- Anthem Blue Cross
- Blue Shield of California
- Blue Shield of California Foundation
- California Academy of Family Physicians
- California Behavioral Health Directors Association
- California Conference of Local Health Officers
- California Department of Public Health
- California Department of Social Services
- The California Endowment
- California Governor's Office of Planning and Research
- California Health and Human Services Agency
- California Health Care Foundation
- California Maternal Quality Care Collaborative
- California Medical Association
- California Pan-Ethnic Health Network
- California Primary Care Association
- California State Association of Counties
- Californians for Safety and Justice
- Center for Youth Wellness
- County Health Executives Association of California
- County Welfare Directors Association of California
- Didi Hirsch Mental Health Services
- First 5 California
- Kaiser Permanente
- L.A. Care Health Plan
- The Permanente Medical Group
- Sutter Health
- University of California, San Francisco

advance our learning.

5. Identify and engage state leadership to support data-driven strategies. Establish systems to monitor and track shared metrics across populations.
6. Establish a shared understanding of community vision and culture of collaboration between health plans, organizations and clinics.
7. Develop a plan to break the intergenerational ACEs cycle that includes appropriate parenting resources and high-tech/high-touch best practices for serving families.
8. Develop and implement a statewide education campaign to raise the public's awareness about ACEs and toxic stress. Develop resource toolkit(s) for diverse audiences.
9. Establish minimum requirements for early periodic screening, diagnosis, and treatment supports that are evidence-based and inclusive of early response efforts.
10. Develop a plan to identify community-based resources and a funding stream to facilitate the adoption of the Health Homes model for children that includes early intervention. Support efforts to establish and sustain public and private partnerships in order to catalyze this work.

In addition to the full committee, the following subcommittees were created to address specific needs:

- **The Clinical Advisory Subcommittee** developed the online training curriculum to certify Medi-Cal providers to receive payment for screening patients for ACEs, and related clinical tools in Fall 2019.
- **The Clinical Implementation Subcommittee** provides input and clinical expertise on developing guidance and tools to help providers: better understand toxic stress physiology and AAHCs; implement ACE screenings to identify risk of toxic stress, evidence-based interventions, and trauma-informed care; and, reduce health disparities. Key areas of focus include practical implementation strategies such as electronic health record integration, advancement of health equity, and continuous review and incorporation of the latest research into ACEs Aware.
- **The Network of Care Subcommittee** will recommend a roadmap for improving collaboration and coordination across the healthcare and community resources necessary to respond to toxic stress—between health plans, health centers, clinicians, and clinical and community organizations. The Network of Care Roadmap, planned for release in December, 2020, will:
  - » Identify key stakeholders and elements in a cross-sector network of care;

  - » Clarify the roles of primary care providers and other stakeholders;
  - » Describe the importance of buffering supports and coordination among providers and key resources; and
  - » Provide considerations for policy and implementation.

- **The Provider Engagement and Education Subcommittee** provides strategic advice on increasing the number of providers who complete an ACEs Aware Core Training and supporting providers in integrating ACE screening and clinical response into their practice. To date, the subcommittee has provided valuable input on:
  - » Communications to increase provider training numbers;
  - » Provider webinar strategy, format, and topics;
  - » ACEs Aware COVID-19 response strategy, EHR strategy, and managed care strategy; and
  - » The forthcoming ACE Screening Implementation Guide for providers.

ACEs Aware managed care plan engagement strategy

In addition to incorporating the input and work of TIPC, its subcommittees, and its member organizations, ACEs Aware is coordinating with managed care plans (MCPs) to enlist their partnership in engaging providers in screening for ACEs and toxic stress. Because approximately 80% of Medi-Cal beneficiaries are enrolled in a Medi-Cal MCP, ACEs Aware recognizes the crucial role MCPs can play in implementing a novel clinical screening effort at scale. In a recent survey of MCP Chief Medical Officers and Medical Directors (with 21 out of 24 responding), 96% said they are engaging with the ACEs Aware initiative and have visited the ACEs Aware website; 87% have communicated with their network of providers about ACEs Aware; 96% have communicated with other staff (case managers, behavioral health providers, and social workers) about ACEs and toxic stress training and/or other resources; and 36% have faced some challenges around updating and configuring health plan information technology or claims systems to reimburse providers for the ACE screening codes.

The goals of the ACEs Aware MCP Engagement Strategy are to ensure that MCPs are encouraging and implementing ACE screening and response among Medi-Cal providers, and to leverage MCP relationships with providers to expand ACE training, screening, and response among Medi-Cal providers. Objectives include ensuring that MCPs and delegated entities understand how to implement and oversee ACE screening, billing, and payment; have the resources and tools to support primary care providers and teams; and develop the internal infrastructure to support primary care providers in implementing ACE screening and response.

ACEs Aware conducted a "nuts and bolts" webinar for MCPs in September 2020. Going forward, the initiative will continue to: engage with delegated entities to identify any additional needs in the managed care ecosystem; develop a robust communications infrastructure to reach plan and delegated-entity staff at multiple levels; conduct quarterly webinars focused on the key implementation supports MCPs have requested and peer-to-peer learning; solicit commitments from MCPs to promote provider Core Training and screening for ACEs as a tool for recognizing risk of toxic stress in primary care; and, leverage quarterly data reports and the provider directory to inform engagement strategy.

ACEs AWARE PHASE III: QUALITY IMPROVEMENT

ACEs Aware Phase III focuses mainly on objective 5, though it aids in the others. The aim of Phase III is to identify and spread best practices and strategies for addressing ACEs and toxic stress in healthcare settings through data-driven quality improvement (QI) efforts. The main mechanism is the California ACEs Learning and Quality Improvement Collaborative (CALQIC), which will generate both qualitative and quantitative data on best practices in ACEs screening and response from 53 clinics in seven California regions over 18 months.

What is QI in healthcare?

The Institute for Healthcare Improvement (IHI) defines the science of improvement as "an applied science that emphasizes innovation, rapid-cycle testing in the field, and spread in order to generate learning about what changes, in which contexts, produce improvements."[1546] QI methods and tools are used to develop innovations on a small scale, identify and leverage key implementation learnings, and scale up and spread them across healthcare systems. One key goal of ACEs Aware is to improve the quality of care received by patients who have experienced ACEs or may be at risk of toxic stress. CALQIC employs implementation science techniques,[1547] including both QI and deeper qualitative inquiry methodologies, to provide the most robust learnings.

Prior success of collaborative QI efforts in California

California has successfully undertaken large public–private collaborative QI efforts at scale that have been extremely effective. Examples include the California Maternal Quality Care Collaborative[1548] and the California Perinatal Quality Care Collaborative[1549] (CMQCC and CPQCC, respectively). While these collaboratives are different from CALQIC in that both are hospital-based, they illustrate the power of well-funded, public–private, statewide collaborative approaches to achieve rigorous, systematic QI in healthcare in the state of California.

CMQCC

The CMQCC includes more than 200 California hospitals covering 95% of all births in the state. It addresses the leading causes of preventable death among pregnant and postpartum women through development and spread of best practices using QI toolkits containing tools and articles, care guidelines, hospital-level implementation guides, and professional education materials. Since implementation of the CMQCC, maternal mortality in California has declined by 55% between 2006 and 2014 (while the national rate continued to rise), saving 9.6 lives per 100,000 through this concerted effort.[1548]

The collaborative has also made significant gains in reducing disparities in maternal morbidity and mortality. For example, 99 hospitals participating in a hemorrhage QI collaborative saw a significant reduction in the gap between Black and White maternal mortality due to severe maternal morbidity from hemorrhage. Before the collaborative, the mortality rate among women with hemorrhage was 22.1% (12,002/54,311), with the highest rate observed among Black women (28.6%; 973/3,404), and the lowest among White women (19.8%; 3,124/15,775). The overall rate fell to 18.5% (3,553/19,165) in the post-intervention period. Both Black and White mothers benefited from the intervention, but the benefit among Black women exceeded that among White women (9.0% vs. 2.1% absolute rate reduction).[1550]

CPQCC

The CPQCC, founded in 1999, established a database that houses critical data on more than 95% of all low-birth-weight deliveries in California. This has allowed the development of data-driven QI efforts, which assisted in significantly reducing catheter-associated infections by 75%, antibiotic utilization by 13.8%, and length of separation between mothers and pre-term babies by an average of three days. It also increased early discharge from 32% to 42% and breastfeeding at discharge from 54% to 64%.[1549]

These large-scale efforts are blueprints for public–private QI processes for advancing best clinical practices to address ACEs and toxic stress. CALQIC adapts and adds to the known QI approaches described above. Systems for data gathering, evaluation, dissemination, and continuous quality improvement, similar to models like the CMQCC and the CPQCC, are crucial to the success of any broad-scale learning collaboratives like CALQIC. CALQIC's goal is to provide a structure for rapid learning regarding processes of care and a structure for a deeper qualitative understanding of necessary elements of practice transformation and optimal relational aspects of care. This public–private QI network aims to drive similar successes as CMQCC and CPQCC at scale for intervening in and stemming the health crisis of ACEs and toxic stress.

California ACEs Learning and Quality Improvement Collaborative

To advance healing approaches to screening and responding to ACEs and toxic stress, CALQIC was created as a collaboration between by the University of California, San Francisco (UCSF), CA-OSG, and DHCS. CALQIC is an 18-month public–private learning collaborative of 53 clinics in seven diverse California regions dedicated to identifying promising clinical practices, tools, resources, and partnerships in responding to ACEs and toxic stress to inform future implementation phases of California's ACEs Aware initiative. CALQIC supports participating clinics to:

- Identify and overcome barriers to ACE screening and response at both the site and organizational levels;
- Develop or strengthen models of care and tools for operationalizing ACE screening and response (i.e., clinical roles, workflows, and scripts);
- Align clinical efforts with the statewide initiative, ACEs Aware, which is working to ensure providers are credentialed, use approved screening tools, and bill using appropriate codes;
- Advance health equity;
- Collect and track data to assess progress in ACE screening and response; and
- Identify and respond to any potential adverse events associated with ACE screening.

Participating clinics receive virtual coaching, technical assistance, site visits to exemplar organizations, and grants. All 53 learning collaborative clinics participate in qualitative and quantitative evaluation activities. CALQIC also includes two "deep dive" evaluations in urban and rural counties to focus on how clinic- and provider-level characteristics and resources affect screening and response for toxic stress, and patient experience (**Figure 33**). In the context of the COVID-19 pandemic and the ongoing California wildfires, CALQIC is also capturing the experiences of screening for and responding to toxic stress for patients experiencing acute on chronic adversity. CALQIC's evaluation will extend the use of telehealth for screening and responding to ACEs, due to changes in care delivery in response to the COVID-19 pandemic.

CALQIC is led by the Center to Advance Trauma-Informed Health Care at UCSF, experts with deep experience in trauma and adversity, implementation science, and health equity. Serving as partners are the RAND Corporation, which is the preeminent California-based nonprofit focused on the evaluation of healthcare innovation, and the Center for Care Innovations, which is the leading California-

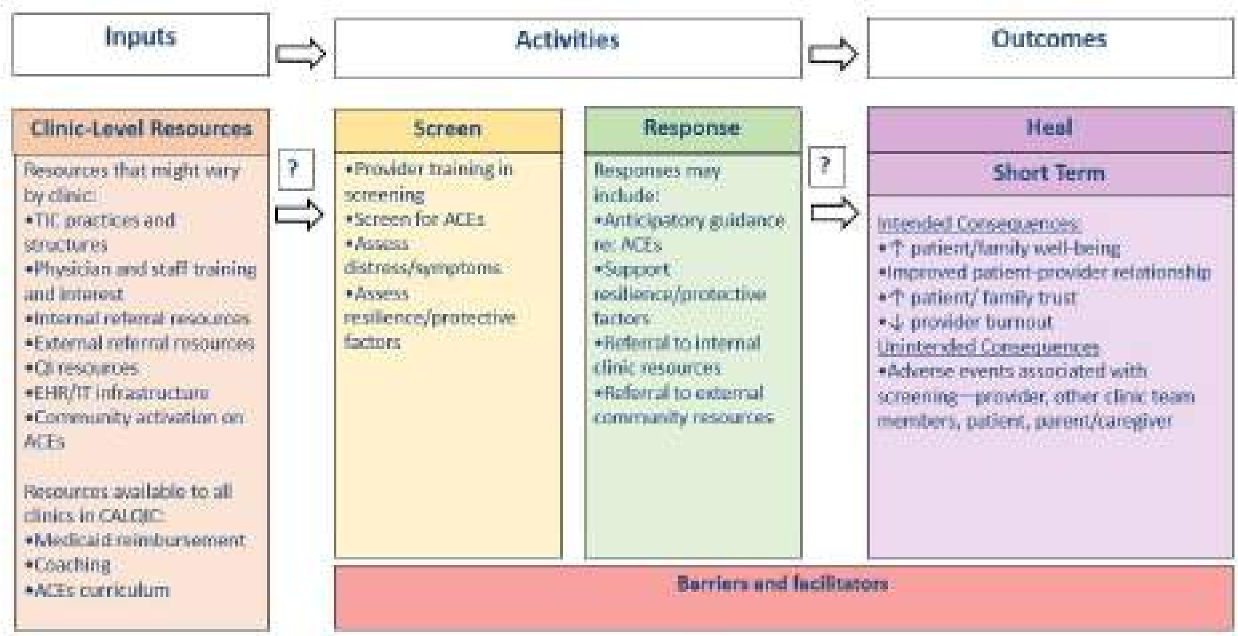


Figure 33. *California ACEs Learning and Quality Improvement Collaborative (CALQIC) logic model for evaluation. Image reproduced with permission from the University of California, San Francisco, Center to Advance Trauma-Informed Health Care (2019); CALQIC.*

Each arrow is an if-then statement, and the goal of the evaluation is to capture the elements in each column to better understand the relationships between each. It is assumed that screening and referral will vary by clinic—according to variations in inputs, or in relationship to variations in other activities. The quantitative assessments of screening success and referral variations, paired with qualitative information on clinic-level resources and capabilities, will be used to better understand the barriers to and facilitators of ACEs screening, and effective potential solutions to address the barriers.

based convener of learning collaboratives focused on healthcare innovations for low-income Medicaid populations. Together, these organizations are applying the science of QI, coupled with qualitative methods, to identify, evaluate, and disseminate facilitators, strategies, and promising practices among the participating clinics.

CALQIC also includes an intentional focus on adverse events (any harms or unintended consequences encountered during or after ACE screening and response). Because potential harms of ACE screening have been speculated on, but have not been well documented or described, the first goal is to rigorously assess any potential harms associated with screening. In addition, CALQIC qualitative interviews will elicit the experience of adverse events from providers, others performing the screening, and patients and parents. CALQIC anticipates that it will use this information to inform a pilot system to collect adverse events in at least one of its "deep dive" evaluation sites. Ultimately, this work could inform a potential future system to collect adverse events, analogous in principle to the federal Vaccine Adverse Event Reporting System, a safety surveillance program co-sponsored by the Food and Drug Administration and the Centers for Disease Control and Prevention.[1551]

The project also integrates health equity and patient/community voice into all aspects and activities of the project team, training of participating clinicians, and development of best practices for the next phases of training of healthcare providers. Ultimately, the lessons learned in CALQIC will inform best practices in ACE screening and response, help avoid unintended harms, and guide future implementation efforts in other clinics and health systems throughout California and nationally.

Clinical Implementation Case Studies

Given the significant prevalence, health consequences, and costs of Adverse Childhood Experiences (ACEs) and toxic stress, the science must be translated into widespread clinical assessment and response in order to improve health outcomes at a population level.[2,15,16,27,30] The current literature captures many examples of successful integration of ACE screening in various clinical settings, including pediatric primary care,[56,722,727-733] adult primary care,[734,735] family medicine,[736] and prenatal care.[678,679] ACE screening is documented to be acceptable to both patients and providers, and emerging evidence shows that it may actually improve patient trust in providers and satisfaction with the healthcare experience, in part because it serves as a welcome bridge to needed prevention and buffering interventions such as parenting, economic, legal, educational, and logistical supports.[678,697,725,731,736,739,794]

As clinical sites work to integrate approaches to mitigating ACEs and toxic stress, current successful clinical implementation efforts of early adopters provide key insights and can help promote the diffusion of this innovative approach. Information gathered in interviews conducted from April to June 2020 with implementation leaders at diverse clinical sites are featured here as case studies, which summarize the sites' unique characteristics and innovations in the realms of provider and staff training, integration of ACE screening and response, and systems change and/or integration. Key metrics (if available), challenges and opportunities (including those related to the coronavirus disease 2019, COVID-19, pandemic), and next steps are also highlighted.

The seven implementation case studies (**Table 11**) presented in this section were selected based on depth and breadth of clinical experience in addressing ACEs and toxic stress, ensuring an adequate variety of practice settings, patient populations, and provider types, as well as a preference for California-based examples (all but one are based in California) to enhance local learning.

Table 11. Summary characteristics of implementation case study sites in ACE screening and response.

Abbreviations used:

ACEs: Adverse Childhood Experiences
BRFSS: Behavioral Risk Factor Surveillance System
CALQIC: California ACEs Learning and Quality Improvement Collaborative
EMR: Electronic medical record
FQHC: Federally qualified health center
NPPC: National Pediatric Practice Community on ACEs
PEARLS: Pediatric ACEs and Related Life-Events Screener
SHARK: Strong, Healthy, and Resilient Kids

Site Description	Who/How Screened	Response	Findings
Southern California Permanente Medical Group (SCPMG) • Large integrated managed care • Pediatric patients in six clinics • Diverse in race/ ethnicity and socioeconomic characteristics • Led by Mercie DiGangi, DO	• Children at 3-, 5-, 10- and 13-year-old well-child visits • De-identified paper screen based on original ACE study tool[3] (but the provider asks the patient/family if they are willing to disclose their specific ACEs) • Moving to PEARLS by Spring 2021 • Results entered in EMR • Began: 2018	• Patients with ≤1 ACE receive handout on ACEs, resilience, stress reduction, and positive parenting • Patients with ≥1 ACE and AAHCs offered referral to social medicine team and connected to SCPMG or community behavioral health services or parenting class	• Published findings:[733] • More than 7,000 children screened • More than 99% of patients who received the screen completed it • Prevalence of ≥1 ACE increased with age: 15% in 3-year-olds, 17.5% in 5-year-olds, 30.5% in 10-year-olds, and 33.8% in 13-year-olds • Among all ages, the prevalence of ≥4 ACEs was very low (≤2.4%) From case interview: • Does not prolong visits • Provides new information • Increases the quality of patient-provider relationships • Is appreciated by families • No adverse events or patient safety concerns

Site Description	Who/How Screened	Response	Findings
Los Angeles County Department of Health Services (LAC-DHS) • Large municipal healthcare • Eight clinics (pediatrics, obstetrics, family medicine, and internal medicine) • Diverse in race/ ethnicity (with large Latinx population) and socioeconomic characteristics; rural and urban • Mostly Medi-Cal, some uninsured • Led by Shannon Thyne, MD and Amy Shekarchi, MD	• Children at 9-, 18-, and 30-month well-child visits • Adolescents yearly • Pregnant women at prenatal care entry • New patients upon establishing care • De-identified paper PEARLS. Identified telehealth screens. • Results entered in EMR • Began: May 2020	• All patients receive handout on ACEs and toxic stress • As needed, eConsult for Behavior, Development, and Adversity, and SHARK program to provide bridge services as children transfer to community services • Social work and behavioral health for acute patient need	• More than 500 screens conducted • Less than 10% of patients had >3 ACEs • Most referrals were due to positive answers to part 2 of PEARLS or optional social determinants of health questions • Resilience questions well received by patients • Currently developing data reports on screening, results, and referrals. • Plan to conduct focus groups on patient, family, provider, and staff perspectives. • Six pediatric clinics have joined CALQIC for streamlined data collection and analysis (in addition to other support).

Site Description	Who/How Screened	Response	Findings
True Care (formerly North County Health Services) • FQHC in North San Diego and Riverside Counties • Pediatrics, adult Medicine, women's health, behavioral health in 11 health centers • Large Spanish-speaking Latinx population • Led by Leon Altamirano, PsyD and Mercedes Dodge, PA-C	• Children annually during well-child visits starting at newborn • Adults on establishing care • Pregnant women and partners on entering prenatal care • All patients as needed based on toxic stress symptoms • Initially used identified paper screen based on original ACE study tool;[3] later transitioned to PEARLS • De-identified data entered in EMR • Began: 2014	• Providers may give handout on ACEs, toxic stress, and relevant patient resources • Providers may refer to True Care behavioral health provider, who may meet the patient on-site for warm handoff • Case managers and care coordinators also help address patients' social determinants of health	Internal data collection: • About 90% of providers have completed the online Becoming ACEs Aware in California Core Training From case interview: • No adverse events or patient safety concerns

Site Description	Who/How Screened	Response	Findings
Sutter Health • Large integrated healthcare system • Sacramento multispecialty clinic • Predominantly White, diverse in age • Internal medicine clinic • Led by Michael Flaningam, MD and Andrew Factor, MD, MPH	• Adults who have symptoms or health conditions that may be related to toxic stress • Identified paper screen based on original ACE study tool[3] • Began: 2019	• Supplement usual care with education on stress and its relationship to ACEs, stress management strategies, and reinforcing patients' existing self-care practices • May refer to behavioral health services, mind-body therapies, stress-management resources	From case interview: • Has helped provide better care • Has increased patients' self-awareness and self-care • Significantly decreased burnout in participating providers

Site Description	Who/How Screened	Response	Findings
Santa Rosa Community Health (SRCH) • FQHC in Sonoma County • One school-based teen clinic; one pediatrics clinic • Large Latinx population, many Spanish-speaking, immigrants, and/or work in agriculture • Led by Deirdre Bernard-Pearl, MD, • Meredith Kieschnick, MD, and Luisa Ramirez	• Children annually during well-child visits starting at 4 months (if <12 years, parents also screened) • Teens screened upon establishing care and annually • Identified paper screen based on original ACE study tool[3] (plus eight questions on resilience/ protective factors) • Results entered in EMR • Began: 2013	• Patients (and parents with ACEs) offered resources based on specific needs. • Providers can refer to integrated behavioral health services, on-site trauma-informed parenting program, parenting program for Spanish-speaking families, community-based parenting groups	Internal data collection: • Over 15,000 ACE screenings conducted From case interview: • Families appreciate being screened for ACEs • Screening adolescents privately has led to increased disclosure of ACEs • No adverse events

Site Description	Who/How Screened	Response	Findings
Dartmouth CO-OP Primary Care Practice-Based Research Network (Dartmouth CO-OP PBRN) • New Hampshire, Vermont, and Maine practice network focused on healthcare research • Family medicine practice in one university-affiliated clinic, one FQHC, and one private practice • Rural, predominantly White; diverse socioeconomic characteristics • Led by Patricia Glowa, MD	• All patients >18 years attending non-acute visits during 2-week pilot • Identified paper screen based on original ACE study tool[3] • Began: 2015 (two-week pilot)	• Patients offered resources based on specific needs • Resources varied by site (for example, university-affiliated site had some behavioral health services and care coordinators who could refer patients to psychiatry or community resources)	Published findings:[736] 100% of patients who received the screen completed it 62% of patients had ≥1 ACE, and 22% had ≥4 ACEs ≥4 ACEs were found in 10% of patients at prevention visits, 30% of patients at chronic illness visits, 33% at other nonacute visits Providers felt that the screen did not interfere with visits, the screen was acceptable to patients, and the screen provided new information Visit length was increased by ≤5 minutes in 91% of visits with patients with ACEs From case interview: • No adverse events or patient safety concerns

Site Description	Who/How Screened	Response	Findings
Kaiser Permanente Northern California (KPNC)[678] • Large integrated managed care • Two obstetric clinics • Diverse in race/ ethnicity and socioeconomic characteristics • Led by Tracy Flanagan, MD, Carey Watson, MD, and Kelly Young-Wolff, PhD, MPH	• English-speaking pregnant patients ≥18 years at 2nd or 3rd prenatal visit between 16 and 23 weeks gestation • Identified paper screen based on BRFSS Questionnaire (plus Connor-Davidson Resilience Scale) • Began: 2016 (four-month pilot)	• All patients received handout on KPNC and community-based resources, such as support groups and classes on depression, anxiety, stress-reduction, and parenting • Providers could refer to KPNC mental/behavioral health services	Published findings: • 88% of patients who received the screen completed it • 54% of patients had 0 ACEs, 28% had 1–2, and 18% had ≥3 • Most patients felt comfortable completing the screen and discussing ACEs • Providers' comfort with ACE screening and response increased after the pilot • Providing adequate training, streamlining workflows, including resilience screening, and ensuring the availability of patient resources were important factors in providers' willingness to screen From case interview: • Few patients required or desired behavioral health services during the pilot

Key learnings from the seven case study sites are highlighted below, grouped thematically. Relevant corollary findings from the literature and information about ACEs Aware recommendations and tools are incorporated where appropriate.

IMPLEMENTING SYSTEMS CHANGE

Case study sites obtained initial buy-in for implementing ACE screening and response from institutional leadership, providers, and staff by presenting data on the health impacts of ACEs and toxic stress. They aligned ACE screening with existing institutional efforts to implement trauma-informed, integrated care to address the health impacts of ACEs and also co-address social determinants of health. For example, True Care implemented ACE screening as a part of an organization-wide initiative to promote integrated care, which included embedding behavioral health providers within each clinical site and service line. Training and engaging leadership is a key element of organizational change in trauma-informed care, which ACEs Aware recommends for all primary care practices.[659,664]

Some case study sites collaborated with external partners for technical and/or funding support. For example, the implementation team at LAC-DHS partnered with First Five LA in the creation of the SHARK program, where specialists in childhood trauma, mental health, behavior, and development collaborate to provide temporary bridge services as children transition to community-based services that may take longer to establish. Six LAC-DHS pediatric clinics have joined the California ACEs Learning and Quality Improvement Collaborative (CALQIC). SRCH also joined the CALQIC, and it obtained an ACEs Aware Supplemental Provider Training grant to support its trauma-informed, ACE screening efforts.

Systems integration

Case study sites engaged both providers and staff to develop ACE screening and response workflows that could be adapted to different clinical settings. Developing these workflows was often an iterative process that incorporated evolving provider and staff feedback. For example, the implementation team at the SCPMG worked with the National Pediatric Practice Community on ACEs (NPPC)[741] to develop a clinical workflow that was piloted by staff at one site and adapted to the others.

Integration of ACE screening results in the electronic medical record (EMR), and electronic prompts for features of screening and response to toxic stress, such as presence of ACE-Associated Health Conditions (AAHCs), and patient education materials, helps streamline care. Four of the seven case study sites (SCPMG, LAC-DHS, True Care, and SRCH) integrated the screening results into their EMR, which was helpful in monitoring screening data longitudinally.[733] The other three sites (Sutter, Dartmouth CO-OP PBRN, and KPNC) did not. (Dartmouth CO-OP PBRN only piloted ACE screening for two weeks, and incorporation into the EMR was not part of that effort.) KPNC reported that clinicians at the ACE screening pilot sites felt that having ACE screening results integrated into the EMR would make screening more accessible and also make tracking impacts of interventions easier, but the organization also reported that "the pros and cons of adding patient ACE scores to the EMR need to be carefully considered."[678]

Some case study sites generated periodic progress reports; others did not have the capacity to systematically collect and analyze data.

Training providers and staff

Both child-serving and adult-serving providers have reported lack of confidence when asking about childhood adversity, and for a variety of reasons, current screening efforts may underestimate the prevalence of ACEs or under-recognize their associated health impacts.[1535,1552,1553] Based on learnings from the NPPC and the Resilient Beginnings Collaborative sufficient provider training on screening for ACEs and toxic stress can not only improve provider comfort with screening, but also increase awareness of health impacts of ACEs, generate support for screening, and establish a common language.[1554]

Most of the case study sites conducted training for both providers and non-clinical staff, like front desk personnel, because of their essential role in implementing ACE screening and response. The training topics included the health impacts of ACEs and toxic stress, the role of resilience and protective factors in buffering toxic stress, the screening tool and clinical workflow, principles of trauma-informed care, and patient resources. Many sites emphasized the importance of training all non-clinical staff to ensure a uniformly trauma-informed workforce. For example, True Care integrated its training into the onboarding process for all new hires. Some sites also conduct refresher courses to review concepts.

High-quality training is recognized as a critical component of successful ACE screening and response, and was thus the focus of the first phase of the ACEs Aware initiative, which included development and promotion of the *Becoming ACEs Aware in California*.[1555] Completion of this training or another approved Core Training is required to receive Medi-Cal payment for ACE screenings.[1538] Since the launch of ACEs Aware, many sites have incorporated the *Becoming ACEs Aware in California* Core Training[1555] into their training curriculum.

Supporting providers and staff

Case study sites recognized that providers and staff may experience vicarious trauma and burnout related to ACE screening and response. Besides including these concepts and highlighting staff resources in their trainings, some sites developed additional supports. For example, SRCH developed a staff support group and also strives to monitor provider and staff burnout through an annual survey, which has shown stable results. Some sites developed robust technical assistance systems. For example, providers at ACE screening sites at LAC-DHS work directly with a coach during the first month of screening. They also have regular check-ins with the coach and access to a website with training materials, phone and email support lines, and an online feedback form. Consistent with the efforts of these case study sites, The Substance Abuse and Mental Health Services Administration guidelines for implementing trauma-informed care describe the necessity of having procedures in place to support providers experiencing vicarious trauma, and providing ongoing workforce training and development.[664]

Screening approaches and tools

Because the published research on specific screening tools for ACEs and toxic stress is somewhat limited,[53,1539,1540] the California Surgeon General convened a clinical advisory team of subject matter experts and physicians experienced in ACE screening to review the literature and develop targeted recommendations. For pediatric ACE screening, the Pediatric ACEs and Related Life-Events Screener (PEARLS), developed by the Bay Area Research Consortium on Toxic Stress and Health (BARC),[1083] was recommended because of the rigorous research framework under which it was developed. It also enables patients' answers to be de-identified, meaning that respondents can disclose the total number of ACEs rather than specifying which ones. According to early data in pediatrics from a single large FQHC, randomization to the de-identified option invites greater patient disclosure and comfort.[1542] PEARLS's initial development, face validation, and concurrent validation with a limited set of health outcomes are published;[56,703] more extensive validation and outcomes evaluation[703] are currently underway. For adult patients, a screening tool based on the original 10 ACE questions, with the questions updated, was recommended.[3] As for the PEARLS, both identified and de-identified formats are available for providers in multiple languages. Data on disclosure quality, and patient and provider preference for adult ACE screening tools is more mixed than in pediatrics.[678,734] These screening tools, the ACEs and Toxic Stress Risk Assessment Algorithms, as well as patient education materials, are available for free at ACEsAware.org.[743]

As recommended by ACEs Aware, all sites except KPNC used either PEARLS or a screening tool based on the original ACE study.[3] KPNC used an identified paper screen based on the Behavioral Risk Factor Surveillance System questionnaire, plus the Connor-Davidson Resilience Scale. In addition to KPNC, SRCH also asked about resilience and protective factors in eight additional questions. More detailed consideration of the impacts of identified and de-identified screening, and screening for protective factors, is presented below under **Patient Safety, Acceptability, and Privacy Considerations**.

Case study sites varied in whom they screen for ACEs. For example, Sutter Health patients were screened as needed based on symptoms or conditions that may be related to toxic stress. True Care takes a systems-level approach and screens all children annually, adults upon establishing care, and pregnant women and their partners upon entering prenatal care. SRCH takes an intergenerational approach by also screening the parents of younger children during preventive health visits. Glowa and colleagues found that higher-risk ACE scores ($\geq$ 4) were present in 10% of adult patients at preventive health visits, compared to 30% at chronic illness follow-up and 33% at other non-acute visits.[736] Three sites included pregnant women in ACE screening. Screening in this population not only helps identify toxic stress-related pregnancy health risks and provide opportunities for interventions that improve pregnancy outcomes, but also offers an early intervention that could prevent toxic stress transmission to the next generation.[422]

ACEs Aware recommends that children be screened for ACEs and provided buffering care as early as possible, because adversity can be biologically embedded as early as the prenatal period,[421] and the signs of toxic stress can manifest even in infancy.[700] Assessment for ACEs should be ongoing, starting in infancy, with the recognition that ACEs tend to accumulate. In a multisite study of children exposed to or at risk of maltreatment, Thompson and colleagues found that by age six, children had an average ACE score of 1.94. Between ages six and 12, on average, they accumulated another 1.53 ACEs, and then between ages of 12 and 16, another 1.15.[742] Thus, continuous assessment is crucial, because health risks increase in a dose–response fashion with each ACE category experienced.[3] Children should thus be rescreened periodically to monitor for additional ACEs that might accumulate over their childhoods. Adults should be screened at least once in adulthood—and though ACEs occur in childhood (by definition) and therefore don't change, patient comfort with disclosure may change over time, so re-screening for adults may be considered.

Only two sites, SCPMG and Dartmouth CO-OP PBRN, tracked and reported the impact of screening on visit duration. Although time constraints were the most-cited anticipated barrier among providers completing the *Becoming ACEs Aware in California* training (71% of participants reported this concern),[1535,1552] Dartmouth CO-OP PBRN tracked and published data on visit duration, finding that visit length increased by less than 5 minutes for 91% of visits,[736] and SCPMG reported that ACE screening did not prolong visit length. These findings cohere with the literature, which has found little (usually adding under five minutes) or no increase in visit times.[736] Two published studies have even found that screening for ACEs increased efficiency of visits and actually reduced visit length.[730,731]

Patient safety, acceptability, and privacy considerations

None of the case study sites reported an increase in patient safety concerns, adverse events or mandated reporting as a result of screening. Because potential harms of ACE screening have been speculated, but have not been well documented or systematically described, one of the goals of the ACEs Aware initiative is to rigorously assess for any potential harms associated with screening as part of the statewide 53-site CALQIC effort.

The case study sites also did not experience challenges or barriers related to patient acceptability of ACE screening and response. This finding is consistent with the literature. Kia-Keating and colleagues reported high pediatric provider and patient acceptability with 92% infant well-child visits receiving an ACEs screening. Key to parent acceptability were the screening being offered by a trusted primary care provider, and receiving immediate education about the results. Providers said ACE screening helped patients understand the connection between mental and physical health.[729] Conn and colleagues also found that parents strongly supported ACE screening as a bridge to needed services, understood the intergenerational impact of ACEs, expressed a desire to break the cycle of adversity, and saw their child's pediatrician as a potential change agent who could help them meet their parenting goals.[728] Adult patients in the primary care and family practice settings have also reportedly expressed comfort with being asked about childhood adversity and recognized the relevance of these questions to their current health.[734,1536]

To enhance patient privacy, some case study sites (SCPMG, LAC-DHS, True Care) used a de-identified screening tool, which asks only for the total number of ACEs, while others (Sutter Health, SRCH, Dartmouth CO-OP PBRN, KPNC) used an identified screening tool, which asks patients to disclose which ACEs they have experienced. In a single large FQHC setting, early pediatric data show that patient randomization to use of the de-identified over the identified PEARLS format is associated with enhanced disclosure rates and patient comfort, and specifically, lower affective activation.[1542] However, some case study sites preferred the use of an identified screen. One of the True Care providers interviewed pointed out the benefits of knowing patients' specific ACEs in order to tailor behavioral health interventions that can assist in trauma recovery. SCPMG balances the benefits of each approach by using a de-identified ACE screening tool while also encouraging patients and families to disclose specific ACEs if they feel comfortable doing so.

ACEs Aware highlights that the ACE screening tool is intended for rapid identification of risk in the primary care setting, where brevity enables routine screening of multiple patients per day. In contrast, the mental health setting typically schedules much longer visits and is therefore conducive to tools designed to encourage more detailed disclosure of trauma histories. Thus, ACEs Aware recommends that primary care providers employ a tool with de-identified scoring as a way to be sensitive to patient comfort and facilitate fuller disclosure, particularly for children and adolescents.[743] For those patents requiring mental health intervention, treatment planning in the mental health setting may be facilitated by a broad suite of validated tools for ascertaining a more detailed trauma history to guide individualized and targeted treatment. Clinical workflows can outline the complementary roles of primary care and mental health providers in the process of ACE screening and response.[686-688]

RESPONDING TO ACEs AND TOXIC STRESS RISK

ACE screening 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 (see more in **Primary and Secondary Prevention Strategies in Healthcare**, in Part II). The ACEs Aware initiative recommends validating existing strengths and protective factors as a key part of clinical assessment and treatment planning for patients identified with ACEs and increased risk for toxic stress.[86]

The case study sites emphasize empathetic listening and building trusting relationships as crucial interventions for patients with ACEs. Patients with a history of adversity report that being listened to with compassion and understanding is one of the most important factors to facilitating their healing.[1556] Building trust between providers and patients is one of the key principles of trauma-informed care[659,664] recommended in this report as a fundamental primary prevention approach for all healthcare settings (again, see **Primary and Secondary Prevention Strategies in Healthcare** for further discussion).

The case study sites recognized the importance of reinforcing patient resilience and strengths in their response to ACE screening. KPNC used an identified paper screen based on the Behavioral Risk Factor Surveillance System questionnaire, plus the Connor-Davidson Resilience Scale. In addition to KPNC, SRCH also asked about resilience and protective factors in eight additional questions. Inquiring about positive experiences and strengths enhances patients' feelings of empowerment and self-efficacy, and helps clinicians and staff gain specific tools to address adversity and toxic stress.[1557] Building on strengths and reinforcing resilience-based coping have been identified as important to promote healing when addressing recent and past trauma in adult healthcare,[1558] and can amplify resilience, help patients feel "known" in positive ways, and increase the likelihood that strengths can be used during the delivery of care.[1557] A study of ACE intervention in low-income Black primary care patients using strengths-based and efficacy-promoting questions to motivate patient-identified health risk behavior change found that participants were well equipped with a variety of adaptive coping skills, numerous strengths, and high motivation to change despite having an ACE history and living in a highly under-resourced environment. The authors of the study concluded that these themes can guide trauma-informed approaches, which "can ultimately advance health equity for marginalized groups."[1559]

Case study sites varied in their interpretation of the ACE score. For example, SCPMG initially offered resources to patients with one to three ACEs and automatically referred those with four or more. However, some patients with low scores required support based on their specific experiences, while some patients with high scores did not require or desire assistance. Thus, providers now refer patients with at least once ACE to resources if they have toxic stress symptoms and want support or if the provider believes that a referral is necessary for any other reason. LAC-DHS providers gave materials related to ACEs, toxic stress, and community resources to all patients because even patients with low ACE scores had other needs (job placements, educational resources, COVID-related services, and housing/food support). The California Surgeon General's Clinical Advisory Subcommittee conducted a comprehensive review of the scientific literature and promising practices in the process of developing screening and response recommendations, including toxic stress risk assessment and response algorithms for both pediatric and adult care.[737] These clinical algorithms synthesize current science and best practice, and help standardize clinical assessment and approaches to addressing risk of toxic stress to improve quality of patient care.

Patient and family resources

The case study sites highlighted the importance of providing patient education on the impacts of ACEs and toxic stress as a clinical intervention. Many sites created their own patient handouts on stress management, parenting tips, and other issues. The ACEs Aware initiative recommends patient education on toxic stress and strategies to regulate the stress response as supplements to usual care for AAHCs. Strategies include supportive relationships (including caregivers for children, other family members, and peers); high-quality, sufficient sleep; balanced nutrition; regular physical activity; mindfulness and meditation; and access to nature (for in-depth discussion of each, see **Tertiary Prevention Strategies in Healthcare**, in Part II).[86,704] The ACEs Aware website also contains patient tools and informational handouts in the provider toolkit.[1560]

For those with neuropsychiatric manifestations of toxic stress, appropriate mental and behavioral healthcare is also necessary. The most commonly used referral resources for the case study sites were integrated or community-based, trauma-informed mental or behavioral health services and parenting programs. Some case study sites developed novel resources, such as the eConsult for Behavior, Development, and Adversity, and the Strong, Healthy, and Resilient Kids program at LAC-DHS.

Many case study sites emphasized the need for further collaboration with county- and community-based resources to develop local networks of care. For example, one interviewee from KPNC highlighted Nurse-Family Partnership, a home visitation program, and the Black Infant Health Program, an evidence-informed intervention that uses a group-based approach to improve infant health among Black women,[1561] as important partners for preventing and addressing the impacts of toxic stress.

OPPORTUNITIES AND CHALLENGES

While most case study sites found it feasible to implement ACE screening and response with institutional support, they aspire to increase access to resources and bolster local networks of care. Due to the COVID-19 pandemic, many have experienced challenges such as increased patient stress and overall disruptions in primary care, including screening. Some case study sites found new opportunities in the pandemic, such as normalizing conversations about toxic stress and increasing telehealth capabilities (see EXAMPLES OF CLINICAL SYSTEMS' ADAPTATIONS TO COVID-19).

Many of the case study sites are planning exciting future initiatives. For example, the Dartmouth CO-OP PBRN plans to conduct a study on resilience factors among patients with ACEs, and LAC-DHS hopes to expand screening to all of its pediatric, women's health, and adult primary care, and juvenile correctional settings. Three of the sites have formally published research findings. Opportunities for the future include securing additional research funding to advance practices for screening and response for ACEs, toxic stress, and AAHCs. Longitudinal studies on longer-term impacts of clinical interventions targeting the toxic stress response are sorely needed.

EXAMPLES OF CLINICAL SYSTEMS' ADAPTATIONS TO COVID-19

The COVID-19 pandemic posed numerous challenges for case study sites, including delays across all sites and programs, increased patient and team stress, and disruptions to care, such as decreased access to medications and insurance, and difficulties in making the technology necessary for telehealth available and accessible to patients. During the height of the pandemic, when non-urgent in-person visits transitioned exclusively to telehealth appointments, difficulties were exacerbated for those most in need of screening and services: families and communities isolated by the digital divide, that is, lacking financial means to own a computer or living in areas without reliable high-speed internet or mobile network service. Even when telehealth services are accessible, not all patients may be familiar or comfortable with the process. Despite these setbacks, some early adopters found that the pandemic provided a few new opportunities, such as normalizing conversations about toxic stress and increasing providers' telehealth capabilities.

Challenges and Next Steps

Southern California Permanente Medical Group. SCPMG slowed its goal of training all pediatricians to screen for ACEs at all well-child visits. Once clinics reopened, ACE screenings restarted as part of in-person visits. The group also continues to work toward developing local coordinated-care networks and is on the way to rolling out PEARLS screening region-wide by spring 2021.

Los Angeles County Department of Health Services. Trainings, visits, and treatment services were converted to virtual interfaces. Ultimately, the county hopes to expand screening to all pediatric clinics, women's health, adult primary care, and juvenile correctional settings.

Santa Rosa Community Health. The organization transitioned most visits to telehealth, although screening continues for younger children at in-person well-child visits. Pediatric providers were meant to complete the online *Becoming ACEs Aware in California* Core Training[1555] and trainings were to be developed for family medicine sites, but both of these efforts were paused. However, SRCH has joined CALQIC and obtained an ACEs Aware Supplemental Provider Training grant to support its trauma-informed ACE screening efforts.

Kaiser Permanente Northern California. The physician ACEs lead built on the lessons learned from the pilot to restart screening efforts at KPNC. Some sites currently screen for ACEs in routine prenatal care for English-speaking women 18 years or younger, and they are considering avenues to expand screening to other patients and sites.

Dartmouth CO-OP Primary Care Practice-Based Research Network. The physician ACEs lead plans to conduct a follow-up study to assess resilience factors among patients

EXAMPLES OF CLINICAL SYSTEMS' ADAPTATIONS TO COVID-19

with ACEs, evaluate the utility of this information, and examine whether patients are interested in pursuing treatment related to their history of ACEs.

True Care. True Care consolidated its clinical sites and is screening for ACEs via telehealth visits. It plans to develop on-site parenting and group-therapy programs, as well, once these activities are safe. Anecdotally, it noted an increase in patients experiencing stress and mental health symptoms and was quickly able to transition its behavioral health services to telehealth.

Sutter Health. Many providers worried about not having enough time or support to implement ACE screening. On the other hand, the ACEs physician lead at Sutter believes that, particularly in light of increased patient stress due to COVID-19, ACE implementation efforts to date have helped to normalize conversations about toxic stress.

Systems–Level Implementation Considerations

Coordinating a thoughtful cross-sector response to address toxic stress as a health condition represents an emerging, evidence-based clinical innovation. By deploying a well-formulated public health approach to prevention, screening, and treatment through the ACEs Aware initiative and coordinated cross-sector efforts, the state of California aims to cut the burden of ACEs and toxic stress in half in the next generation.

This report has provided the evidence to support a broad effort to finance and implement a coordinated response system for intervening on toxic stress across California.

Screening for and responding to toxic stress in primary care addresses a significant upstream root cause for myriad poor health and social outcomes, enhances family and community resilience, and can help advance health equity. Such cutting-edge clinical innovation relies on well-coordinated, rigorously designed implementation science and quality improvement (QI) principles and efforts.[1562-1570] Success requires integration of complementary efforts across systems partners, including primary care providers, mental health and social service providers, and cross-sector leaders, including in education, justice, early childhood, public health, social services, and entities that regulate and pay for services. Cross-sector trauma-informed and toxic stress-responsive training for all relevant workforces is essential.

Across the spectrum of desired goals—prioritizing prevention, catalyzing practice transformation, and fostering research and innovation—specific implementation strategies emerge as crucial to success (**Figure 34**). Prevention involves a sustained plan of action to promote safe, stable, nurturing relationships and environments and to address the structural determinants of health and well-being through evidence-based policies and programs.[23,31] These efforts require coordinating the expertise of myriad community and ecological partners into a thoughtful network of care and response. Practice transformation requires universal screening for

Figure 34. The spectrum of coordinated interventions needed to achieve prevention, practice transformation, research, and ongoing innovation. Reproduced with permission from the Center for Youth Wellness.[1532]

ACEs to identify risk for toxic stress, effective referral systems, a comprehensive and coordinated service array, and adequate payment for these services.

This report has provided the evidence to support a broad effort to finance and implement a coordinated response system for intervening on toxic stress across California. This includes creating methods for continuous QI, promoting trauma-informed and patient-centered medical homes, reimbursement strategies, addressing adequacy of mental healthcare services, innovating on data-sharing and integration platforms, deep provider engagement and training, implementation of best and promising practices, avoiding unintended harms, expanding available networks of referrals and supports to address toxic stress, and supporting systems-level policies to coordinate these resources. Effective implementation requires alignment of health services, health delivery, and allied service systems.

ACEs Aware is guided by the best evidence to date and incorporates rigorous analysis and planning to bring to bear the substantial body of science on effective interventions to address the myriad impacts of ACEs and toxic stress. A secondary aim is to advance the knowledge base in regard to clinical approaches to screening and coordinated cross-sector responses for toxic stress, utilizing QI and qualitative inquiry methodologies through the California ACEs Learning and Quality Improvement Collaborative (CALQIC). Further, ongoing investment in research is an important part of the pipeline, as exemplified by the $9 million investment in the California Initiative to Advance Precision Medicine, to hone precision medicine approaches for advancing diagnostic and therapeutic capabilities to address toxic stress.[337]

SYSTEMS FOR QUALITY IMPROVEMENT

ACEs Aware seeks to embed thoughtfully designed strategies around coordinated data gathering, evaluation, dissemination, and continuous QI among key partners. CALQIC serves as a centerpiece of ACEs Aware. This 18-month public-private partnership is focused on rigorously and iteratively studying implementation of

ACE screening and response in 53 clinics in seven diverse California regions. Led by the University of California, San Francisco, with partners at the RAND Corporation and the Center for Care Innovations, CALQIC methodically assesses best practices and monitors for adverse events to inform the next phases of implementation and learning, with a focus on promoting health equity. Participating organizations receive on-site and virtual coaching, technical assistance, site visits to exemplar organizations, and grants. The CALQIC network was designed to drive QI at scale for intervening upon and stemming the crisis of ACEs and toxic stress, while surfacing and responding to unintended consequences. Authentic community engagement, a health-equity lens, and awareness of historical and ongoing disparities are vital components at every stage of program implementation (see **The ACEs Aware Initiative**, earlier in Part III, for more details).

ACEs Aware seeks to accelerate adoption and spread of best practices to advance successful prevention, screening, and treatment for the impacts of ACEs and toxic stress in the healthcare setting. Innovation theorists often classify adopters of new practices into five categories: innovators, early adopters, early majority, late majority, and laggards (**Figure 35**). Once innovators and early adopters have embraced a change, they pave the way for the early majority by problem-solving and persevering through obstacles to implementation and sharing their learnings. Subsequently, as those in the early majority experience the benefit of the innovation, they serve as proof points to demonstrate efficacy of the innovation, and in so doing, induce the late majority.[1566] Using these principles of

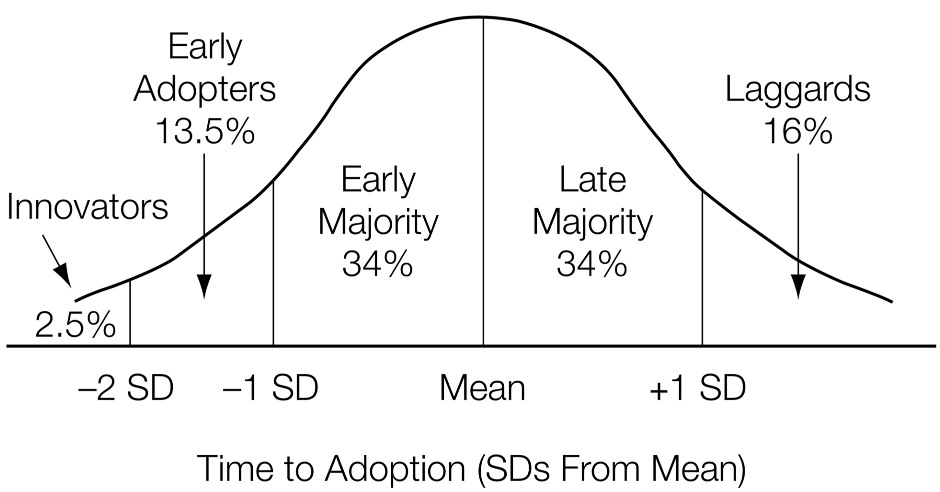


Figure 35. *Innovation adopter categories. Reproduced with permission from JAMA. 2003. 289(15): 1969-1975.* [1566]

innovation diffusion, ACEs Aware is finding and supporting innovators, investing in early adopters, and facilitating visibility and shared learning through grant funding, training and capacity-building, communications strategies, and through its learning collaborative (CALQIC).

Trauma-informed practice and the Patient-Centered Medical Home model

The medical home philosophy emphasizes primary care coordination that is patient-centered, accessible, culturally competent, and focused on comprehensive, high-quality support.[1571] The capacity for a medical home to become a trauma-informed, multidisciplinary system is a foundational building block of this initiative. Universal implementation of **trauma-informed care** (TIC) improves care for all patients, but especially for those with a history of adversity.[659] Its principles support a strengths-based and non-judgmental approach to toxic stress assessment and intervention, and help prevent inadvertent re-traumatization of patients. Providers can also empathize, motivate, and empower patients or clients with active listening skills and motivational interviewing techniques.[660,661] TIC is therefore beneficial for all patients, providers, and staff. The TIC framework, adapted by ACEs Aware from the Substance Abuse and Mental Health Services Administration with an enhanced focus on the health impacts of adversity, involves the following key principles:[659,664]

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.

Another key element in trauma-informed care is self-care. Just as all healthcare workers are trained in measures of infection control to limit risk of contracting a communicable disease, all staff working with trauma-exposed patients must also learn to recognize and attend to compassion fatigue, secondary or vicarious trauma, and burnout.[628,1046,1572] A recent study found a 2.5-fold increased risk of burnout for physicians with four or more ACEs.[1573] Practicing compassionate resilience to maintain provider well-being while caring for patients is an important step for combatting staff compassion fatigue, burnout, secondary traumatic stress, vicarious trauma, and other workforce concerns. Systems must be in place to help support the health and well-being of staff who are implementing ACE screening as a tool for identifying risk of toxic stress and applying evidence-based staff interventions like supportive coaching to enhance the success of their clinicians and reduce risk of turnover.[1574]

These principles can be used within the Patient-Centered Medical Home (PCMH) model to create a safe and healing experience for children, families, and adults who have experienced ACEs.[56,1040,1575] PCMHs dedicated to preventing and healing toxic stress should train all staff in TIC principles, and how to clinically assess risk for and intervene on toxic stress physiology, and in doing so, provide care coordination for a range of clinical and community interventions and resources within an integrated, multidisciplinary system of care (see **Primary and Secondary Prevention Strategies in Healthcare** and **Tertiary Prevention Strategies in Healthcare** in Part II for more details).

California's existing PCMH infrastructure and transformation efforts can be leveraged to meet the prevention, early intervention, and healing goals of toxic stress screening.[1576-1578] Key PCMH components relate to access to care, teamwork, and the technology to coordinate referrals, data, and care.[1579] Attention is also needed in regard to developing an organizational climate that encourages implementation optimization and use of evidence-based interventions in PCMH settings.[1564,1580] Yet even with these structural elements in place, research shows that patients and families often do not experience care or the outcomes intended for the PCMH model.[1576] Several key competencies for optimized outcomes are required:

- Establish *safe environments and trusting, ongoing relationships* between clinical care teams and patients so families can feel safe when they disclose personal experiences and know they can count on clinical teams for their care.
- Conduct and anchor care to *whole person and integrated screening and assessments* of patient and family risks, needs, strengths, and context, including conditions and resources in their communities.
- Engage patients and families in relationship-centered, *shared decision-making* discussions that prioritize goals and troubleshoot problems so families can take steps toward prevention and healing.
- Conduct pre-visit planning to prepare and *optimize encounter time* to implement brief interventions, such as personalized education and counseling.
- Establish *relationships and coordination methods with the wraparound*

services and additional treatment to support patients and families in need so that referrals are successful and follow-up and integration of care is achieved. This includes supporting behavioral health integration and multidisciplinary approaches within the clinic, as well as expanding access to external resources through the development of networks of care.

A systems-level approach to support trauma-informed, patient-centered medical homes would include (a) funding and incentives for best practices; (b) creating, disseminating, and coordinating efforts to expand this model across federally qualified health centers in California; (c) creating performance measurement standards and requirements, (d) offering free provider trainings with Continuing Medical Education (CME) and Maintenance of Certification (MOC) credit;[1555] and (e) supporting QI efforts.

Systems–level changes

State and local policymakers, payers, and leaders of community collaborations can contribute to the success of California's vision to reduce ACEs and toxic stress by half in a generation by coordinating the many interlocking systems, policies, funding streams, and programs that affect the capacity of California's healthcare providers and communities. This coordination will advance successful screening for, preventing, treating, and healing the impacts of ACEs and toxic stress. Such alignment of activities is key for effective implementation and sustainment.[1564]

To support the systems-level changes needed to effectively prevent and address ACEs and toxic stress, ACEs Aware is using the following strategies.

Creating standardized clinical workflows and algorithms to guide screening and response.

ACEs Aware has developed screening workflows and toxic stress risk assessment and response algorithms for both pediatric and adult care.[737] These clinical algorithms were developed to standardize clinical assessment and approaches to addressing risk of toxic stress to improve the quality of patient care. Recommendations include patient education on toxic stress and strategies to regulate the stress response as an adjunct to usual care for ACE-Associated Health Conditions (AAHCs), including: supportive relationships; high-quality, sufficient sleep; balanced nutrition; regular physical activity; mindfulness practices; access to nature; and appropriate mental and behavioral healthcare (especially in the context of integrated primary care and behavioral health where available) as needed.[603,704,1035] Coordination with other sectors, such as schools, child care, justice, welfare, and public health, can be done sustainably when providers leverage the healthcare team.[686-688]

Providing grants to support providers and build their capacity.

ACEs Aware awarded $14.3 million in grants to 100 organizations in the areas of provider engagement, training, and communications, in order to deepen engagement and encourage the proliferation and sharing of best practices and strategies.

Building and supporting functional networks of care.

ACEs Aware is creating a Network of Care Roadmap to improve collaboration and coordination across the healthcare and cross-sector systems to address toxic stress. Networks of care can be locally established between health plans, health centers, clinicians, and clinical and community organizations in addressing ACEs and toxic stress in primary care.

In addition to providing payment, training, and implementation support, the success of the ACEs Aware initiative also requires supportive "top-down" policies and the integration of requirements related to ACE screening, such as:

- Evidence-based or evidence-informed screening and preventive care guidelines related to toxic stress and care management in the context of specific AAHCs;
- Performance metrics and performance feedback to drive continuous QI in prevention, identification and response to ACEs, toxic stress, and AAHCs;
- Programs to identify and financially reward providers and clinics that are meeting or exceeding performance metrics to incentivize high quality of care for ACEs, toxic stress, and AAHCs (value-based purchasing programs);
- Continuing to offer ways to meet provider maintenance-of-certification requirements through continuing education on screening for and addressing ACEs and toxic stress;
- Population health management strategies to identify and focus care for patients at higher risk due to ACEs and toxic stress;
- Effective use of the electronic medical record (EMR) to streamline care for ACEs, toxic stress, and AAHCs;
- Implementation of increasingly effective and relevant evidence-based interventions for preventing, screening for, and responding to ACEs and toxic stress, through investment in toxic stress research and clinical innovation; and
- Support for building system capacity to deliver appropriate targeted services to meet patient and family needs arising from exposure to ACEs and toxic stress.

Billing and referrals to comprehensive services

Currently, ACEs Aware reimburses trained providers to screen for ACEs in primary care and other specified settings. Also important is the alignment of diagnostic services and billing codes to ensure that providers can receive reimbursement for addressing the needs and opportunities to promote healing that are revealed through ACE screening. A systems-level approach is required to consider and facilitate enhanced models of care, payment models for preventive visits, acute hospital and emergency room visits, and resources for individuals with emergent and/or chronic conditions. Creating diagnostic and service codes for symptoms of toxic stress physiology, such as AAHCs, with EMR prompts, will help improve coordination of care, reimbursement for services, and QI measurement.

Currently, clinicians can only choose a diagnostic code for physical, mental, or developmental health diagnoses; they cannot add a unifying diagnosis of toxic stress physiology. This may limit interdisciplinary and root-cause approaches to the medical management of AAHCs, and inhibit efforts to provide trauma-informed and healing-centered interventions.[64] These intervention approaches could target the root impacts on the nervous system, immune system, endocrine system, metabolic systems, and/or genetic regulatory systems.[6-8,11,12,603,1420,1581] Shifts in diagnostic and billing codes for AAHCs and different clinical risk levels for toxic stress, combined with enhanced payment models to support brief interventions, care coordination, referrals, and frequency of follow-up, will enable more effective and coordinated action to prevent and heal the impacts of ACEs.

From a systems perspective, strengthened closed-loop referral systems are necessary to help enact evidence-based interventions for toxic stress mitigation in children, adults, and families. The goal is for patients to be able to seamlessly access appropriately targeted services that can interrupt or mitigate the toxic stress physiology. This will also require enhanced availability of the comprehensive services to address ACEs, toxic stress, and accompanying social determinants of health that can be coordinated through a primary care home, especially in rural and underserved communities.

Intervening on toxic stress requires a coordinated and often multidisciplinary approach. In addition to the primary care provider, there are important roles for, among others, educators, wellness navigators, care coordinators, home visitors, peer support, and referrals are often needed to services such as biofeedback, neurofeedback, mindfulness, meditation, nutritional support, parenting support, and behavioral health services like psychotherapy and psychiatry.[722,1035,1582,1583] In adopting medical home principles, practices and hospital systems should start to identify and amplify their multidisciplinary partners and local referral networks.

Resources and services could include linkages to economic supports, legal supports (including medical-legal partnerships), high-quality evidence-based home visitation services, child care, preschool and school enrichment with family engagement, and parenting or family relational skill-building.[23,31,685,1584,1585]

Policies that allow for the credentialing and/or compensation for non-licensed professionals and non-medical supports could be helpful. Many roles contribute to optimal results, including care coordinators, health educators, patient navigators, and family-to-family and peer-to-peer professionals who are also experts in (1) healthy parenting and establishing healthy parent–child attachment, (2) strategies to coach and activate patients in self-care, and (3) evidence-based trauma healing approaches that build resilience, including fostering healthy responses to stress, restoring a healthy sense of self, and supporting positive relational skills often diminished through exposure to ACEs. Nonmedical certification programs are largely absent in behavioral health, unlike for geriatric care.[1586]

MENTAL AND BEHAVIORAL HEALTH WORKFORCE

It is important to note that most patients with non-neuropsychiatric manifestations of toxic stress will not require a mental or behavioral health referral. However, for those who do require this set of resources, there are some relevant considerations to be made.

In 1991, public mental health services in California shifted to a decentralized system whereby counties became the primary providers for Medi-Cal and uninsured, low-income clients. Through a mix of federal matching funds, Mental Health Services Act funds, and other local revenues, local mental health plans provide a range of services, including inpatient treatment, adult residential treatment, day rehabilitation, case management, and crisis intervention, among others. The Affordable Care Act increased access by deeming behavioral health as one of 10 essential health benefits. California chose to cover all essential health benefits, resulting in a substantial expansion of behavioral health services. At that time, most low-to-moderate-intensity behavioral health services shifted to the responsibility of Medi-Cal managed care plans, leaving counties to continue to provide services for adults with more intensive conditions. Although progress has been made in insurance coverage for behavioral services, there remains a shortage of behavioral healthcare workers to satisfy the growing needs, especially in low-density regions of the state like the Inland Empire and the San Joaquin Valley.[1587] The coronavirus disease 2019 (COVID-19) pandemic has further increased the demand for behavioral health professionals.[1588]

In 2016, there were just over 80,000 licensed behavioral health professionals in California. Many current license holders are close to retirement; 45% of psychiatrists and 37% of psychologists are over the age of 60.[1587] There is an urgent need to invest in building and fortifying a racially and ethnically diverse behavioral health workforce and to ensure equitable regional distribution, possibly by harnessing the potential of technologies such as telehealth.[1589]

Integrated primary care and behavioral health within the same settings is one promising model[686-688,1035] and should be a key goal of statewide efforts. Though models that allow for warm handoffs and true interdisciplinarity in care planning are the gold standard, there are other ways to expand access to behavioral and mental healthcare when it is needed. These include supporting primary care providers to prescribe psychiatric medications for uncomplicated patients under the guidance of psychiatrists, via telehealth or other consultation. This practice requires education efforts that help primary care providers acquire the knowledge and skills as well as attend to their attitudes around mental health interventions and evidence-based medicine.[1590,1591] California's expansion of reimbursement for telehealth-provided services will provide payments comparable to in-person visits and opens the opportunity for greater coordination between behavioral health and primary care providers.[1592]

DATA SHARING AND INTEGRATION

EMR technology presents challenges as well as opportunities for any healthcare innovation or transformation. Under privacy and security laws, health data are heavily regulated to protect the collection and sharing of individuals' information within and across systems. In addition, data are collected in many different formats, creating obstacles to simple transfers from one program to the next.[1593] Currently, over 85% of office-based physicians use an EMR system.[1594] Though they can increase administrative burden,[1595,1596] EMRs have been associated in several studies with reductions in medication errors, improved health system costs, and improved communication among providers, patients, and other clinicians.[1597-1599]

Novel frameworks are beginning to capture the cross-sector and cross-disciplinary data needed to track ACEs. For example, the Semantic Platform for ACEs Surveillance integrates information streams from multiple sources, including databases and the literature.[1600,1601] By overcoming interoperability challenges, the system aims to assist clinicians, public health agencies, social services, and researchers in studying ACEs and toxic stress, delineating clinical and population-level trends, and coordinating and carrying out preventive or therapeutic strategies. Other efforts focus on providing patients with data-sharing platforms to complete screening tools and share data with providers voluntarily in ways that do not violate privacy or confidentiality regulations, such as the Well-Visit Planner and the CHADIS.[1602,1603]

Platforms for electronic prompts for features of screening and response to toxic stress, such as assessing for presence of AAHCs, and patient education materials, would streamline care. The sharing of key data across the services and programs that are part of the care team would amplify efficiency and positive outcomes.[1604] This is especially important in order to avoid multiple and uncoordinated efforts to screen the same child or adult for ACEs across different service providers and programs. This is also important to coordinate the care of families receiving care separately, for example, in the child and adult health systems. As noted, engaging patients and families to carry and share their own data as they wish is one option to consider. Assessment of methods to enable this option is underway.

In addition to improving patient care, robust data-sharing systems are needed to advance scientific investigation of ACEs, toxic stress, and AAHCs. Optimized data systems are ones in which data are discoverable (so users can find what they need), open (with open and timely access to data), linked (readily associated with related and supporting data, to enable insightful understanding), useful (presented in a compelling, understandable way), and safe (from deterioration, hacks, or becoming obsolete). Because successful data-sharing systems will require participation across multiple sectors, development and management of effective data systems is complex. Developing and maintaining optimal data systems will require communication not just across the sectors involved in advancing the science of ACEs and toxic stress, but also between data users and data system developers, employing a flexible, collaborative approach.[1604]

California also has a wide array of community-based city, county, and regional initiatives that foster a shared vision for well-being and healing, with sustainable cross-agency and cross-sector collaboration to integrate and improve health, education, justice, early childhood, public health, and social services. Increasingly, innovations are emerging to braid and blend funding in ways that optimize the availability, efficiency, and effectiveness of services (see **Part II**). One example is the Handle with Care initiative, currently being implemented in two California counties, which helps law enforcement communicate with schools when children are present at the scene of a traumatic encounter (such as a domestic disturbance). Without communicating any confidential information, the program enables the child's school to be notified that he or she should be "handled with care" and engages educational personnel to surround the child with extra precautions in days that follow a traumatic event to prevent further harms. Such cross-sector initiatives will play a central role in the systems coordination required to successfully recognize, prevent, mitigate, and heal the population-wide and intergenerational impact of ACEs and toxic stress in California.

Approach to Environmental Scans of Statewide Trauma-Informed Work

In 2019, Governor Newsom appointed Dr. Nadine Burke Harris as California's first-ever Surgeon General. One of her first actions was a fact-finding process to learn about what was already being done and working well to address Adverse Childhood Experiences (ACEs) and toxic stress among children, families, and communities in California. This exploratory effort, which included a statewide listening tour and environmental scans to assess cross-governmental and community efforts, was designed to inform the planning process for cross-sector strategies to address ACEs and toxic stress statewide.

Multiple California state agencies collaborated with stakeholders to further the collective understanding of trauma-informed practices and policies that have been adopted and/or implemented across the state. The Injury and Violence Prevention Branch of the California Department of Public Health, the Office of Child Abuse Prevention of the California Department of Social Services, and the Essentials for Childhood (EfC) Initiative coalition and its Trauma-Informed Practices Subcommittee identified a need to determine what baseline efforts were underway across state organizations and agencies to make California a more trauma-informed and resilient state. To strengthen understanding in this area, a survey was initiated in March 2020 to collect information on current trauma-informed practices and policies in order to develop tools, trainings, and supports to help California state departments and agencies expand and build upon their existing efforts.

Further, ACEs Connection—an information-exchange catalyst and social network community of practice in the worldwide ACEs and toxic stress movement—had been working in partnership with the EfC Initiative to identify and document ACEs-related activities (e.g., trainings or events) at the local level. In this effort, ACEs Connection developed a mapping tool for displaying ACEs and trauma-informed organizational activities geographically and by sector.[1529] Three California counties (Fresno, San Diego, and Santa Barbara) have been piloting its use to help track their local ACEs-related work.

These multiple efforts to assess what state and local agencies and organizations are doing to address ACEs and toxic stress were brought together through a partnership with the California Office of the Surgeon General (CA-OSG), Health in All Policies Task Force (HiAP), Public Health Institute, ACEs Connection, and the EfC Initiative. As a result of this collaborative partnership, these separate activities were coordinated using similar information-gathering processes with allied aims and tactics. Specifically, in consultation with the other partners, the CA-OSG developed a formal environmental scan survey to assess ACEs-related activities at the county level; and ACEs Connection and the EfC Initiative developed a state-governmental-level survey to document current state-level ACEs activities. The EfC Initiative workgroup, including ACEs Connection and the California Strategic Growth Council, piloted the state survey before it was released to the field in May 2020. As the two surveys were being developed, a coordinated effort was made to align the two sets of survey questions for consistency and comparability.

The two surveys were undertaken at a critical moment when many drivers of trauma, such as systemic racism and economic insecurity, had been laid bare and government systems tasked with addressing these ever-changing and complex issues were strained by added demands as a result of the coronavirus disease 2019 (COVID-19) pandemic and historic wildfires. Trauma-informed systems, practices, and policies are one very important way to address these multifaceted and complex issues. Thus, there was a clear need to understand and advance the status of current state and local adoption and implementation of trauma-informed efforts.

PURPOSE OF THE STATE AND COUNTY SURVEYS

The purpose of both surveys was to develop a baseline state-of-the-state understanding of the current level of awareness; training and education efforts; and adoption and implementation of ACEs-related and trauma-informed policies and practices throughout California.

The results of the surveys are intended to inform the cross-sector strategies, including of the ACEs Aware and EfC initiatives, around state- and local-level efforts to incorporate trauma-informed approaches into their systems and ultimately reduce ACEs. Results of the surveys will also be used to assess the state's capacity to enhance current efforts and inform future implementation of ACEs Aware. Results will also be used more broadly to aid the CA-OSG, California Department of Health Care Services, California Department of Public Health, Health in All Policies Task Force, the EfC Initiative, and Governor Gavin Newsom's administration in better supporting families and children, including those who have experienced ACEs or trauma. The survey results will also enable identification and promotion of existing promising practices, and pinpointing of where work at the state and county levels can be supported and strengthened.

SURVEY QUESTIONS

The surveys asked respondents about the reach and extent of their organization's work related to ACEs, toxic stress, and trauma-informed care, including training, screening, existing supports, funding, and challenges. Sample questions on both the state and county surveys include:

1. What steps has your organization taken to implement ACEs/toxic stress-responsive and/or trauma-informed practices, policies, or environments at an organizational/programmatic level?
2. What steps have staff in your organization taken to build awareness of ACEs science/toxic stress and/or incorporate trauma-informed practices, policies, or environments at an organizational level?
3. What training model does your organization use to incorporate ACEs/toxic stress-responsive and/or trauma-informed practices, policies, or environments?
4. What other factors have facilitated the ability of your organization to support ACEs/toxic stress-responsive and/or trauma-informed practices, policies, and environments, if any?
5. What other factors have challenged the ability of your organization to support ACEs/toxic stress-responsive and/or trauma-informed practices, policies, and environments, if any?
6. What resources are needed to support future implementation of ACEs/toxic stress- responsive and/or trauma-informed practices, policies, or environments?

The questions for both the state and local surveys were informed by ACEs Connection's Milestone Tracker,[1605] which organizations use to monitor progress toward to becoming more trauma-informed.

STATE SURVEY DISTRIBUTION

In August 2020, the state survey was sent to contacts in healthcare and allied sectors, such as public health, education, early childhood, home visitation, justice, and social services. The state survey was distributed utilizing a broad methodology that relied on formal state organizational structure, and a targeted methodology using personal connections by the survey team to: key leaders at six state agencies and personal colleagues in work groups, task forces, and similar bodies linked to the EfC Initiative, Health in All Policies Task Force, and

CA-OSG.

In September 2020, initial outreach for the state survey reached approximately 330 individuals in approximately 40 state agencies, departments, boards, and offices. During the data collection period, the survey team identified gaps in participation and sent additional messages to increase the response rate. In all, approximately 400 individuals from 50 state departments were emailed directly about the survey.

COUNTY SURVEY DISTRIBUTION

Also in August 2020, the county survey was distributed using a broad methodology to reach cross-sector county leaders from all 58 counties and 61 local health jurisdictions via personalized emails sent from the California Surgeon General, which also requested that they share the survey with other relevant parties in their county departments and agencies. The survey was also distributed using a targeted methodology: the survey team used their network of ACEs champions across the state to do further promotion, including asking key state partners to forward the survey request from CA-OSG to targeted county staff.

County staff that were contacted included health officers, maternal child adolescent health, public health, social services, behavioral health, substance use, and social services directors, chief probation officers, First 5 directors, superintendents of schools, and contacts within child abuse prevention coordinators and councils, and Help Me Grow. In all, approximately 550 individuals from 58 county organizations were emailed directly about the survey.

SURVEY RESPONSES

In total, 261 individuals at 32 state departments responded to the state survey in September 2020. Of those respondents, most individuals worked at the program level (119) or branch/center/division level (106), while a few reported working at the department or agency-level (36). Some 257 individuals serving 57 of the 58 counties in California responded to the county survey. Respondents represented the healthcare, public health, social services, early childhood, justice, and education sectors, and included respondents from organizations such as First Five, Help Me Grow, and Parks and Recreation. This response rate was considered remarkable given the challenges facing state and county agencies in the midst of the COVID-19 pandemic.

NEXT STEPS

Full analysis of the state and county surveys was not available at time of publication of this report. Plans include one or more written reports communicating these results, with release in spring 2021. These reports will include a summary of the results of the two surveys, as well as recommendations for state and local agencies and organizations regarding promising practices that can be used to make California a resilient and trauma-informed state, how to better meet the needs of the Californians who have faced adversity, and how to best support the staff who provide those services.

Preliminary review of the survey responses indicates significant activity underway in California's efforts to become a trauma-informed state. The findings will be used to educate stakeholders about the opportunity to engage best practices within state and local efforts to promote well-being and reduce negative health outcomes associated with ACEs and toxic stress. Survey results will also be used to identify where state- and county-level policies, programs, and interventions can be strengthened, aligned, and coordinated.

The survey team is deeply appreciative of the individuals who took time to respond to the local- and state-level environmental scan surveys. Despite the tremendous pressures brought about by the events of 2020, hundreds of individuals shared their existing efforts and recommendations to assist collaborative efforts and ensure that California becomes a more resilient and trauma-informed state.

PART IV

What Lies Ahead

ACEs Aware Phase IV: Evaluation

Adverse Childhood Experiences (ACEs) and toxic stress are major root causes (drivers) of multiple short- and long-term negative health and well-being outcomes among children and adults in California. Implementation of the statewide ACEs Aware initiative, starting with provider training towards the comprehensive integration of ACEs and toxic stress screening and treatment into existing healthcare systems, and partnered with enhanced allied cross-sector efforts, is a key first step towards achieving the overarching goal of cutting ACEs and toxic stress in half within a generation.

Given that the ACEs Aware initiative represents the first statewide ACEs and toxic stress screening and treatment program of this scale, a strong evaluation plan is an integral part of ensuring continuous quality improvement (QI), assessing program effectiveness, and generating implementation lessons. The evaluation

KEY OBJECTIVES OF THE ACES AWARE INITIATIVE

1. To inform and empower primary care clinicians with the latest evidence on how to recognize, address, and prevent ACEs and toxic stress.
2. To incentivize early detection and early intervention for toxic stress by reimbursing providers for screening for ACEs, which includes 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.
3. To increase awareness and utilization of cross-sectoral, evidence-based and promising clinical and community interventions for preventing and addressing the toxic stress response.
4. To build clinical capacity for screening for—and clinical and cross-sector community capacity for response—to ACEs and toxic stress by investing in clinical quality improvement and community networks for response.
5. To improve clinical outcomes and health equity by enhancing the quality and specificity of healthcare provided to individuals exposed to ACEs and/or at risk for toxic stress, through rigorous, evidence-informed methods.

plan has three components:

1. Collection (already ongoing) of key clinic, provider, and patient-level outcomes related to optimal clinical response to risk of toxic stress, by the California ACEs Learning and Quality Improvement Collaborative (CALQIC);
2. Quarterly internal tracking (already ongoing) of provider screening efforts by the California Department of Health Care Services (DHCS) and the Office of the California Surgeon General (CA-OSG); and
3. A future external evaluation (planned but not yet funded) that independently assesses overall systems-level changes in healthcare outcomes, utilization, and costs, by combining inputs from the two efforts listed above, plus supplemental administrative data.

In the short term, CALQIC is providing training and technical assistance for 18 months to a subset of regional healthcare systems, including 53 clinical systems and their providers in seven regions across the state. As part of this QI effort, CALQIC will be collecting and tracking detailed process data on patient and family health and well-being, patient–provider relationships, patient and family trust, provider burnout, and unintended adverse events associated with screening (for details, see **The ACEs Aware Initiative** in Part III). All 53 learning collaborative clinics participate in qualitative and quantitative evaluation activities. CALQIC also includes two "deep dive" evaluations in urban and rural counties to focus on how clinic- and provider-level characteristics and resources affect screening and response for toxic stress, and patient experience. Together, these organizations are applying the science of QI, coupled with qualitative methods, to identify, evaluate, and disseminate facilitators, strategies, and promising practices among the participating clinics. The external statewide evaluation of the ACEs Aware initiative will build upon and incorporate many of the process and outcomes indicators and data collection tools from CALQIC.

Evaluation efforts will be guided by the CALQIC Logic Model for Evaluation (**Figure 36**). Each arrow in the Figure represents an if-then statement. The goal of the evaluation is to capture the elements in each column to better understand the relationships between them. Screening and referral will vary by clinic according to variations in inputs, or in relationship to variations in other activities. Indicators of activities to be tracked include the screening rates and the rates of internal and external referrals by ACE score resulting in appointments. The quantitative assessments of screening implementation and referral variations, paired with qualitative information regarding clinic-level resources and capabilities, will be used to better understand the barriers to and facilitators of ACEs screening, and to

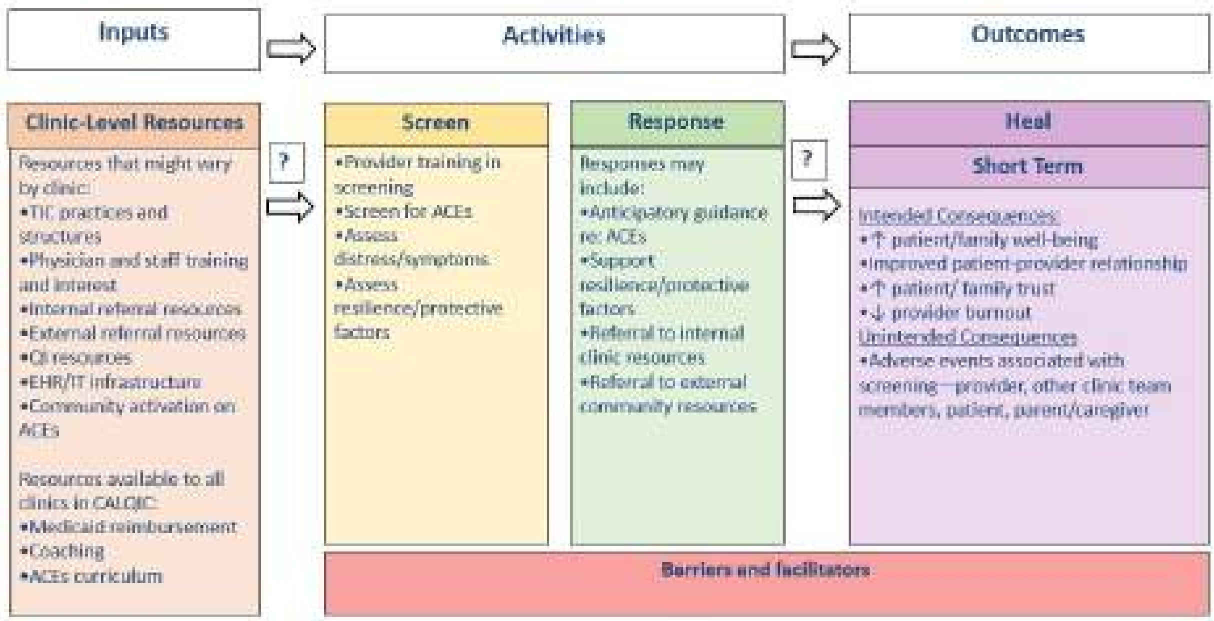


Figure 36. California ACEs Learning and Quality Improvement Collaborative (CALQIC) logic model for evaluation. Image reproduced with permission from the University of California, San Francisco, Center to Advance Trauma-Informed Health Care (2019); CALQIC.

identify effective potential solutions to address the barriers. Outcomes assessed by clinic and patient characteristics will include: patient/family health and well-being, patient-provider relationship trust, patient perceptions of helpfulness of referrals, and provider burnout, as well as unintended consequences.

As part of the second evaluation component, Medi-Cal claims data is being collected and reported quarterly by DHCS and CA-OSG, to include systems-level information about all Medi-Cal providers who are screening and responding to ACEs in primary care. This will include a tabulation of total ACE screenings and stratification by relevant patient and healthcare-setting characteristics, such as stratification of patient results by high-risk or low-risk screens and by provider type, delivery system, and region. Specifically, the DHCS quarterly ACEs Aware Medi-Cal Claims report will stratify these results by procedure code, high-risk screens (HCPCS code G9919) and low-risk screens (G9920). Other data reported will include:

- Total ACE screening visits
- ACE screenings by age of beneficiary
- ACE screenings by sex of beneficiary
- ACE screenings by age and sex
- ACE screenings by ethnicity of beneficiary

- ACE screenings by delivery system
- ACE screenings by California region
- ACE screenings by provider type
- ACE screenings by physician specialty
- ACE screening rate for each Medi-Cal managed care plan

The ACEs Aware initiative will continue to collect and report data on the numbers and types of providers who have taken an ACEs Aware Core Training. In the future, it may also be possible to assess the extent to which particular screening results are associated with specific types of referrals and clinical interventions.

The overall purposes of the external ACEs Aware initiative evaluation are to assess the statewide implementation of ACEs/toxic stress screening and response for Medi-Cal recipients and the resultant changes in healthcare systems, and to document the impacts on utilization of healthcare and other services, related health outcomes (e.g. rates and severity of ACE-Associated Health Conditions, AAHCs), and potentially, associated systems-level cost consequences (i.e., related to AAHCs). An evaluation team, consisting of members of state agencies, contractors, healthcare systems, and subject matter experts, is planned to coordinate the overall evaluation strategy and integrate these efforts across the three evaluation components. A **three-year** time frame has been established for this external evaluation to allow sufficient time for at least short-term AAHCs to be monitored.

The evaluation team will create an updated Logic Model to focus on wider practice and outcome questions, with sub-models to document the multiple inputs, activities, and outcomes, highlighting the potential wider systems-level changes and outcomes across all sites serving Medi-Cal beneficiaries statewide (not just the CALQIC sites). The Logic Model will incorporate the full scope of the evaluation of the statewide ACEs Aware initiative and identify a series of overarching evaluation questions. Based on the Logic Model and related evaluation questions, key indicators (and existing and new data sources for these indicators) will be identified. Implementation of the evaluation plan, including data collection, analysis, and iterative QI efforts based on findings, will include closely monitoring process and outcome indicators and producing regular evaluation reports.

The following process evaluation questions could be assessed by an external evaluation plan that combines inputs from CALQIC, DHCS, CA-OSG, and other administrative sources:

- What was the overall feasibility or practicality of implementing ACEs/toxic stress screening and response in primary care with engagement of cross-sector response networks?

- What was the scope and reach of program uptake and implementation, including documentation of implementation and timelines across sites (e.g., degree and nature of implementation activities)?
- What systems and organizational policy and practice changes were implemented?
- What organizational and clinical challenges were encountered, and what solutions were developed?
- What was the practitioner and client experience like (e.g., acceptability of screening, stigma)?
- What were the impacts of the program, both intended and unintended? How can the unintended consequences be minimized?

The following outcome evaluation questions are intended to be addressed as well, comparing screened clients by ACE score/toxic stress risk status and with unscreened clients over time:

- What was the incidence and prevalence of ACEs (and toxic stress risk level) by program site and client factors (e.g., ACEs score/risks identified, demographic characteristics)?
- What types of referrals were made and completed?
- What healthcare utilization patterns/changes took place (e.g., changes in usage of emergency services, mental/behavioral healthcare, community resources, and specialty care)?
- What differences were seen by seen in frequency, severity, and mortality related to AAHCs, by screening status, ACEs score, and/or toxic stress risk?

Cost-effectiveness and cost-benefit analyses should also be conducted once program and utilization services costs are documented, including associated impacts on rates of health outcomes (patient and program benefits) and service utilization trends.

Because the ACEs Aware initiative involves implementation of clinical and systems-level interventions for ACEs and toxic stress, a mixed-methods (quantitative and qualitative) quasi-experimental study design should be used for tracking implementation processes, systems changes and outcomes (both intended and unintended). The rationale for this approach to evaluation in this large-scale field application is based on the voluntary nature of the participation of organizations/clinics, professionals, and patients. In this situation, there is no random assignment of sites or patients to receive or not receive ACEs and toxic stress screening and response interventions, so strong causal interpretations of the results would not be valid. The primary limitation of this design is that alternative explanations for all the findings cannot be easily ruled out, due to both potential selection bias in those who choose to participate (or not) and unmeasured or confounding historical or other factors.

A thoughtful evaluation strategy to address these limitations should combine data from a rigorous qualitative assessment with tracking data from the detailed quantitative indicators. The qualitative evaluation component will be especially critical to document both the policy and system changes in healthcare and their ancillary wrap-around support systems. The consultant evaluation team should include strong subject matter expertise in qualitative data analyses, as well as in healthcare policy and financial analyses. Data-collection methods should include interviews of major stakeholders and policy analyses of systems challenges and changes. An important aspect of this component will be to capture and describe the contextual and qualitative differences in clinical implementation across sites, and attempt to distill and disseminate best practices that promote optimal health and social outcomes.

Documentation and analysis of the extent of program implementation at each system/site to test for dose–response impacts is also planned. The primary quantitative data source for the statewide assessment of ACEs/toxic stress screening and treatment implementation and healthcare utilization will be Medi-Cal claims data over time. At the patient level, pre- and post-intervention assessment time frames will be used (e.g., six months to one year prior to screening and one to three years after) to track service utilization over time among those screened for ACEs and toxic stress (by toxic stress risk category). De-identified aggregate data sets of screened patients will be created and matched with aggregate control group data for further comparison analyses. Using these aggregate data, referral and treatment service claims data will also be identified and tracked, including:

- Use of Centers for Medicare and Medicaid Services (CMS) core indicators (and any unique California standards);
- Within healthcare systems and sites: diagnosis codes; further screening and/or work-up codes; treatment and referral codes; case management codes; and total claims and related costs incurred; and
- Internal and external referrals and services used, tracked by the above systems indictors, where available.

For the quantitative evaluation, three types of comparison conditions could be used: 1) use of statewide Medi-Cal claims service usage data as baseline; 2) use of clinical practice and service utilization data at each implementation system or site and, when possible, at (selected or comparable) non-implementation sites; and 3) early adopters versus late adopters (comparing pre- and post-intervention outcomes).

For the selected AAHCs to be tracked, a similar set of indicators will be used, including the CMS core (and any unique California standard) indicators, with the status of each condition measured at baseline before the first ACE screening and for comparison groups, including prior treatment patterns (e.g., treatment services, prescriptions, emergency department visits, and hospitalizations), and overall claims and costs, at standard follow-up time periods (e.g., six months or annually) for screened and comparison groups.

Looking Ahead: California's Next Steps

The California ACEs Aware initiative is founded on the best scientific evidence on addressing the impacts of ACEs and toxic stress on the health of California's people. ACEs Aware is intended as an engine to advance evidence-informed interventions in healthcare and to drive more precise targeting and effectiveness of the cross-sector approaches needed to prevent and mitigate the health effects of ACEs and toxic stress. This initiative provides an unprecedented opportunity to execute a cautiously scaled statewide approach to reduce medical, mental health, behavioral, and social consequences of ACEs and toxic stress, in a way that proactively uplifts families and communities. The science and policy landscape are aligning in powerful ways to reveal the possibilities for preventing and healing impacts of ACEs and toxic stress, and fostering community and individual flourishing.

The state of California has set a bold goal to cut the burden of toxic stress and ACEs in half in the next generation by implementing a well-formulated public health approach to prevention, early detection, treatment and cross-sectoral action. To do this, California is addressing upstream factors, supporting family and community resilience, and prioritizing equity in achieving health and social outcomes. The keystone of this initiative is a statewide effort to detect and intervene on toxic stress in primary care and to deploy cross-sector expertise to ensure the availability, quality, and success of interventions. Screening for ACEs and toxic stress in primary care is essential and a foundational step toward coordinating robust cross-sector systems of prevention and healing to reduce the negative impacts of toxic stress on health and social outcomes. The focus on primary care screening and intervention is being implemented in ways that engage and align the cross-sector expertise needed to both reduce health impacts of toxic stress once they have occurred (secondary and tertiary prevention), and ultimately, to reduce the incidence of ACEs and toxic stress in the first place (primary prevention).

Development of **clinical diagnostic criteria for toxic stress** is a key milestone that has the potential to greatly improve quality, efficacy, and coordination of care, and reimbursement for services. Shifts in diagnostic and billing codes for ACE-Associated Health Conditions (AAHCs) and more precision tools for assessment of treatment efficacy and prognostication of risk, combined with enhanced payment models to support brief interventions, care coordination, referrals, and more frequent follow-up, can catalyze more effective and coordinated action to prevent and heal the impacts of ACEs.

Primary prevention efforts promote the sustainable presence of safe, stable, nurturing relationships and environments and co-address the social and structural determinants of health and well-being. Primary prevention-oriented policies and programs include connecting parents and caregivers to high-quality, family-focused physical and mental healthcare and establishing strong networks of buffering resources for children, families, and adults, in order to prevent toxic stress from ever occurring and from worsening once in place. This includes linkages to high-quality home visitation, child care, preschool and school enrichment with family engagement, optimizing social-emotional learning at home, promoting healthy relationship norms, parenting and family relationship skill-building, connecting youth to caring adults and activities, and economic and legal supports.[23,31,41,42,44,45,100,564,604,755,1606] Providing this cross-sector network of care will require **strengthening linkages** to social services and mental/behavioral healthcare in the primary care setting, either through integrated care models or through strong partnerships. Preventing interpersonal and structural discrimination and oppression of all types is also critical to interrupt a significant contributor of toxic stress for individuals and communities.

California already has rich resources in a growing number of communities, with cross-sector partnerships promoting well-being and equity by addressing ACEs and associated social determinants of health. Today, California hosts a wide array of city, county, regional, and statewide efforts engaging in sustainable cross-agency and cross-sector collaboration to integrate trauma-informed health, education, social services, and other allied work. Increasingly, these efforts recognize and seek to heal the collective adversity faced by the community due to toxic stress from ACEs, as well as from related adversities like racism, poverty, lack of equitable opportunities, and housing insecurity. They also aspire to promote the transformational resilience needed to meet existing and emerging adversities in an engaged, creative, and connected manner. Nearly all seek to foster citizen engagement in making the cultural shifts required to integrate the science of toxic stress and resilience amid adversity.

Other key components of this cross-sector effort should be increasingly integrated and **sustained collaborations** between the healthcare, public health, social services, education, justice, and other allied sectors—undergirded by a shared vision, responsive iteration of best practices, and shared data integration systems.[623] These strategies should be paired with and may be reinforced by a **coordinated public education campaign** to raise awareness about impacts of ACEs and toxic stress, as well as effective intervention and prevention tactics. Changing common narratives and social norms can help promote healthy relationships, enhance public knowledge about how to thrive despite having faced these challenges, and can improve the efficacy of cross-sector initiatives.[31]

Decades of research and innovation have informed California's collaborative ACEs Aware initiative to integrate best science into practice to improve the early and lifelong health of children, youth, families, and communities. Next steps for the movement include advancing a **robust toxic stress research agenda**. Key objectives should include:

1. Development of **clinically relevant biomarkers** to help more precisely diagnose, classify, and assess treatment efficacy for toxic stress in clinical settings. These biomarkers could greatly improve clinicians' ability to risk-stratify and assess prognosis for patients experiencing toxic stress and its potential subtypes (e.g., immune, metabolic, neuropsychiatric, and/or endocrine).
2. **Guidelines for clinical management of ACE-Associated Health Conditions (AAHCs)** in the setting of toxic stress. For instance, in asthma, toxic stress can alter expression and function of beta-adrenergic and glucocorticoid receptors, and lead to changes in inflammatory cytokines and stress reactivity in ways that render traditional treatments such as beta-agonists and corticosteroids less effective (see **Tertiary Prevention Strategies in Healthcare**, in Part II, for details).[230] However, current stepwise treatment algorithms for asthma do not take these biological differences into account.
3. **Identification of therapeutic targets** for regulating the toxic stress response. Just as antiretroviral medications were a critical tool for public health efforts to stem the human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) epidemic, therapeutic agents to regulate the stress response and avert or mitigate the neuro-endocrine-immune-metabolic and genetic regulatory derangements of toxic stress are needed.
4. Elucidation of the complex interactions of how **individual differences** in underlying biological susceptibility or exposures (including timing, severity, duration and developmental interactions) might affect clinical presentation of toxic stress or inform individualized treatment strategies.
5. **Longitudinal studies** to better understand the specific and longer-term impacts of clinical interventions that target the toxic stress response, especially for metrics like prevalence and severity of AAHCs, social

outcomes, healthcare utilization, systems-level costs, and health equity. Tracking and preventing unanticipated harms will be of paramount importance.

6. As a first step in advancing these goals, the Office of the California Surgeon General has partnered with the California Initiative to Advance Precision Medicine of the California Governor's Office of Planning and Research to launch a $9 million initiative to investigate precision medicine approaches to detect and mitigate toxic stress.[337]

ACEs Aware and allied cross-sector efforts across the state of California represent policy innovation to intervene on a challenging public health crisis, through a carefully scaled approach to primary, secondary, and tertiary prevention of ACEs and toxic stress. As this report has shown, to enable lasting change, healthcare-based innovations must be closely coordinated with cross-sector response, practice transformation, research and innovation, and public education efforts. In California, education and capacity-building within healthcare was prioritized as an important first phase, to ensure that providers were prepared to act in advance of public education. By deploying a well-formulated public health approach to prevention, screening, and treatment, ACEs Aware and related programs seek to cut toxic stress and ACEs in half in the next generation. For California and states with similar ambitions, this is an unprecedented opportunity to execute a visionary, data-driven, and evidence-informed set of clinical and public health interventions, using a cautiously scaled approach to enable clinical and population-level promotion of mitigation of toxic stress and building resilience, while generating a data-driven approach to understanding and propagating best practices and avoiding unintended harms.

NEXT STEPS FOR THE ACEs AWARE MOVEMENT

1. Enhanced policy efforts to support prevention of and early intervention for ACEs and toxic stress, including access to treatment based on risk of toxic stress rather than diagnosis of downstream harms.
2. Coordination of a robust network of clinical and community interventions, including clear guidelines for response to clinical risk of toxic stress, and technology and data infrastructure for bidirectional communication (within the appropriate protection of patient privacy rights).
3. Adequate mental and behavioral health treatment infrastructure integrated or closely aligned with primary care.
4. Cross-sector training for recognition and trauma-informed response to ACEs and toxic stress in every sector, including law enforcement, education, judicial system, early care and education, business and economic sectors, public health, social services, immigration, legal services, and healthcare.
5. Scaling of promising cross-sector efforts to address ACEs and toxic stress, such as Handle With Care, Adverse Childhood Experiences Response Team (ACERT), Healthy Environment and Response to Trauma in Schools (HEARTS), as highlighted in previous sections of the report (especially Part II).
6. A public education campaign on:
   - How ACEs and toxic stress impact well-being,
   - The structural and systemic conditions that can make ACEs and toxic stress more or less likely to occur, and
   - Strong messages of hope, including practical strategies for buffering factors and scaffolding protective factors that can improve outcomes for a child or adult at risk for or experiencing toxic stress to prevent further harm—and how to break the intergenerational cycle of adversity.
7. Implementation of a robust research agenda for improved detection and treatment of toxic stress including development of clinically relevant biomarkers, therapeutic targets, clinical guidelines, individualized treatment strategies and longitudinal studies.

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APPENDIX A: MEASURING ADVERSE CHILDHOOD EXPERIENCES IN CALIFORNIA

Childhood adversity has been addressed in multiple surveys in recent years. Some surveys closely align with the original Kaiser Permanente and Centers for Disease Control and Prevention (CDC) Adverse Childhood Experiences (ACEs) study, while others use an expanded notion of childhood adversity. Three surveys, the Behavioral Risk Factor Surveillance System (BRFSS), National Survey of Children's Health (NSCH), and Maternal and Infant Health Assessment (MIHA), most explicitly address childhood adversity as well as resilience in California. Additional surveys ask about particular types of adverse experiences.

The BRFSS, NSCH, and MIHA surveys provide a rich and conceptually similar perspective on childhood adversity. Taken together, they present a broad framework for child adversity across the lifespan and provide useful data to inform and facilitate interventions. Each of these data sources produces at least one overall index of childhood adversity. An overall index should be viewed as a more comprehensive measure than any one of its individual items alone because it captures the cumulative magnitude of experiencing hardship. However, given their differences in methodology, data from the three sources should not be combined or directly compared.

The BRFSS ACEs Module was adapted from the original ACEs study conducted by Kaiser Permanente and the CDC. Data are based on adults' recollections of their childhood experiences during the first 17 years of life. Although these retrospective data shed light on the conditions in which children are currently being raised, they do not provide information about the current status of California's children.

NSCH data were collected by the US Census Bureau on behalf of the Maternal and Child Health Bureau of the Department of Health and Human Services. NSCH uses a set of family, economic, and community adversity indicators to ask parents about current adverse and positive experiences to which their children (ages 0 to 17) have been exposed. This is the most timely population-based survey measure of adversity and resilience among California children because it asks parents about the trauma and protective buffers their children have experienced while they are still children, compared to the more traditional surveys that ask adults to recall their childhood experiences.

MIHA is a collaborative effort of the Maternal, Child and Adolescent Health Division and the Women, Infants, and Children Division of the California Department of Public Health and the Center on Social Disparities in Health at the University of California, San Francisco. MIHA surveys postpartum women (15 years and older) who delivered a live birth about their own hardships prior to age 14 as well as current hardships during the pregnancy.

Among these three data sources, the NSCH indicators are the most contemporary because they tap into parents' views of their children's current experiences. MIHA adds an intergenerational perspective by providing information about the childhood hardships experienced by mothers of newborns and their hardships during pregnancy. BRFSS provides a well-established standard measure of adult retrospective reports of ACEs that produces standard relative risks which allow for comparisons with existing research based on the traditional ACEs. Both NSCH and MIHA include a wider range of potentially adverse experiences, such as exposure to extreme poverty, community violence, and food and housing insecurity, whereas the BRFSS ACEs Module focuses primarily on family experiences from the original ACEs study (i.e., child abuse and household challenges).

Table 1 compares the NSCH, MIHA, and BRFSS on population, methodology, sampling, and timeframes. **Table 2** compares the surveys on content. **Table 3** lists verbatim questions from these three surveys.

Some data sources, not detailed here, measure certain broad aspects of childhood adversity, though not from a youth or child proxy perspective. For example, the California Child Welfare Indicators Project tracks child maltreatment and foster care involvement, and multiple sources measure family poverty, such as the California Poverty Measure (Public Policy Institute of California and Stanford Center on Poverty and Inequality) and the federal poverty threshold (American Community Survey).

In addition to the surveys that are addressed here, we examined additional websites and data sources, but concluded that they are less useful as a primary resource for measuring childhood adversity. Some are indices or clearinghouses that draw on other primary sources and some do not measure childhood adversity outcomes directly. However, indices are useful as a broad measure of child well-being. Sources that measure outcomes, such as cancer, rather than experiences, could also be useful for a broad understanding of potential outcomes of repeated and prolonged exposure to childhood adversity, but these sources do not directly tie adversity with outcomes. Additional sources of relevance to California children's health and well-being status include: The California Healthy Kids Survey, the California Health Interview Survey, the National Longitudinal Study of Adolescent to Adult Health, Fragile Families and Child Well-being study, Panel Study of Income Dynamics, California Health and Human Services Open Data Portal, California Department of Health Care Services Medi-Cal Managed Care Reports, California's Office of Statewide Health Planning and Development Health Care Payments Database, California Evidence-Based Clearinghouse for Child Welfare, Children Now Children's Report Card, Annie E. Casey

Foundation's KIDS COUNT Data Book, Robert Wood Johnson Foundation County Health Rankings & Roadmaps, Measure of America, Opportunity Index, Neighborhood Atlas Area Deprivation Index, California Kids Cancer Registry and California Cancer Registry, Index of Deep Disadvantage, and Brain Health Registry.

Table 1. Comparison of the Behavioral Risk Factor Surveillance System, National Survey of Children's Health, and Maternal and Infant Health Assessment in California

Characteristic	Behavioral Risk Factor Surveillance System (BRFSS)	National Survey of Children's Health (NSCH)	Maternal and Infant Health Assessment (MIHA)
Survey population and mode	Adults reported on own childhood experiences, by telephone	Parents reported on child's experiences, by web and paper survey	Postpartum mothers reported on own childhood experiences, by mailed survey with telephone follow-up
Conceptual meaning	Most traditional measure of ACEs and its potential intergenerational transmission	Most timely measure of contemporary child adversity experiences	Most timely measure of potential intergenerational transmission of ACEs
Sample size	Approximately 8,000 to 12,000 per year	Approximately 3,000 to 6,000 per year	Approximately 7,000 per year
Sample size assessment	Sufficient sample size for California's larger counties; To generate reliable estimates in small counties, need to combine counties, combine years, use methodological approaches, and/or seek oversample*	Sufficient sample size for California's larger counties; To generate reliable estimates in small counties, need to combine counties, combine years, use methodological approaches, and/or seek oversample**	Sufficient sample size for California's larger counties; smaller counties included in regional reports; to generate reliable estimates in small counties, need to combine counties, combine years, or use other methodological approaches
Historical longitudinal measurement	No data prior to 2008	No comparable data prior to 2016	No data prior to 2011

Characteristic	Behavioral Risk Factor Surveillance System (BRFSS)	National Survey of Children's Health (NSCH)	Maternal and Infant Health Assessment (MIHA)
Future longitudinal measurement	California BRFSS ACEs module is administered every other year on the odd years (e.g., 2015, 2017, 2019)	Reliable longitudinal data expected yearly from 2016 onward	ACEs-related survey questions cycle on and off survey; currently off cycle; expected return in 2022
Time periods available	One set of combined years: 2011-2013-2015-2017	One set of combined years: 2016-2018	Two sets of combined years: 2011-12, 2013-14
Level of reporting	Most California counties	All California counties and county groups	35 California counties with regional aggregation
Types of indicators	> Number of ACEs (0, 1-3, 4+) > By households with and without children	> Number of ACEs (0, 1, 2+) > Number of ACEs (0, 1, 2, 3, 4+) (CA only) > Types of ACEs (California only) > Resilience factors	> Number of ACEs (0, 1, 2-3, 4+) > By demographic groups (California only)

** Teams at the California Department of Public Health's Essentials for Childhood and Violence Prevention Initiative, All Children Thrive, and the University of California, Davis's Violence Prevention Research Program, developed a methodology to maximize BRFSS data availability for counties.*

*** To increase NSCH data availability and reliability, yearly oversamples can be purchased from the Census Bureau. The Population Reference Bureau has completed preliminary work on methodological approaches in collaboration with Census Bureau.*

Table 2: Types of measures by survey

Types of measures	Behavioral Risk Factor Surveillance System (BRFSS)	National Survey of Children's Health (NSCH)	Maternal and Infant Health Assessment (MIHA)
Emotional abuse*	x		
Physical abuse*	x		
Sexual abuse*	x		
Intimate partner violence*	x	x	
Substance abuse*	x	x	x
Mental illness in household*	x	x	
Incarcerated household member*	x	x	x
Parent separation or divorce*	x	x	x
Physical neglect*	Only in 2008-09, 2013		
Emotional neglect*			x
Neighborhood violence		x	
Parent death		x	
Treated unfairly due to race/ ethnicity		x	
Economic hardship		x	x
Foster care			x
Housing instability		x	x
Hunger		x	x

* *Similar to the type of measure that appeared in the original Kaiser Permanente/CDC ACE Study.*

Tables 3: Verbatim questions from surveys addressing childhood adversity

Survey	Adversity measurement category	Verbatim question
Behavioral Risk Factor Surveillance System (2009, 2019)	Emotional abuse*	Before age 18…How often did a parent or adult in your home ever swear at you, insult you, or put you down?
	Physical abuse*	Before age 18…How often did a parent or adult in your home ever hit, beat, kick, or physically hurt you in any way? Do not include spanking.
	Sexual abuse*	Before age 18…How often did anyone at least 5 years older than you or an adult, ever touch you sexually?
	Sexual abuse*	Before age 18…How often did anyone at least 5 years older than you or an adult, force you to have sex?
	Sexual abuse*	Before age 18…How often did anyone at least 5 years older than you or an adult, try to make you touch sexually?
	Incarcerated household member*	Before age 18…Did you live with anyone who served time or was sentenced to serve time in a prison, jail, or other correctional facility?
	Intimate partner violence*	Before age 18…How often did your parents or adults in your home ever slap, hit, kick, punch or beat each other up?
	Mental illness in household*	Before age 18…Did you live with anyone who was depressed, mentally ill, or suicidal?
	Parent separation or divorce*	Before age 18…Were your parents separated or divorced?
	Substance abuse*	Before age 18…Did you live with anyone who was a problem drinker or alcoholic?
	Substance abuse*	Before age 18…Did you live with anyone who used illegal street drugs or who abused prescription medications?

Survey	Adversity measurement category	Verbatim question
Behavioral Risk Factor Surveillance System (2009, 2019)	Physical neglect* (only included in 2008-09, 2013)	Before age 18...Did a parent or adult caretaker ever fail to provide for your basic needs, such as food, clothing, medical care, hygiene, or fail to protect you from known dangers?

* *Similar to the type of measure that appeared in the original Kaiser Permanente/CDC ACE Study.*

The BRFSS ACE module includes 11 questions about previous childhood trauma adapted from the original CDC-Kaiser ACEs Study (Table 1). The two questions about alcohol and drug use and the three questions about child sexual abuse have been combined in this analysis. Domestic violence, child physical abuse, and child emotional abuse were assessed using slightly different but comparable questions in 2011 versus 2013, 2015, and 2017. Child neglect was not used to calculate the ACE score. Physical neglect only was included in the BRFSS ACE module in 2013, but not thereafter. The total ACE score used in this analysis ranges from 0 to 8, with higher scores indicating greater exposure.

APPENDIX B:
TEXT OF SELECTED CALIFORNIA LEGISLATIVE BILLS OR RESOLUTIONS ON CHILDHOOD ADVERSITY OR TOXIC STRESS

Assembly Bill 340

CHAPTER 700

An act to add Section 14132.19 to the Welfare and Institutions Code, relating to Medi-Cal.

[Approved by Governor - October 12, 2017. Filed with Secretary of State - October 12, 2017.]

LEGISLATIVE COUNSEL'S DIGEST

AB 340, Arambula.

Early and Periodic Screening, Diagnosis, and Treatment Program: trauma screening.

Existing law provides for the Medi-Cal program, which is administered by the State Department of Health Care Services, under which qualified low-income individuals receive health care services, including early and periodic screening, diagnosis, and treatment (EPSDT) for any individual under 21 years of age who is covered under Medi-Cal consistent with the requirements under federal law. The Medi-Cal program is, in part, governed and funded by federal Medicaid program provisions.

Existing federal law provides that EPSDT services include periodic screening services, vision services, dental services, hearing services, and other necessary services to correct or ameliorate defects and physical and mental illnesses and conditions discovered by the screening services, whether or not the services are covered under the state plan.

In addition to the required periodic screening services, existing federal law provides that Medicaid-eligible children are entitled to interperiodic screenings in order to identify a suspected illness or condition not present or discovered during the periodic examination.

This bill would require the department, in consultation with the State Department of Social Services and others, to convene, by May 1, 2018, an advisory working group to update, amend, or develop, if appropriate, tools and protocols for screening children for trauma as defined, within the EPSDT benefit, as specified.

The bill would require this group to report its findings and recommendations, as well as any appropriations necessary to implement those recommendations, to the department and to the Legislature's budget subcommittees on health and human services no later than May 1, 2019, and would provide that this group would be disbanded on December 31, 2019. The bill would also require, on or before May 1, 2019, the department to identify an existing advisory working group to periodically review and consider the protocols for the screening of trauma in children at least once every 5 years, or upon the request of the department. The bill would authorize the department to implement, interpret, or make specific these provisions by means of all-county letters, plan letters, or plan or provider bulletins, as specified.

DIGEST KEY

Vote: majority Appropriation: no Fiscal Committee: yes Local Program: no

BILL TEXT

THE PEOPLE OF THE STATE OF CALIFORNIA DO ENACT AS FOLLOWS:

SECTION 1.

Section 14132.19 is added to the Welfare and Institutions Code, to read:

14132.19.

(a) (1) The department, in consultation with the State Department of Social Services, county mental health experts, managed care plan experts, behavioral health experts, child welfare experts, and stakeholders, shall convene an advisory working group to update, amend, or develop, if appropriate, tools and protocols for the screening of children for trauma, within the Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) benefit, consistent with existing law and this section. The advisory working group shall consider both of the following:

(A) Existing screening tools used in the Medi-Cal program, including, but not limited to, the Staying Healthy Assessment developed by the department, the United States Preventive Services Task Force grade "A" or "B" recommendations, and the American Academy of Pediatrics Bright Futures periodicity schedule and anticipatory guidance.

(B) The efficacy and appropriateness of the types of providers authorized to administer screenings.

(2) The department shall convene the advisory working group by May 1, 2018. The advisory working group shall report its findings and recommendations, as well as any appropriations necessary to implement those recommendations, to the department and to the Legislature's budget subcommittees on health and human services no later than May 1, 2019. The advisory working group shall be disbanded on December 31, 2019.

(3) Findings or recommendations of the advisory working group that cannot be implemented without a subsequent appropriation by the Legislature, as determined by the department, shall not be implemented until the appropriation is made.

(4) On or before May 1, 2019, the department shall identify an existing advisory working group to periodically review and consider the protocols for the screening of trauma in children consistent with subparagraphs (A) and (B) of paragraph (1). The group created pursuant to this section may, as part of its work, recommend to the department an existing group appropriate to conduct this review. The advisory working group identified by department shall review and consider the protocols for the screening of trauma in children at least once every five years, or upon the request of the department.

(b) Notwithstanding Chapter 3.5 (commencing with Section 11340) of Part 1 of Division 3 of Title 2 of the Government Code, the department may implement, interpret, or make specific this section by means of all-county letters, plan letters, plan or provider bulletins, or similar instructions, without taking regulatory action.

(c) This section shall be implemented only if and to the extent that federal financial participation under Title XIX of the federal Social Security Act (42 U.S.C. Sec. 1396 et seq.) is not jeopardized and all necessary federal approvals have been obtained.

(d) "Trauma," as used in this section, means the result of an event, series of events, or set of circumstances that is experienced by an individual as physically or emotionally harmful or threatening and that has lasting adverse effects on the individual's functioning and physical, social, emotional, or spiritual well-being.

Assembly Concurrent Resolution No. 155

CHAPTER 144

Relative to childhood brain development.

[Filed with Secretary of State September 02, 2014.]

LEGISLATIVE COUNSEL'S DIGEST

ACR 155, Bocanegra. Childhood brain development: adverse experiences: toxic stress.

This measure would urge the Governor to identify evidence-based solutions to reduce children's exposure to adverse childhood experiences, address the impacts of those experiences, and invest in preventive health care and mental health and wellness interventions.

DIGEST KEY

Fiscal Committee: no

BILL TEXT

WHEREAS, Research over the last two decades in the evolving fields of neuroscience, molecular biology, public health, genomics, and epigenetics reveals that experiences in the first few years of life build changes into the biology of the human body that, in turn, influence the person's physical and mental health over his or her lifetime; and

WHEREAS, Adverse childhood experiences are traumatic experiences that occur during childhood, including physical, emotional or sexual abuse, physical and emotional neglect, household dysfunction, including substance abuse, untreated mental illness or incarceration of a household member, domestic violence, or separation or divorce involving household members, that can have a profound effect on a child's developing brain and body and can result in poor health during the person's adulthood; and

WHEREAS, The original 1998 Adverse Childhood Experiences Study, which surveyed approximately 17,000 adult Californians, found that two-thirds of participants had at least one adverse childhood experience and one in six participants had four or more adverse childhood experiences; and

WHEREAS, The Adverse Childhood Experience Study also found a strong correlation between the number of adverse childhood experiences and a person's risk for disease and negative health behaviors; and

WHEREAS, Researchers found that a person with four or more adverse childhood experiences was 2.4 times more likely to have a stroke, 2.2 times more likely to have ischemic heart disease, 2 times more likely to have chronic pulmonary obstructive disease, 1.9 times more likely to have a type of cancer, and 1.6 times more likely to have diabetes; and

WHEREAS, Researchers found that a person with four or more adverse childhood experiences was 12.2 times more likely to attempt suicide, 10.3 times more likely to use injection drugs, and 7.4 times more likely to be an alcoholic; and

WHEREAS, The life expectancy of a person with six or more adverse childhood experiences is 20 years shorter than a person with no adverse childhood experiences; and

WHEREAS, These early adverse experiences literally shape the physical architecture of a child's developing brain and establish either a sturdy or a fragile foundation for all the learning, health, and behavior that follow; and

WHEREAS, Strong, frequent, or prolonged stress in childhood caused by adverse childhood experiences can become toxic stress, impacting the development of a child's fundamental brain architecture and stress response systems; and

WHEREAS, Early childhood offers a unique window of opportunity to prevent and heal the impacts of adverse childhood experiences and toxic stress on a child's brain and body; and

WHEREAS, A child's brain continues to develop through adolescence and into young adulthood; and

WHEREAS, The emerging science and research on toxic stress and adverse childhood experiences evidence a growing public health crisis for the state with implications for the state's educational, juvenile justice, criminal justice, and public health systems; and

WHEREAS, Adverse childhood experiences can significantly impact a child's success in education; and

WHEREAS, The Trauma and Learning Policy Initiative (TLPI) found that neurobiological, epigenetics, and psychological studies have shown that traumatic experiences in childhood and adolescence can diminish concentration, memory, and the organizational and language abilities students need to succeed in school, thereby negatively impacting a student's academic performance, classroom behavior, and the ability to form relationships; and

WHEREAS, A child with four or more adverse childhood experiences is 46 times more likely to have learning or emotional problems; and

WHEREAS, A woman with seven or more adverse childhood experiences is 5.5 times more likely to become pregnant as a teenager; and

WHEREAS, Adverse childhood experiences can affect a child's future contact with the criminal justice system; and

WHEREAS, A woman with three violent adverse childhood experiences is 3.5 times more likely to become the victim of intimate partner violence, while a man with three violent adverse childhood experiences is 3.8 times more likely to perpetrate intimate partner violence; and

WHEREAS, A critical factor in buffering children from the effects of toxic stress and adverse childhood experiences is the existence of supportive, stable relationships between children and their families, caregivers, and other important adults in their lives; and

WHEREAS, Positively influencing the architecture of a child's developing brain is more effective and less costly than attempting to correct poor learning, health, and behaviors later in life; now, therefore, be it

Resolved by the Assembly of the State of California, the Senate thereof concurring, That the Legislature urges the Governor to reduce children's exposure to adverse childhood experiences, address the impacts of those experiences, and invest in preventive health care and mental health and wellness interventions; and be it further

Resolved, That the Legislature urges the Governor of California, in doing the foregoing, to consider the principles of brain development, the intimate connection between mental and physical health, the concepts of toxic stress, adverse childhood experiences, buffering relationships, and the roles of early intervention and investment in children as important strategies; and be it further

Resolved, That the Chief Clerk of the Assembly transmit copies of this resolution to the author for appropriate distribution.

Assembly Concurrent Resolution No. 235

CHAPTER 99

Relative to Trauma-Informed Awareness Day.

[Filed with Secretary of State June 13, 2018.]

LEGISLATIVE COUNSEL'S DIGEST

ACR 235, Arambula. Trauma-Informed Awareness Day.

This measure would designate May 22, 2018, as Trauma-Informed Awareness Day in California, in conjunction with National Trauma-Informed Awareness Day, to highlight the impact of trauma and the importance of prevention and community resilience through trauma-informed care.

DIGEST KEY

Fiscal Committee: no

BILL TEXT

WHEREAS, The California Legislature unanimously passed Assembly Concurrent Resolution No. 155 in 2014, urging the Governor to reduce children's exposure to adverse childhood experiences, address the impacts of those experiences, and build and promote resilience and protective factors, while investing in preventive health care and mental health and wellness interventions; and

WHEREAS, Forty-two percent of California children and 61 percent of California adults have experienced one or more adverse childhood experiences (ACEs); and

WHEREAS, ACEs are stressful or traumatic experiences that include abuse, neglect, racism, and household instability; and

WHEREAS, ACEs are recognized as a proxy for toxic stress, which can affect brain and body development, and if not addressed, can lead to mental, emotional, and physical health consequences affecting health and well-being across the lifespan of a person; and

WHEREAS, ACEs are determinants of major public health problems in California, such as heart disease, substance abuse, and mental illness. Detrimental effects can be buffered by building resiliency and promoting protective factors in a child's life through early intervention; and

WHEREAS, Trauma-informed care is an approach that can bring greater understanding and more effective ways to prevent, identify, and support and serve children, adults, families, and communities affected by ACEs, trauma, adversity, and toxic stress; and

WHEREAS, By adopting trauma-informed approaches that build resiliency and promote protective factors in all public, private, and charter schools, workplaces, communities, and government programs, training and licensing can aid in preventing mental, emotional, physical, and social issues for people impacted by ACEs, trauma, adversity, and toxic stress; and

WHEREAS, Trauma-informed care has been promoted and established in nearly one-half of California's 58 counties, in both urban and rural communities, including, but not limited to, the following:

(1) The County of Los Angeles Trauma and Resiliency-Informed Systems Change Initiative has convened over 100 stakeholders from county systems, philanthropy and community-based organizations, and academia to advance a countywide agenda to embed trauma-informed policies and practices across the county's child and family serving systems.

(2) Resilient Sacramento provided education and support to First 5 Sacramento Commission as the agency initiated trauma-informed practices. As a result, the commission incorporated language on the importance of trauma-informed approaches into its 2018 Strategic Plan, and included a contract requirement that all funded partners participate in trauma-informed training throughout the year.

(3) The County of Fresno Trauma and Resilience Network has assembled over 80 different organizational leaders that are learning together and working toward being a trauma-informed community, while developing practices that build resilience in kids, families, and neighborhoods. The group is collecting data on individual and community ACEs to have a more accurate awareness of the depth of trauma victims are facing.

(4) The Safe Long Beach Violence Prevention Plan (Safe Long Beach) was adopted in May 2014 by the Long Beach City Council to address a broad safety agenda aimed at reducing all forms of violence, including domestic abuse, child abuse, elder abuse, hate crimes, bullying, gang violence, and violent crime. Safe Long Beach draws upon the city's many existing assets to target violence at its root and build a safer Long Beach by 2020. The Trauma Induced Task Force of Long Beach (TITFLB) is an integral part of establishing Long Beach as a trauma-informed city. In its first year, the TITFLB established a framework for acceptance, engagement, and promotion of trauma-informed approaches for the City of Long Beach, and continues to be an integral part of establishing Long Beach as a trauma-informed city.

(5) A broad coalition of agencies, nonprofits, and individuals in the County of Del Norte are providing education and training focused on building community resilience and trauma-informed practices. The education committee of the Del Norte Child Abuse Prevention Council is partnering with the Del Norte County Unified School District to provide trauma-informed and resilience practices training for all teachers and administrators.

(6) The Healthy Mendocino Project regional childhood trauma action teams are developing local messaging, collaborating on trauma-informed trainings, and creating opportunities for resilience building. The Mendocino County Health and Human Services Agency Community Outreach Unit is collaborating with the University of California at Davis, Champions Project, on a pilot program to provide trauma-informed services to children who have experienced trauma through adulthood. FIRST 5 Mendocino offers agencies, providers, and community members specialized tools and strategies to mitigate the impacts of trauma and by using the Community Resiliency Model and the Trauma Resiliency Model. The County of Mendocino recognizes that those in the helping profession also experience trauma, and are helping those professionals and their employers understand the importance of operationalizing self-care in their work environment; and

WHEREAS, The Substance Abuse and Mental Health Services Administration and many other agencies and organizations provide substantial resources to better engage individuals and communities across the United States in order to implement trauma-informed care; now, therefore, be it

Resolved by the Assembly of the State of California, the Senate thereof concurring, That the Legislature designates May 22, 2018, as Trauma-Informed Awareness Day in California, in conjunction with National Trauma-Informed Awareness Day, to highlight the impact of trauma and the importance of prevention and community resilience through trauma-informed care; and be it further

Resolved, That the Chief Clerk of the Assembly transmit copies of this resolution to the author for appropriate distribution.