March 25, 2025

# Charting A Course: An Evidence-Based Approach to Addressing ACEs and Toxic Stress at Scale

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# ACES & TOXIC STRESS ARE A PUBLIC HEALTH

# CRISIS

# ADVERSE CHILDHOOD EXPERIENCES (ACES)

**Abuse**

Physical | Emotional | Sexual

**Neglect**

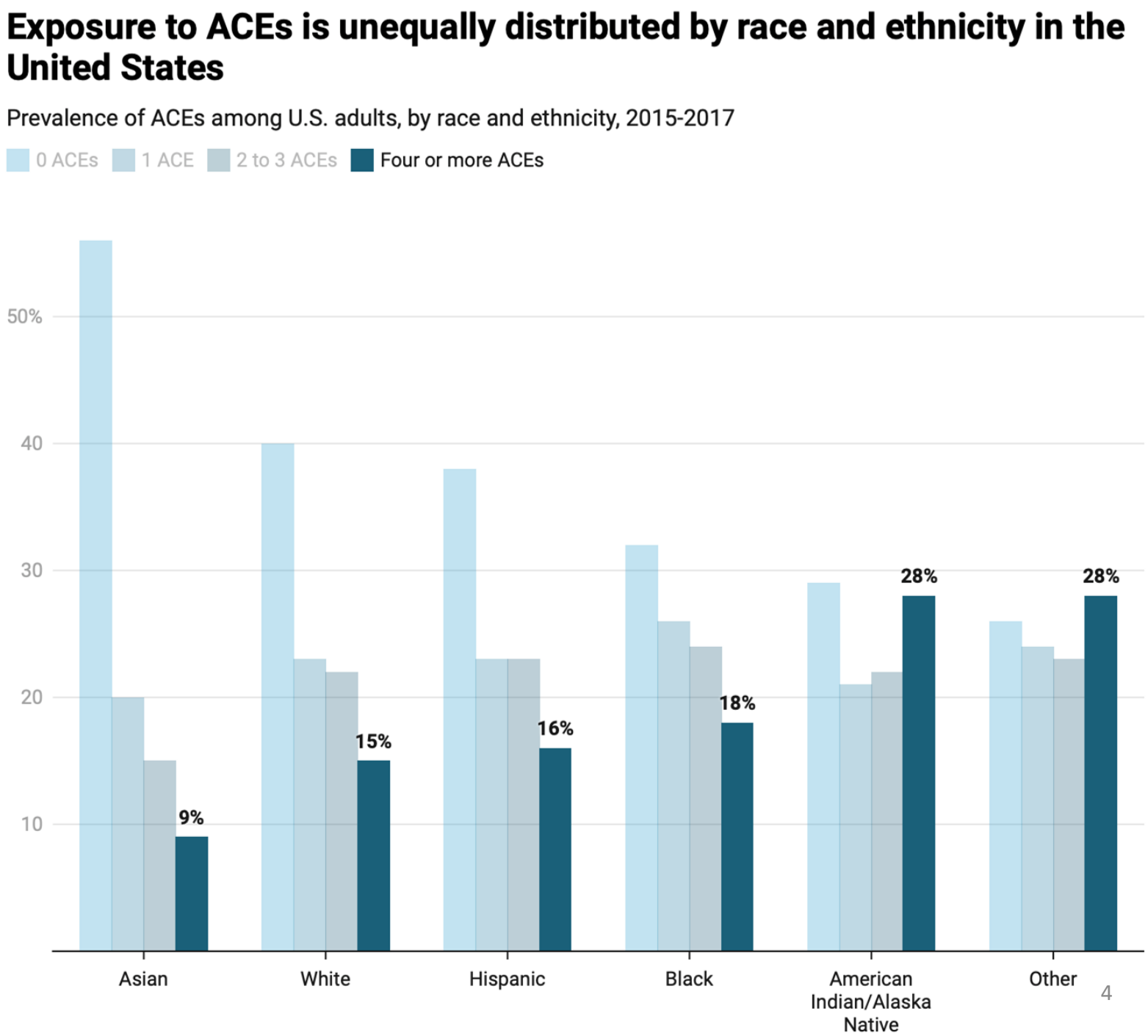
Physical | Emotional

**Household Challenges**

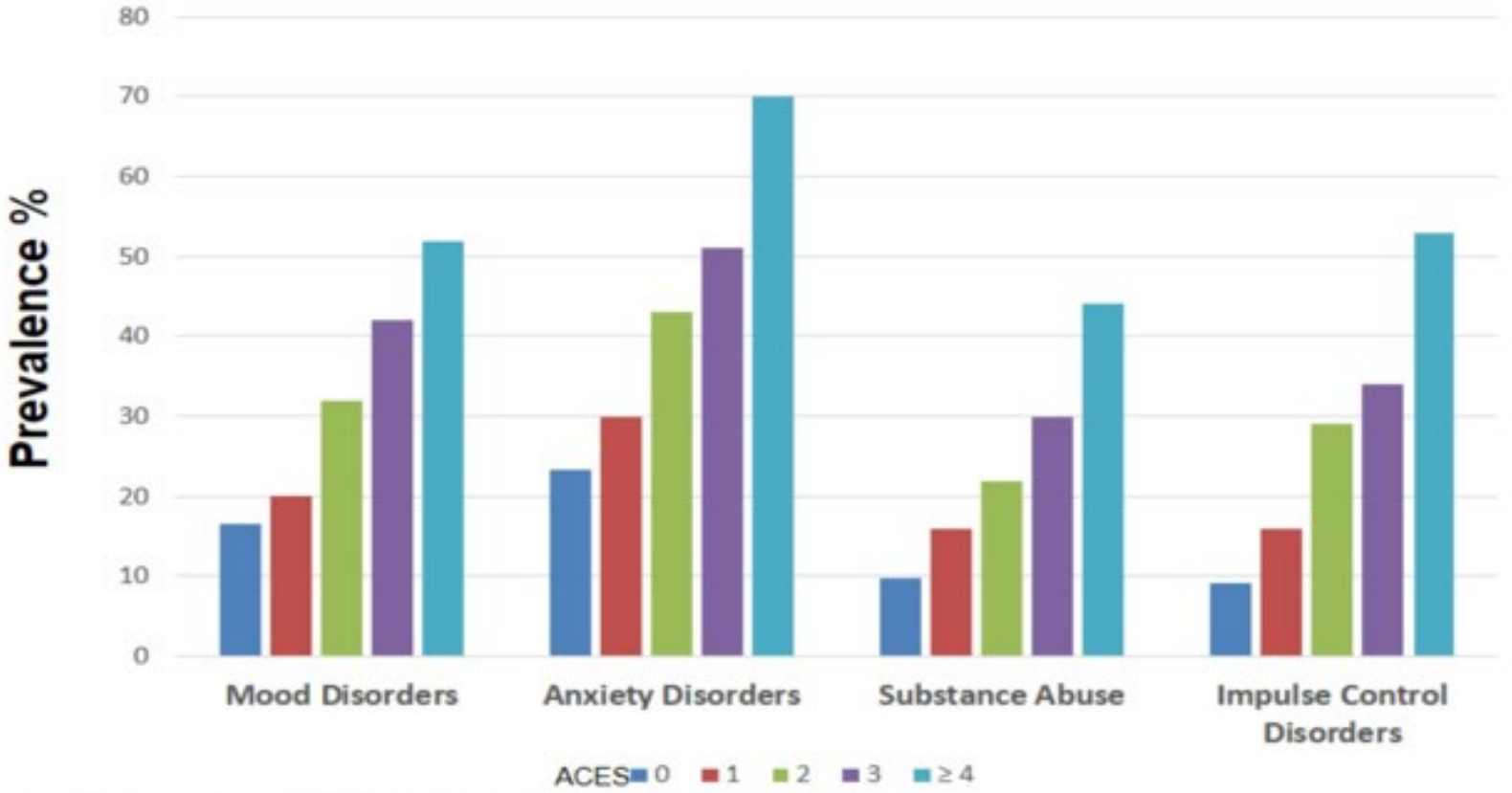
Mental Illness | Intimate Partner Violence | Parental Separation or Divorce | Incarceration | Substance Misuse or Dependence

While almost 2/3 of U.S. adults have experienced ACEs, exposure is unequally distributed by race and ethnicity

*Sociodemographic characteristics of adults in the study population, by adverse childhood experience score* — Behavioral Risk Factor Surveillance System (BRFSS), 25 states,† 2015–2017; Source: US Department of Health and Human Services/Centers for Disease Control and Prevention MMWR / November 8, 2019 / Vol. 68 / No. 44.



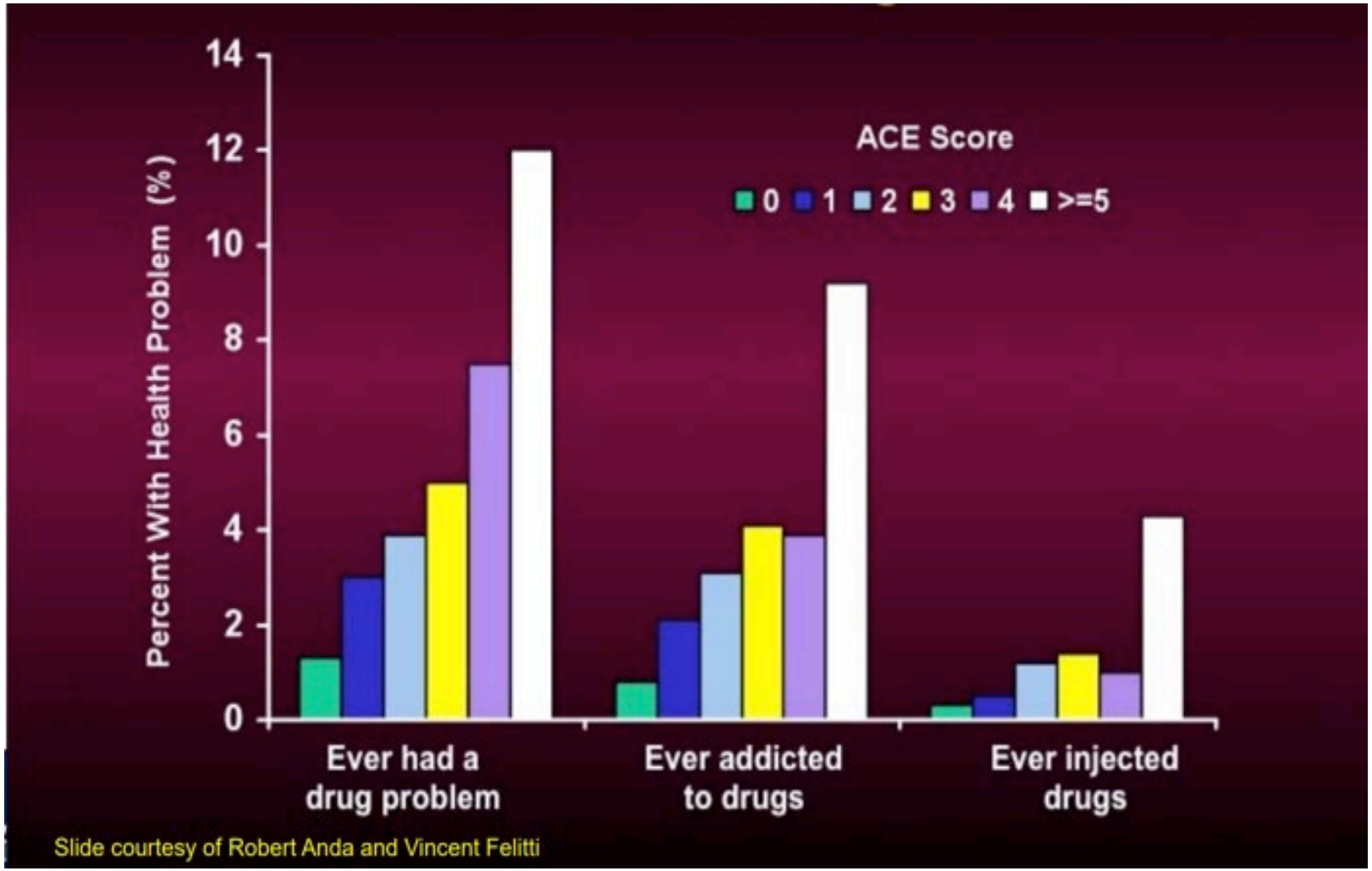
# Cumulative ACEs & Mental Health[1,2]

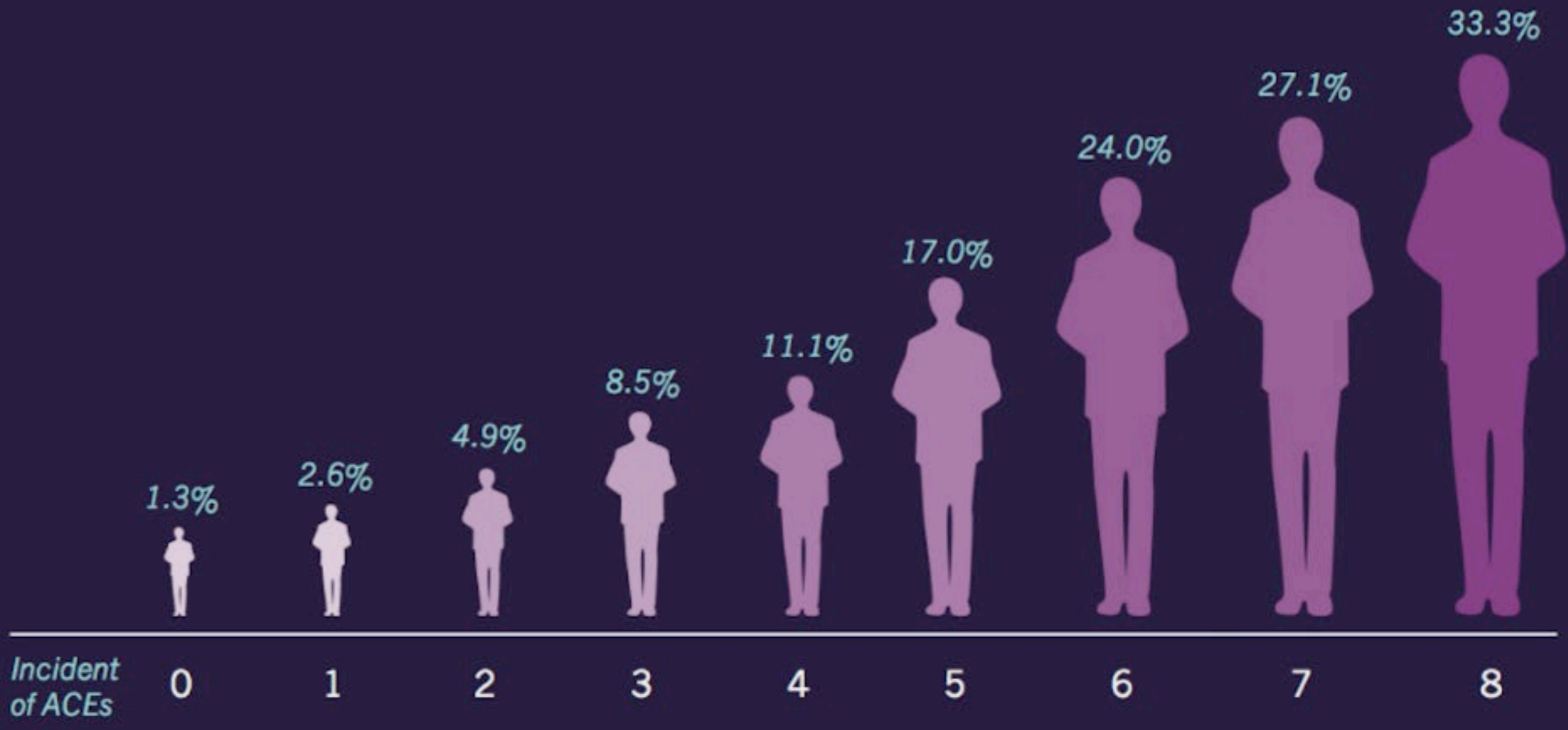



[1]Data from the National Comorbidity Survey-Replication Sample (NCS-R).
[2]Putnam, Harris, Putnam, J Traumatic Stress, 26:435-442, 2013.

CANarratives.org

# ACE Score and Substance Use






**ACE Score and Relation to Adult Homelessness**

*Proportion of Washington residents experiencing adult homelessness (among participants in Washington's Behavioral Risk Factor Surveillance System).*[3]

# ACES ARE ASSOCIATED WITH INCREASED RISK FOR 9 OF THE 10 LEADING CAUSES OF DEATH IN THE U.S.

| Leading Causes of Death in the U.S., 2021 | | Odds Ratios for ≥ 4 ACEs (relative to no ACEs) |
|---|---|---|
| 1 | **Heart disease** | 2.1 |
| 2 | **Cancer** | 2.3 |
| 3 | COVID-19 | Unknown |
| 4 | **Accidents** (unintentional injuries) | 2.6 |
| 5 | **Stroke** | 2.0 |
| 6 | **Chronic lower respiratory disease** | 3.1 |
| 7 | **Alzheimer's disease** or dementia | 11.2 |
| 8 | **Diabetes** | 1.4 |
| 9 | **Chronic liver disease** | 2.4 |
| 10 | **Kidney disease** | 1.7 |

# Annual Cost of ACEs in the U.S.

Heart disease

Stroke

Cancer

Diabetes

Arthritis

Asthma

COPD

Kidney Disease


Smoking

Heavy Drinking

Overweight and Obesity

Illicit Drug Use

Anxiety

Depression

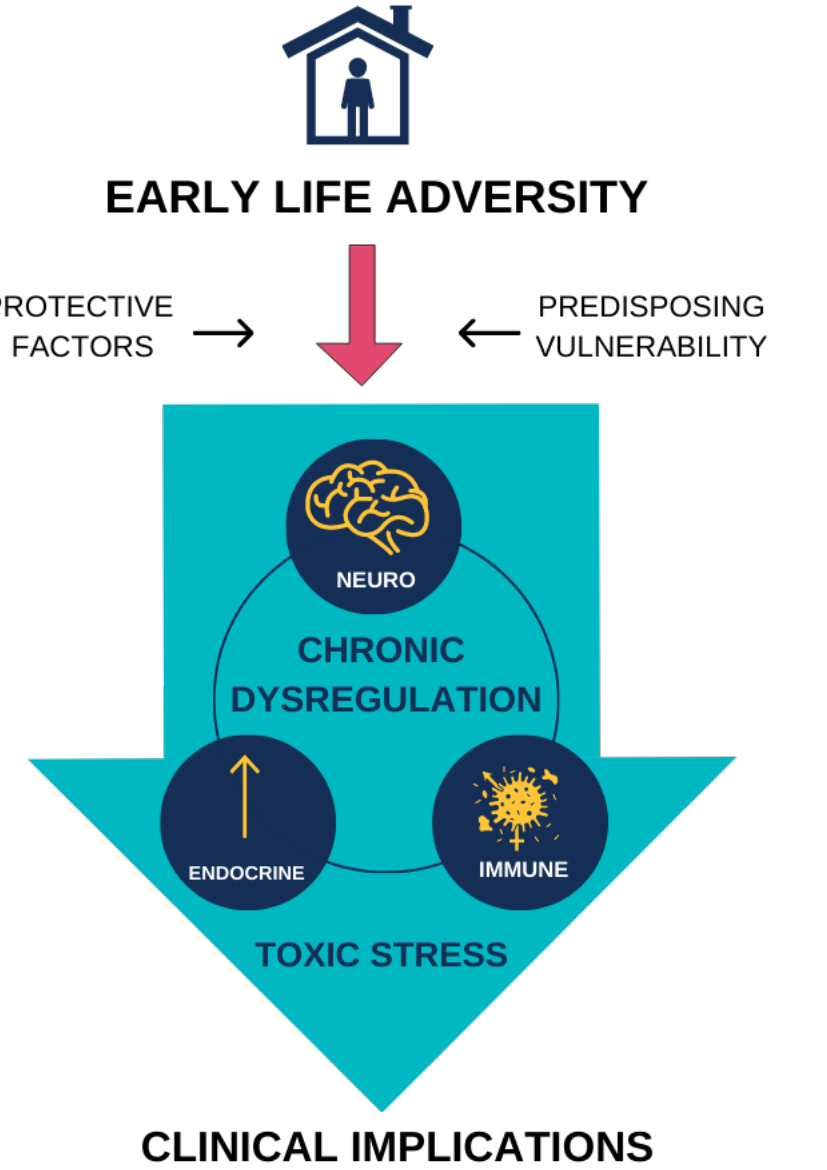
Violence

Peterson C, Aslam MV, Niolon PH, Bacon S, Bellis MA, Mercy JA, Florence C. Economic Burden of Health Conditions Associated With Adverse Childhood Experiences Among US Adults. JAMA Netw Open. 2023 Dec 1;6(12):e2346323. doi: 10.1001/jamanetworkopen.2023.46323. PMID: 38055277; PMCID: PMC10701608.

# THE BIOLOGY OF ADVERSITY

# THE 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…"***




Source: National Academies of Sciences, Engineering, and Medicine. Vibrant and healthy kids: *Aligning science, practice, and policy to advance health equity*. Washington, DC: National Academies Press, 2019.; Nelson CA, Bhutta ZA, Burke Harris N, Danese A, Samara M. Adversity in childhood is linked to mental and physical health throughout life. *BMJ (Clinical Research Edition)* 2020; 371: m3048.

# Biological systems disrupted by toxic stress

| SYSTEM | MECHANISM(S) | HEALTH IMPACT |
|---|---|---|
| **Neurologic; Neuroendocrine** | - Dysregulation of SAM and HPA axes; 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 |
| | - VTA and reward processing dysregulation | Increased risky behaviors and risk of addiction |
| **Immunologic; Inflammatory** | - Increased inflammatory markers, especially Th2 response; inhibition of anti-inflammatory pathways; gut microbiome dysbiosis | Increased risk of infection, auto-immune disorders, cancers, chronic inflammation; cardiometabolic disorders |
| **Endocrine/ Metabolic** | - Changes in growth hormone, thyroid hormone, and pubertal hormonal axes | Changes in growth, development, basal metabolism, and pubertal events |
| | - Changes to leptin, ghrelin, lipid and glucose metabolism, and other metabolic pathways | Increased risk of overweight, obesity, cardiometabolic disorders, and insulin resistance |
| **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 |

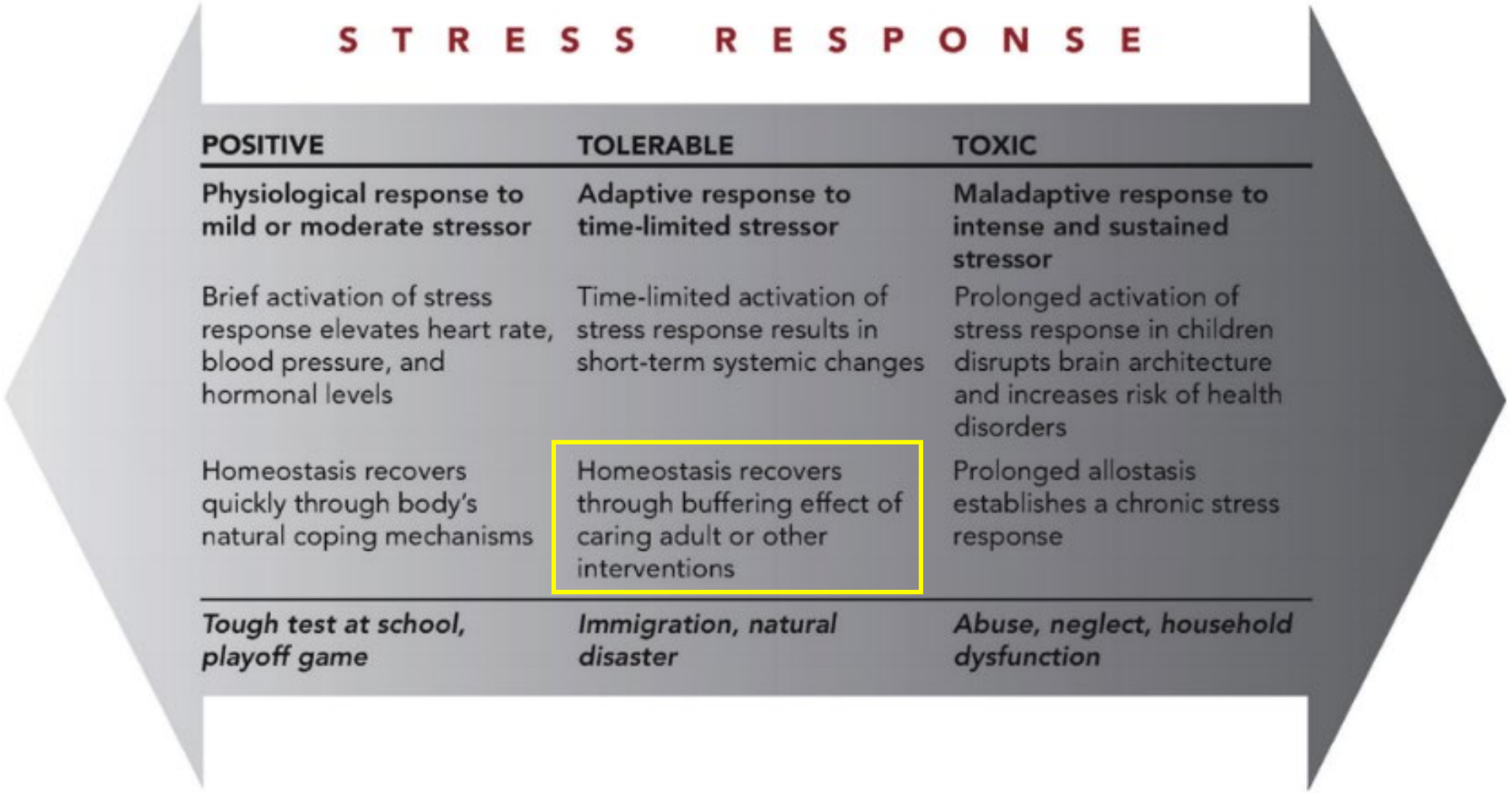



**Fig. 2.** Spectrum of the stress response: positive, tolerable, and toxic.

Source: Bucci, M., S. S. Marques, D. Oh, and N. B. Harris. 2016. Toxic stress in children and adolescents. *Advances in Pediatrics* **63**(1):403–428.

# Buffering the Toxic Stress Response

**Neurologic/Neuroendocrine**: MRI studies found that institutionalized children randomized to **high-quality nurturant caregiving** showed normalization of the developmental trajectory of white matter structures. **Responsive caregiving** also improves cortisol reactivity in children. **Time in nature** reduces sympathetic nervous system activity and increases parasympathetic activity.

**Immunologic**: **Meditation** was associated with decreased IFN-γ and NK cell production of IL-10 and with increased T cell production of IL-4 (anti-inflammatory). **Healthy sleep** reduces infection risk and improves vaccination response, increasing NK cell activity, IL-6, and TNF-alpha levels. **Moderate exercise** decreases infection risk.

**Endocrine/Metabolic**: **Oxytocin** inhibits the stress response, enhances bonding, protects against stress-induced cell death, has anti-inflammatory effects, enhances metabolic homeostasis, and protects vascular endothelium. **Social support** buffers stress-related cardiovascular reactivity and decreases catecholamine levels. The **Mediterranean diet** reduces inflammation and risk for depression, cardiovascular disease, diabetes, and mortality.

**Epigenetic**: Meany and colleagues found that **nurturant caregiving** was associated with epigenetic changes that led to greater stress tolerance, more normal functioning of the stress response, and improved cognitive performance. Child Parent Psychotherapy is associated with improved cortisol regulation and delays in epigenetic aging.

Sources: Bick et al, 2015, Feldman et al, 2014, Kandola et al, 2016, Cohen et al, 2015, Carlson et al, Irwin, et al, 2015, Boufleur et al, 2013, Blaisdell et al, 2019, Grewen et al., 2005, Irwin, 2015, Besedovsky et al, 2019, Keicolt-Glaser et al, 2017, Gleeson et al, 2011, Jedrychowski et al, 2001, Kuo 2015

# Toxic Stress is Amenable to Treatment

- New opportunities to more precisely interrupt the toxic stress response, break the intergenerational cycle of ACEs and toxic stress, and promote an intergenerational cycle of health.

- Early intervention can improve brain, immune, hormonal, and genetic regulatory control of development.

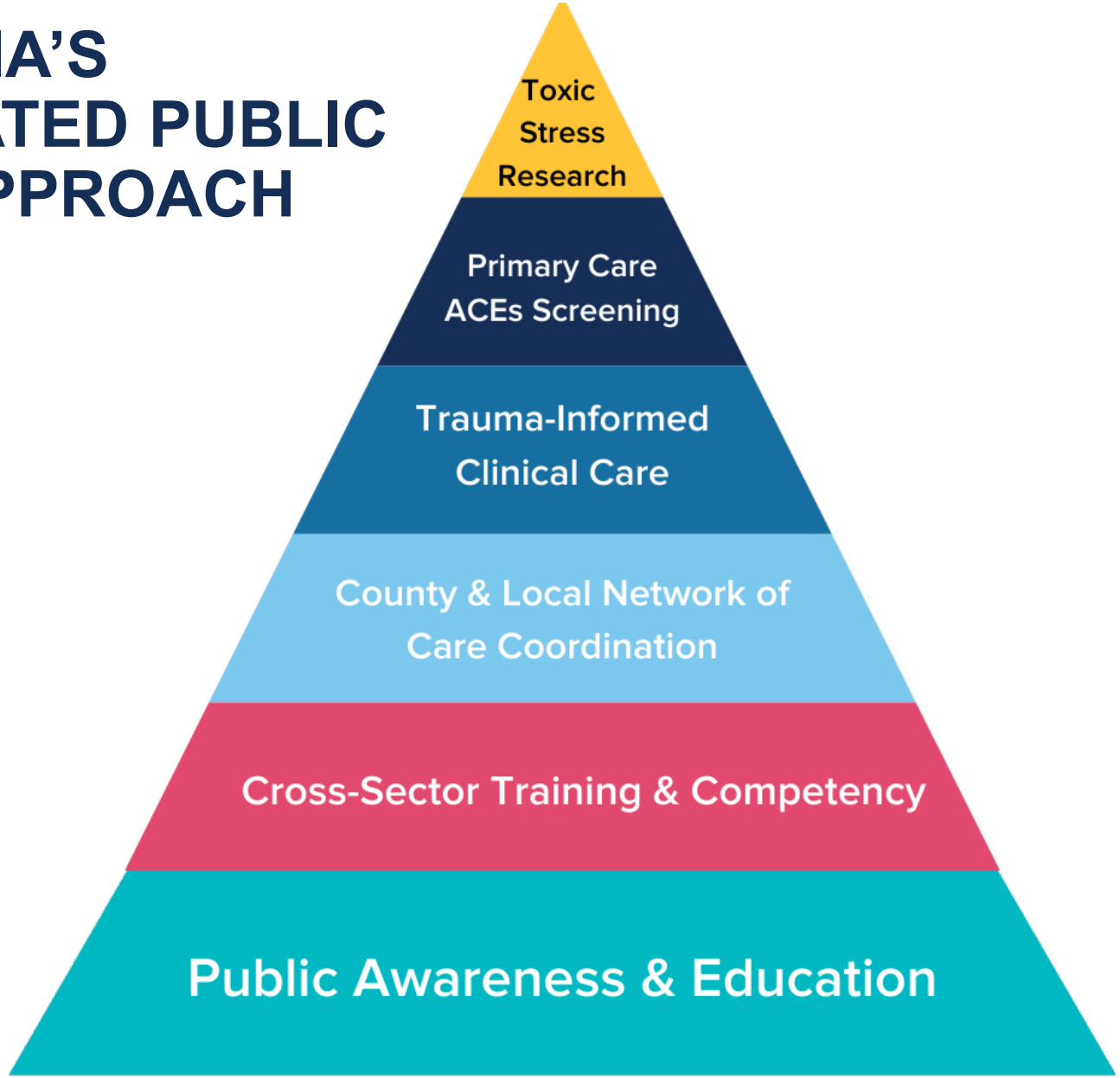
- Treatment of toxic stress in adults may prevent transmission of neuro-endocrine-immune-metabolic and genetic regulatory disruptions in offspring.

Source: Sources: Chino M, Debruyn L. Building true capacity: Indigenous models for Indigenous communities. American Journal of Public Health 2006; 96(4): 596-9.; Bick J, et al. Effect of early institutionalization and foster care on long-term white matter development: A randomized clinical trial. JAMA Pediatrics 2015; 169(3): 211-9.; Miller GE, et al. A family-oriented psychosocial intervention reduces inflammation in low-SES African American youth. Proceedings of the National Academy of Sciences 2014; 111(31): 11287- 92.

# NO SINGLE SECTOR OR CATEGORY OF PREVENTION IS SUFFICIENT ALONE


| Healthcare | Public Health | Social Services | Early Childhood | Education | Justice |
|---|---|---|---|---|---|

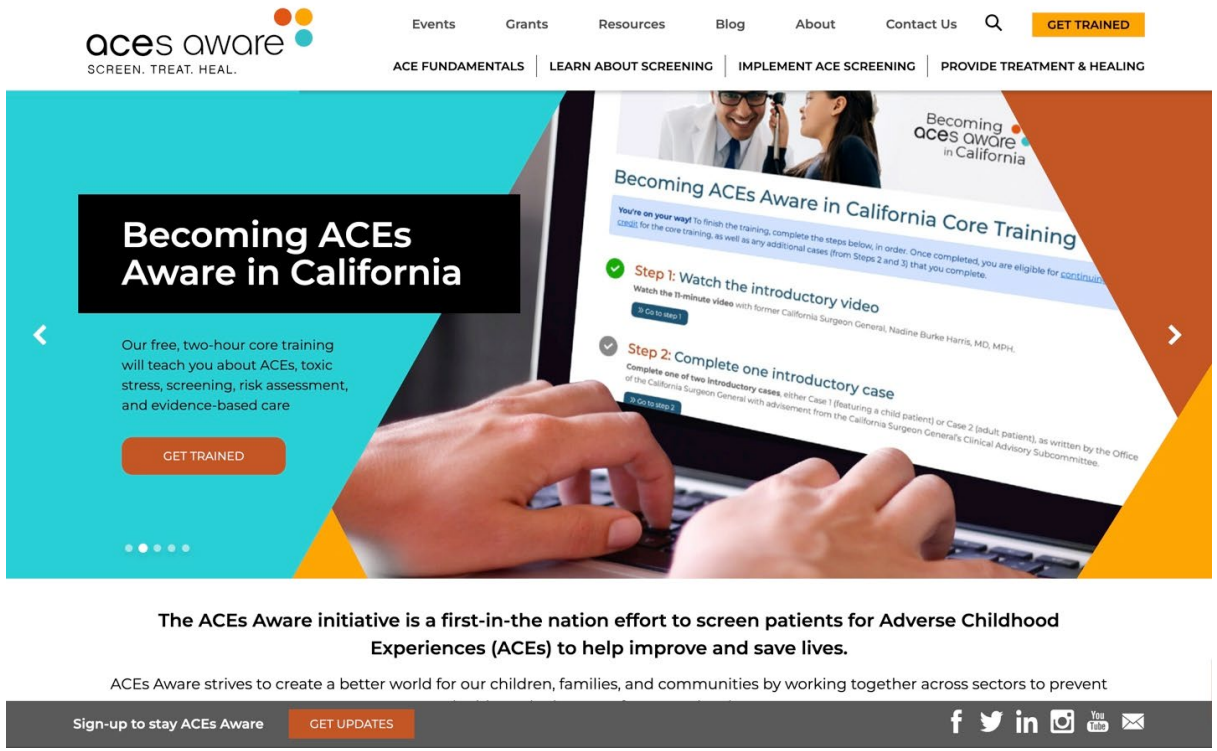
# CALIFORNIA'S COORDINATED PUBLIC HEALTH APPROACH

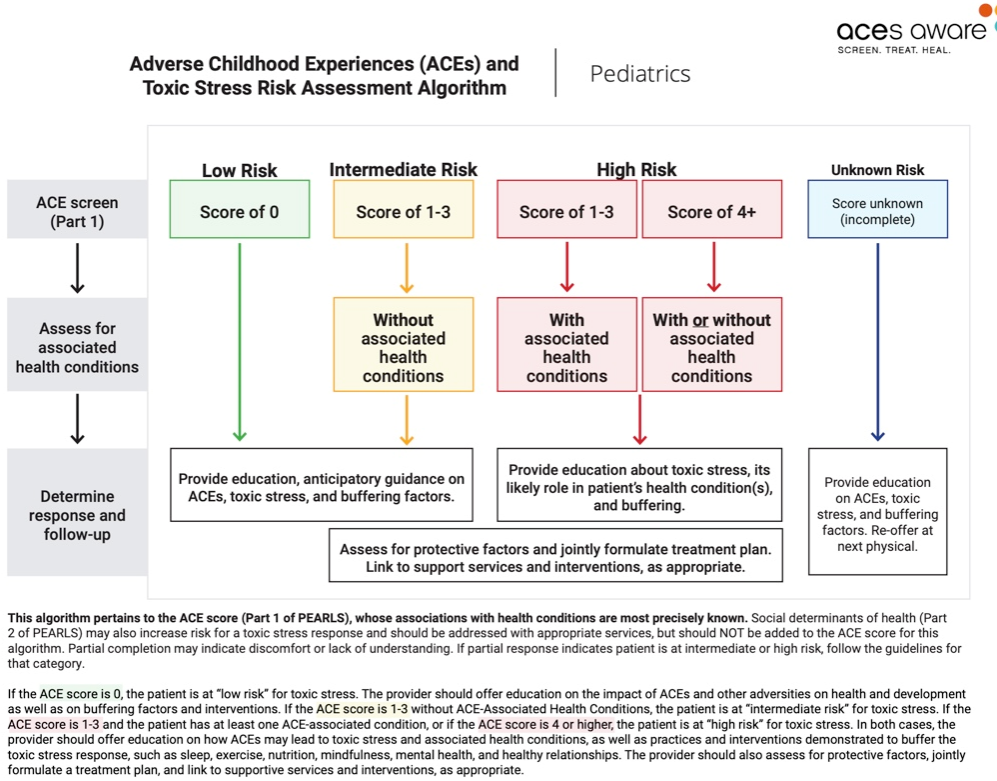


# Toxic Stress Research: California Initiative to Advance Precision Medicine

- **$20M for 7 demonstration projects:**
  - **Children's Hospital Los Angeles:** *Scalable Measurement and Clinical Deployment of Mitochondrial Biomarkers of Toxic Stress*
  - **Loma Linda University:** *A Multi-Component Intervention to Strengthen Families and Build Youth Resilience*
  - **Stanford University:** *Systems-based, Multidisciplinary Assessment of Adversity and Toxic Stress for Individualized Care (The SYSTEMAATIC Project)*
  - **University of California, Irvine:** *Using Precision Medicine to Tackle Impacts of Adverse and Unpredictable Experiences on Children's Neurodevelopment*
  - **University of California, Los Angeles:** *Identifying Social, Molecular, & Immunological Processes for Mitigating Toxic Stress & Enhancing Personalized Resilience*
  - **University of California, San Diego:** *San Diego County, UC San Diego, & Community Partners Better Address ACEs with Precision Medicine & Organizational Change*
  - **University of California, San Francisco:** *The Collaborative approach to examining Adversity and building Resilience (CARE) Program*

# Primary Care ACE Screening and Toxic Stress Risk Assessment



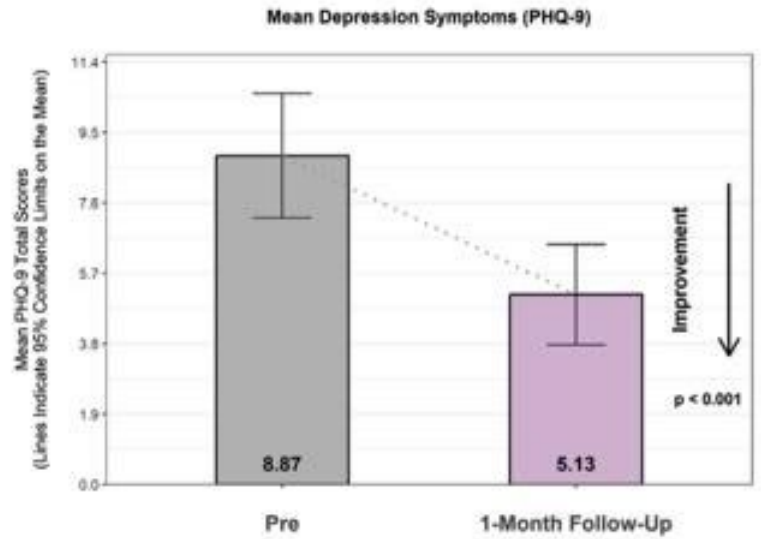

**This algorithm pertains to the ACE score (Part 1 of PEARLS), whose associations with health conditions are most precisely known.** Social determinants of health (Part 2 of PEARLS) may also increase risk for a toxic stress response and should be addressed with appropriate services, but should NOT be added to the ACE score for this algorithm. Partial completion may indicate discomfort or lack of understanding. If partial response indicates patient is at intermediate or high risk, follow the guidelines for that category.

If the ACE score is 0, the patient is at "low risk" for toxic stress. The provider should offer education on the impact of ACEs and other adversities on health and development as well as on buffering factors and interventions. If the ACE score is 1-3 without ACE-Associated Health Conditions, the patient is at "intermediate risk" for toxic stress. If the ACE score is 1-3 and the patient has at least one ACE-associated condition, or if the ACE score is 4 or higher, the patient is at "high risk" for toxic stress. In both cases, the provider should offer education on how ACEs may lead to toxic stress and associated health conditions, as well as practices and interventions demonstrated to buffer the toxic stress response, such as sleep, exercise, nutrition, mindfulness, mental health, and healthy relationships. The provider should also assess for protective factors, jointly formulate a treatment plan, and link to supportive services and interventions, as appropriate.

# Improved Health Outcomes

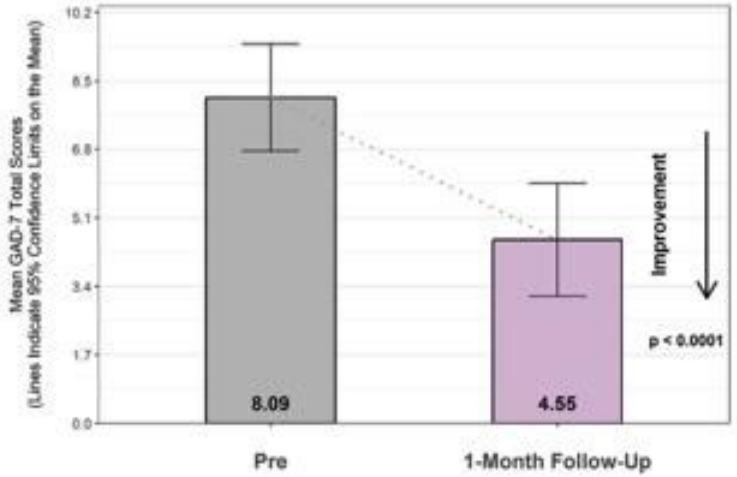


**Figure 4.** Changes in Depression Symptoms (PHQ-9) Pre- and Post-Enrollment (Virtual Meditation as a Response to Adverse Childhood Events)



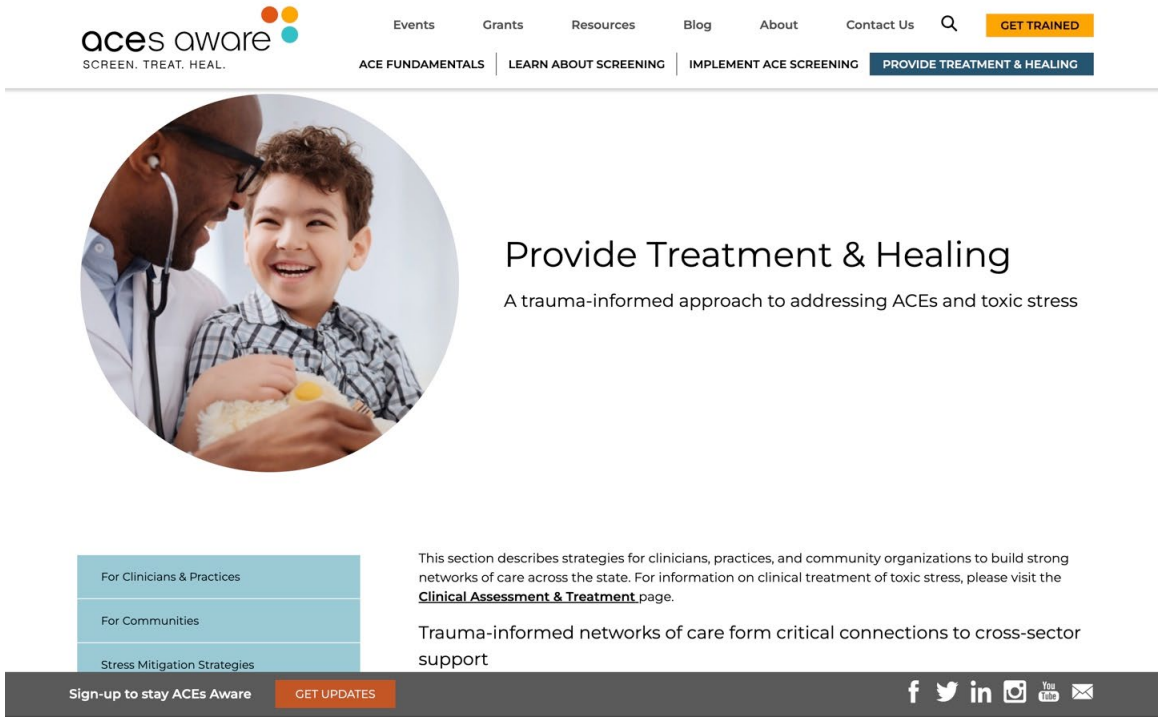

SHARK: October 2022 - July 2023
N = 47 Participating Youth
Wilcoxon Signed-Rank Test
≥ 10 Indicates Clinically Meaningful Depression Risk

**Figure 5.** Changes in Anxiety Scores (GAD7) Pre- and Post-Enrollment (Virtual Meditation as a Response to Adverse Childhood Events)




SHARK: October 2022 - July 2023
N = 47 Participating Youth
Wilcoxon Signed-Rank Test
≥ 10 Indicates Clinically Meaningful Anxiety Risk

# Trauma Informed Clinical Care and Network of Care Coordination




## CalAIM

**Behavioral Health Initiative**
Medi-Cal is strengthening mental health and substance use disorder services and better integrating them with physical health care.

**Community Supports**
New services as part of the transformation of Medi-Cal help members address unmet basic needs that can impact their health, whether they're clinical or non-clinical. These include support to secure and maintain housing, and access to medically tailored meals to support short term recovery.

**Dental Initiative**
Medi-Cal is expanding dental benefits for children and those with conditions that are more likely to lead to dental disease.

**Enhanced Care Management**
Medi-Cal is providing high-need members with in-person care where they live.

**Incentive Payment Program**
Medi-Cal is supporting the implementation and expansion of Enhanced Care Management, Community Supports and other initiatives by providing incentives to Medi-Cal managed care plans to invest in improving the quality of care, reducing health disparities, and promoting health equity.

**Integrated Care for Dual Eligible Members**
Medi-Cal is better integrating care for members who are dually enrolled in both Medicare and Medi-Cal.

**Justice-Involved Initiative**
Medi-Cal is providing services to justice-involved adults and youth while they are incarcerated, and as they re-enter their communities.

**Population Health Management**
Medi-Cal is requiring managed care plans to use a concentrated holistic approach to improving the health outcomes of a group of individuals.

**Providing Access and Transforming Health (PATH)**
PATH funds are an investment in the capacity and infrastructure of local community-based organizations to provide services to Medi-Cal members in their communities.

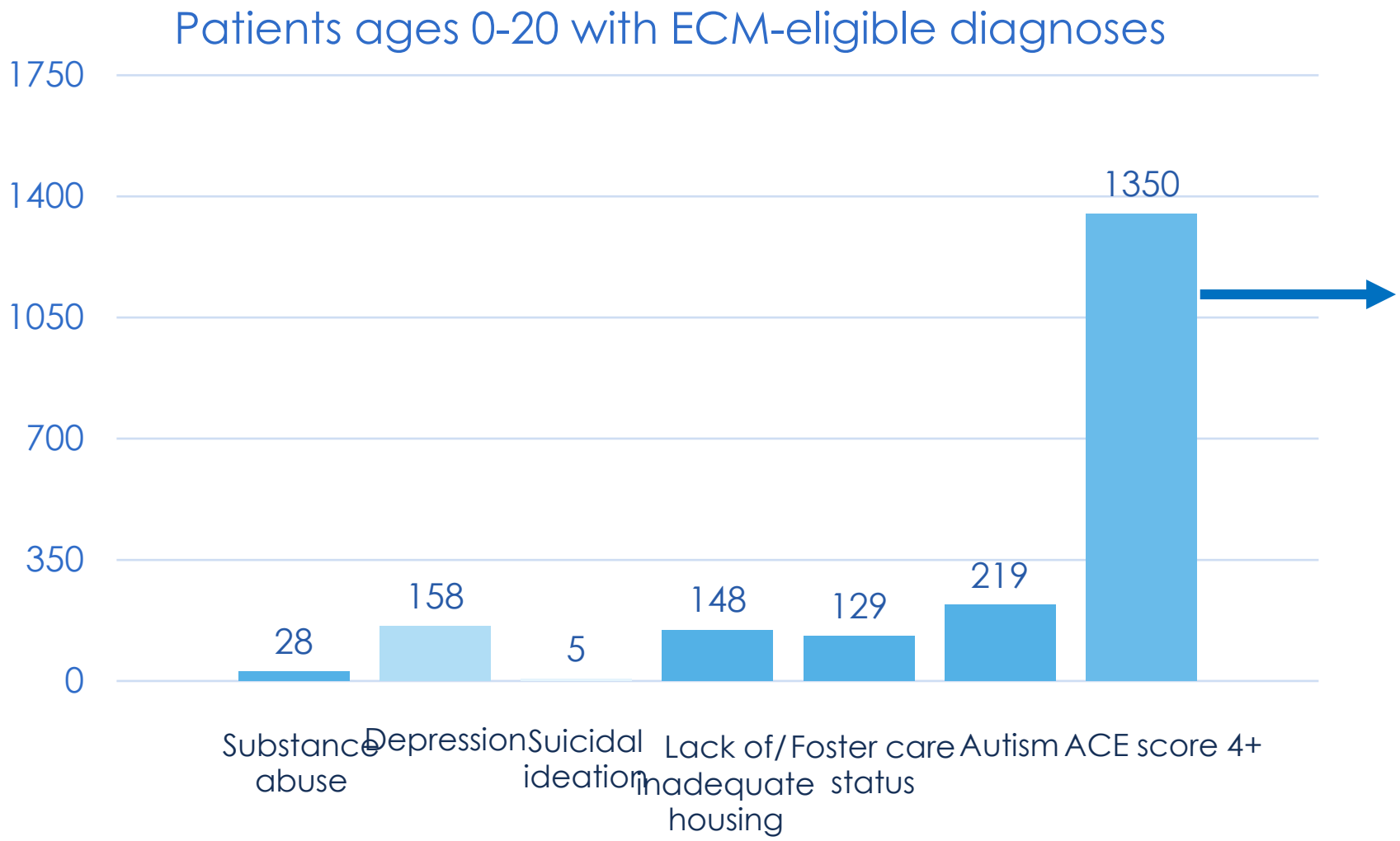
**Statewide Managed Long-Term Care**
Medi-Cal is introducing a better way to coordinate care for those with very complex or long-term care needs.

**Supporting Health and Opportunity for Children and Families**
Medi-Cal is improving the health of children in California, supporting their families, reducing disparities in care, and strengthening accountability and oversight of children's services.

ACEs LA

# Enhanced Care Management

## Eligibility by Diagnosis at LA County DHS

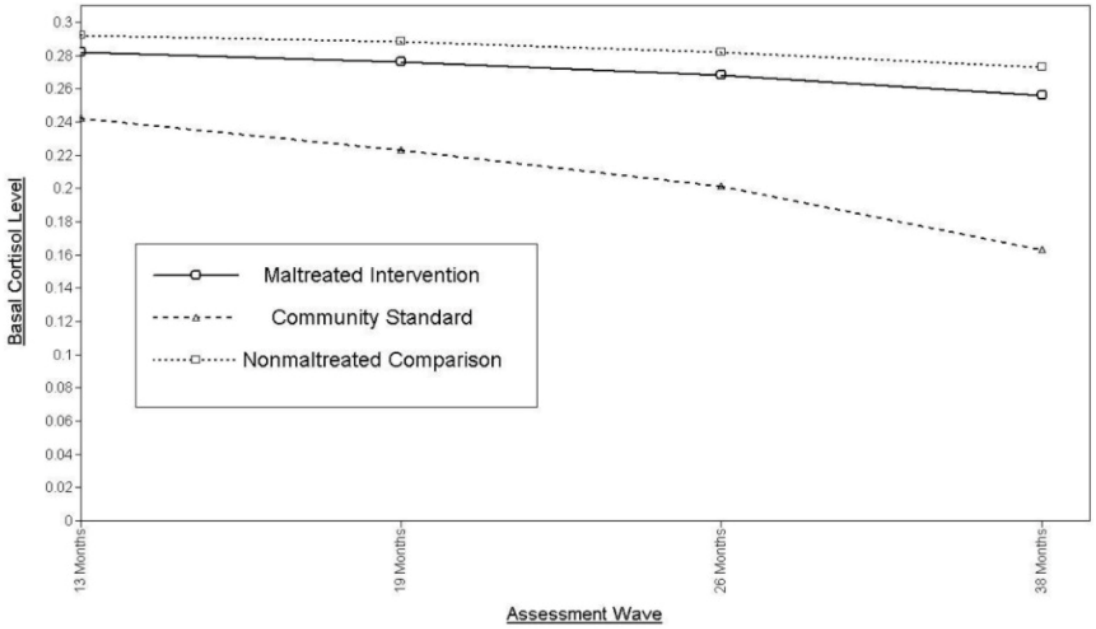



Only 71 patients with ACE score of 4+ have another of these ECM eligible diagnoses

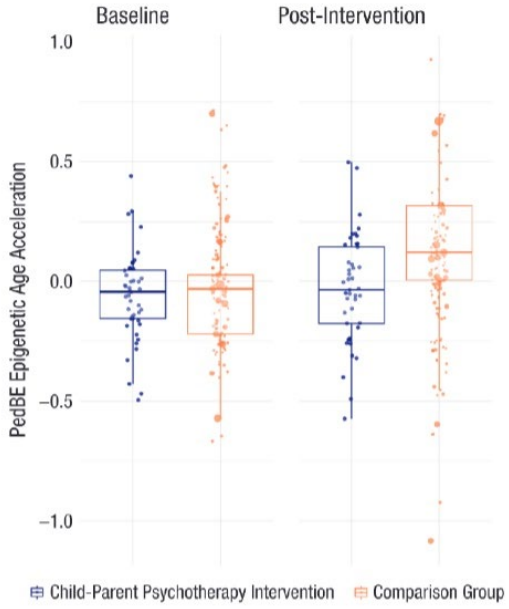
UCLA

Health Services
LOS ANGELES COUNTY

# Child Parent Psychotherapy Improves Cortisol Regulation and Reduces Epigenetic Age Acceleration




- Fig 1:



# Cross Sector Training and Competency: Education

OFFICE OF THE CALIFORNIA SURGEON GENERAL

ABOUT PRIORITIES NEWS RESOURCES CONTACT

Safe Spaces

Foundations of Trauma-Informed Practice for Educational and Care Settings

## New Training Creates Safe Spaces for Kids

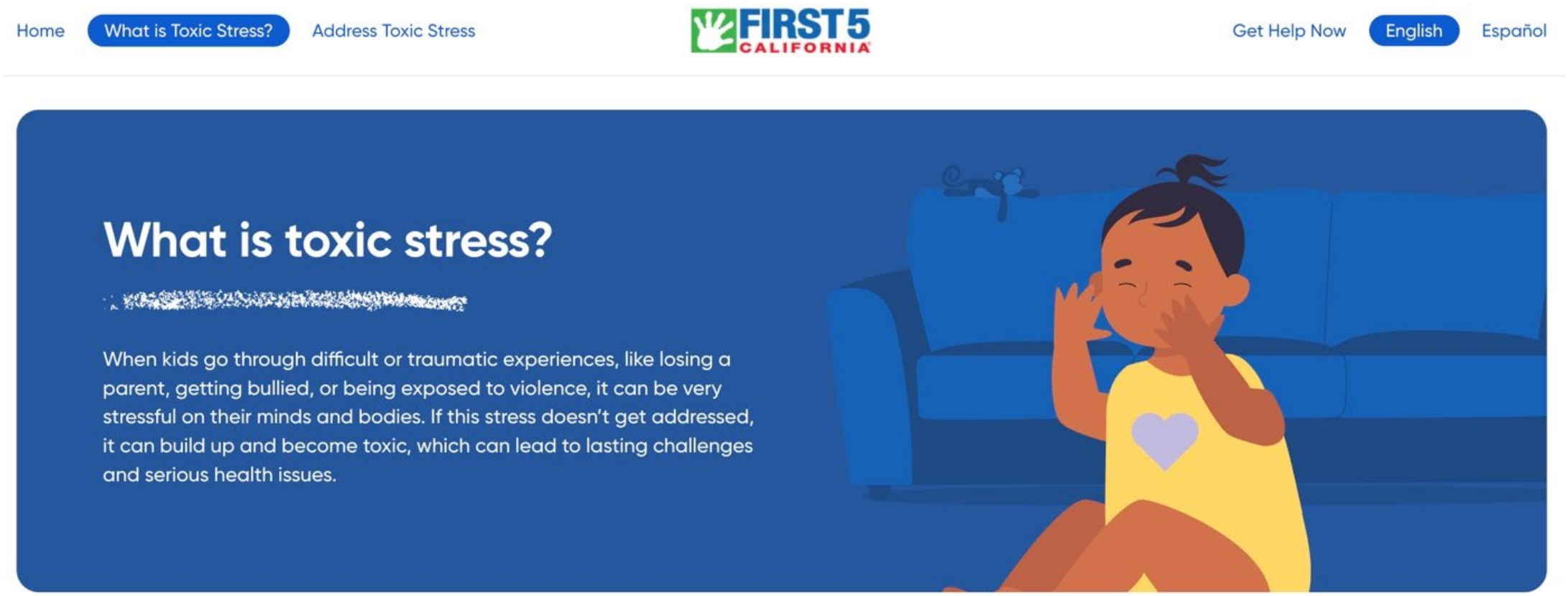
Safe spaces is a free, online training designed to help early care providers, TK-12 educators and other school personnel recognize and respond to trauma and stress in children.

TRAINING NOW LIVE!

# Cross Sector Training and Competency: Corrections and Rehabilitation


Becoming a Trauma-Informed Organization: CDCR and CCHCS are committed to improving the practices, policies, and culture of the entire department by educating staff at all levels to recognize the impacts of trauma and ensure the physical and emotional safety of all staff and incarcerated individuals.

# Public Awareness and Education



# Key Evaluation Results

## Knowledge & Awareness

**92% Awareness**
California Caregivers Aware of Stronger Starts

**2.4X Increase**
Knowledge of "Toxic Stress"
(from 22% to 74%)

**2X Increase**
Knowledge of "ACEs"
(from 20% to 60%)

## Seeking Help

**2.4X Increase**
Caregivers Looking for How to Help Children Manage Trauma, Avoid Toxic Stress
(from 20% to 67%)

**3.6X Increase**
Caregivers Seeking Info About Toxic Stress
(from 14% to 64%)

## Actions & Motivations

**90% Motivated**
Learn What Actions I Can Take to Overcome Toxic Stress

**93% Intend**
Take Actions to Manage Toxic Stress in Themselves & Kids

**42% Increase**
Helping Children Understand Negative Feelings

**81% Engaged**
Actively Engaged Online or Took Action with Friends

## Beliefs

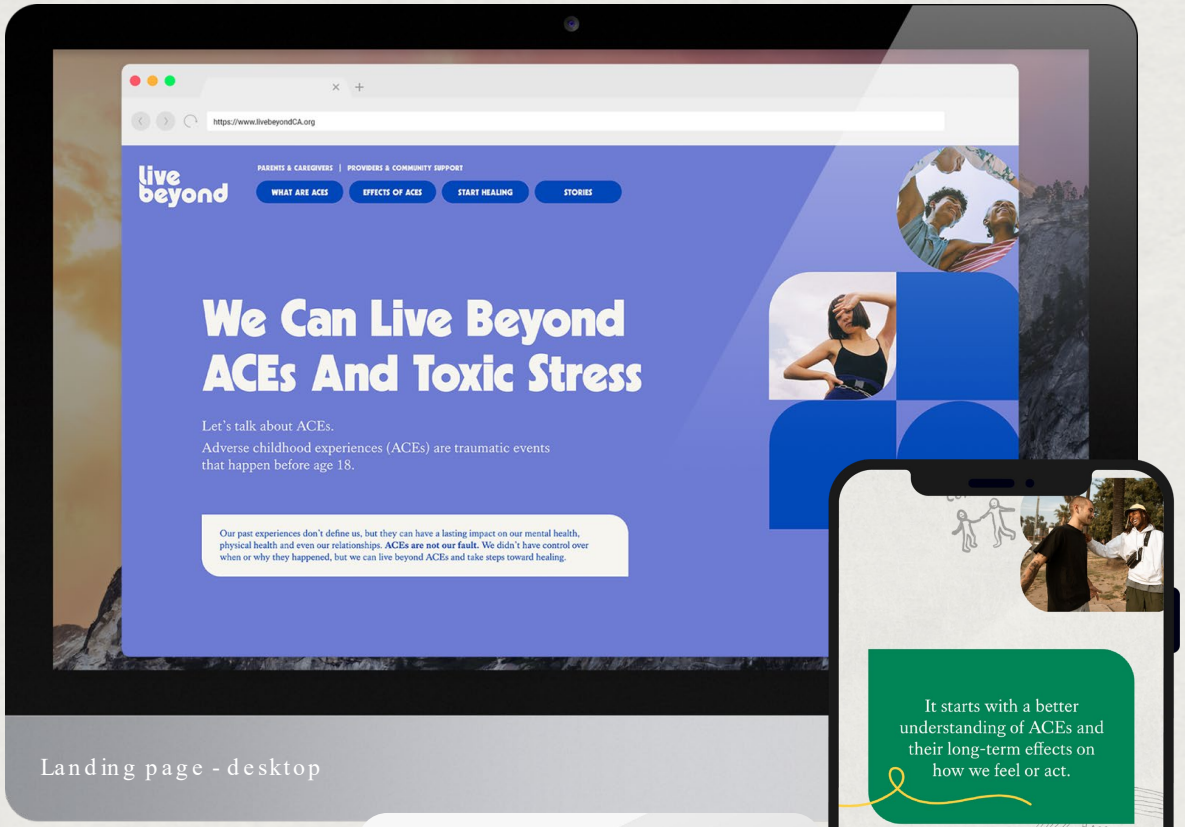
**89% Believe**
It's Possible to Help Children Heal from Trauma

**88% Believe**
Can Break the Cycle of Toxic Stress for Their Child

**87% Believe**
Having Toxic Stress Impacts the Way I Parent My Child

**91% Agree**
Learning about Toxic Stress is Relevant to Their Lives

# For Youth By Youth

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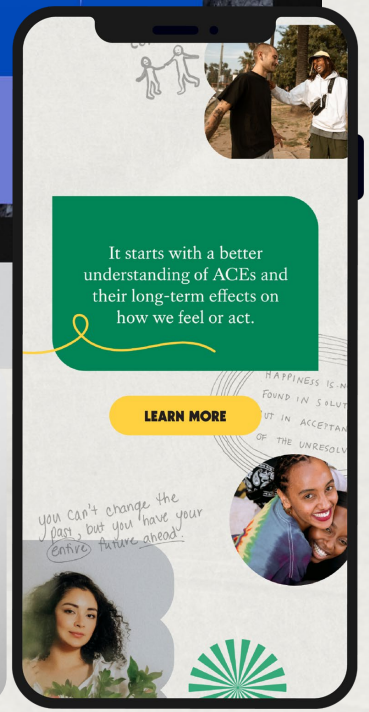
Stickers

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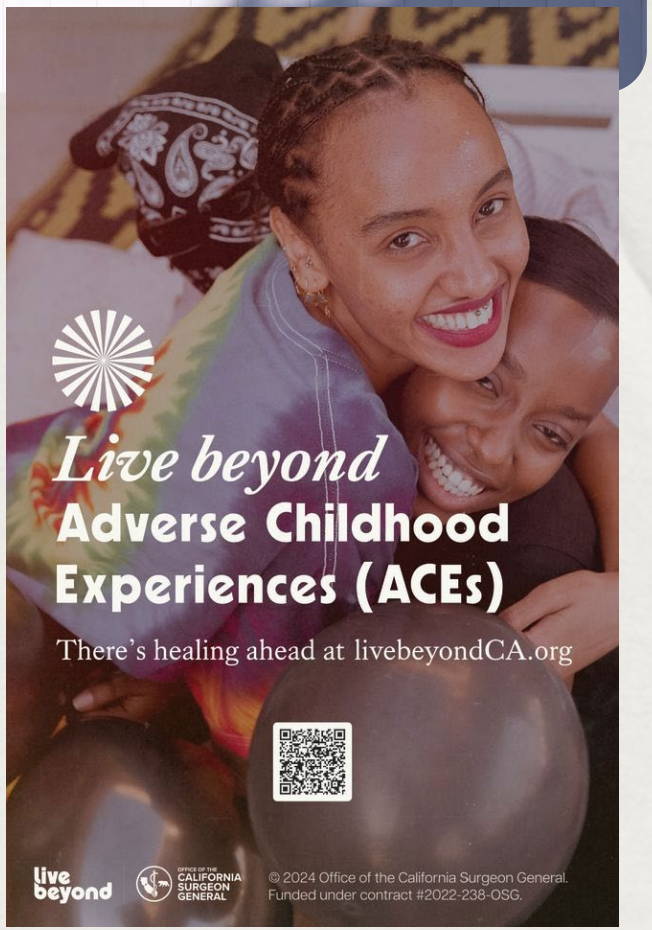


live beyond

# Further Research is Necessary

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.

2. Guidelines for **clinical management** of ACE-Associated Health Conditions (AAHC's) in the setting of toxic stress.

3. Identification of **therapeutic targets** for regulating the toxic stress response.

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 or inform individualized treatment strategies.

5. **Longitudinal studies** are needed to better understand the specific and longer-term impacts of clinical interventions that target the toxic stress response.

# THANK YOU!