aces aware
SCREEN. TREAT. HEAL.

The Science of ACEs and Toxic Stress (Part 1)

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Adverse Childhood Experiences (ACEs)

Abuse

Physical, emotional, or sexual

Physical

Emotional

Sexual

Neglect

Physical or emotional

Physical

Emotional

HOUSEHOLD CHALLENGES

Growing up in a household with incarceration, mental illness, substance misuse or dependence, absence due to separation or divorce, or intimate partner violence

Mental Illness

Intimate Partner Violence

Parental Separation or Divorce

Incarceration

Substance Misuse or Dependence

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SCREEN. TREAT. HEAL.

The Toxic Stress Response Defined

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

"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.

Recognizing Other Risk Factors for Toxic Stress

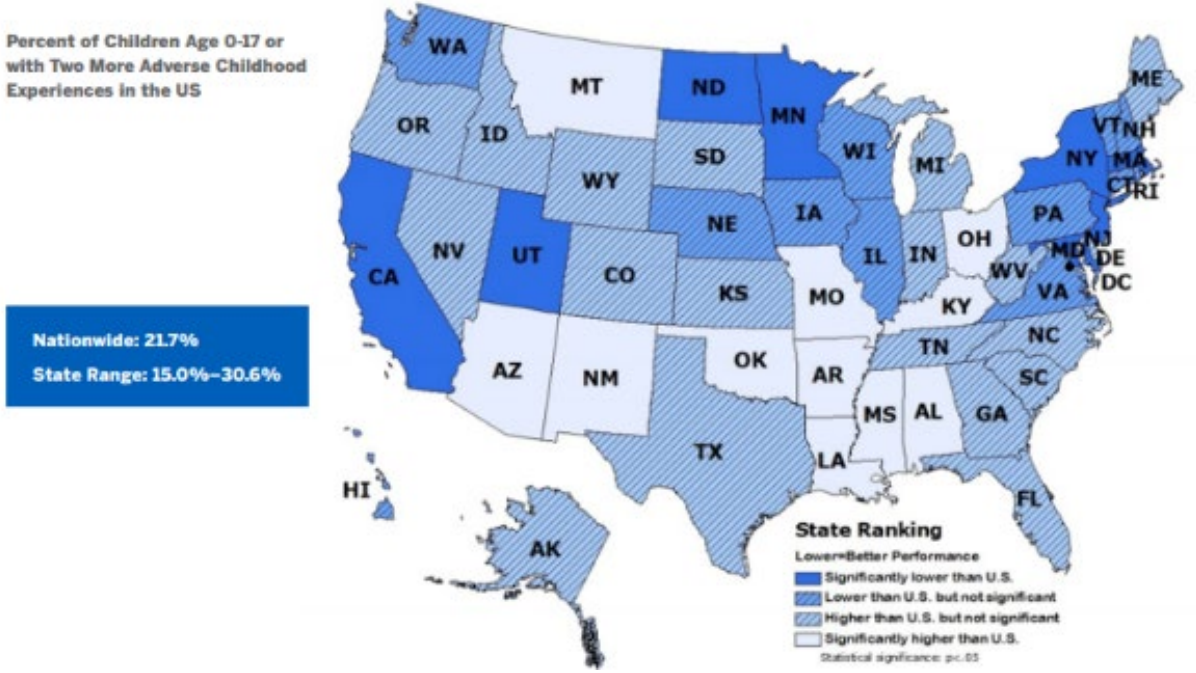
A circumstance, exposure, or condition with documented associations with increased likelihood or susceptibility of development of the toxic stress response.

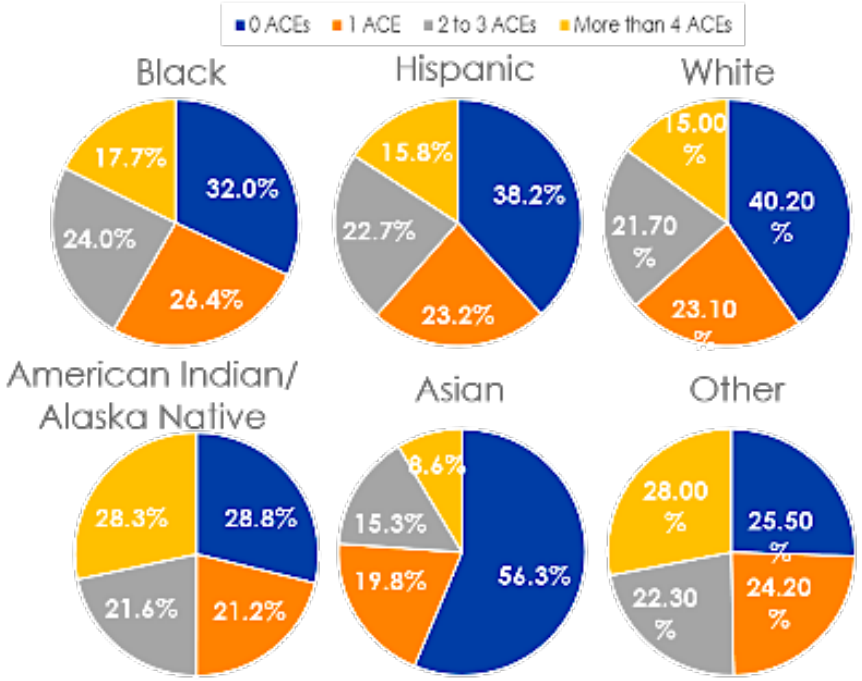
In addition to ACEs, ***other risk factors for toxic stress include poverty, exposure to discrimination, and exposure to the atrocities of war****.*

Source: 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.

61.6% of US adults have ≥ 1 ACE
15.8% have ≥ 4 ACEs

62.3% Californians have ≥1 ACEs 16.3% have ≥ 4 ACEs





Sources: Merrick et al., Prevalence of adverse childhood experiences from the 2011-2014 Behavioral Risk Factor Surveillance System in 23 states. *JAMA Pediatrics* 2018; 172: 1038.; Merrick et al., Vital Signs: Estimated Proportion of Adult Health Problems Attributable to Adverse Childhood Experiences and Implications for Prevention — 25 States, 2015–2017. *MMWR Morb Mortal Wkly Rep* 2019;68:999-1005; Bethell et al., Issue Brief: A national and across state profile on adverse childhood experiences among children and possibilities to heal and thrive. Johns Hopkins Bloomberg School of Public Health, October 2017.

ACEs Dramatically Increase Risk for at least 9 of the 10 Leading Causes of Death in the U.S.

	Leading Causes of Death in the U.S., 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

Source of causes of death: CDC, 2017; Sources of odds ratios: Hughes et al., 2017 for 1, 2, 4, 7, 10; Petrucelli et al., 2019 for 3 (injuries with fracture), 5; Center for Youth Wellness, 2014 for 6 (Alzheimer's or dementia); Center for Youth Wellness, 2014 and Merrick et al., 2019 for 9.

Annual Cost of ACEs to California

Select Health Conditions	Child Abuse and Neglect: Other Sectors
$112.5 billion	**$19.3 billion**
• Asthma • Arthritis • COPD • Depression • Smoking • Cardiovascular disease • Heavy Drinking • Obesity	• Education • Welfare • Criminal justice • Lifetime productivity • Healthcare, early death

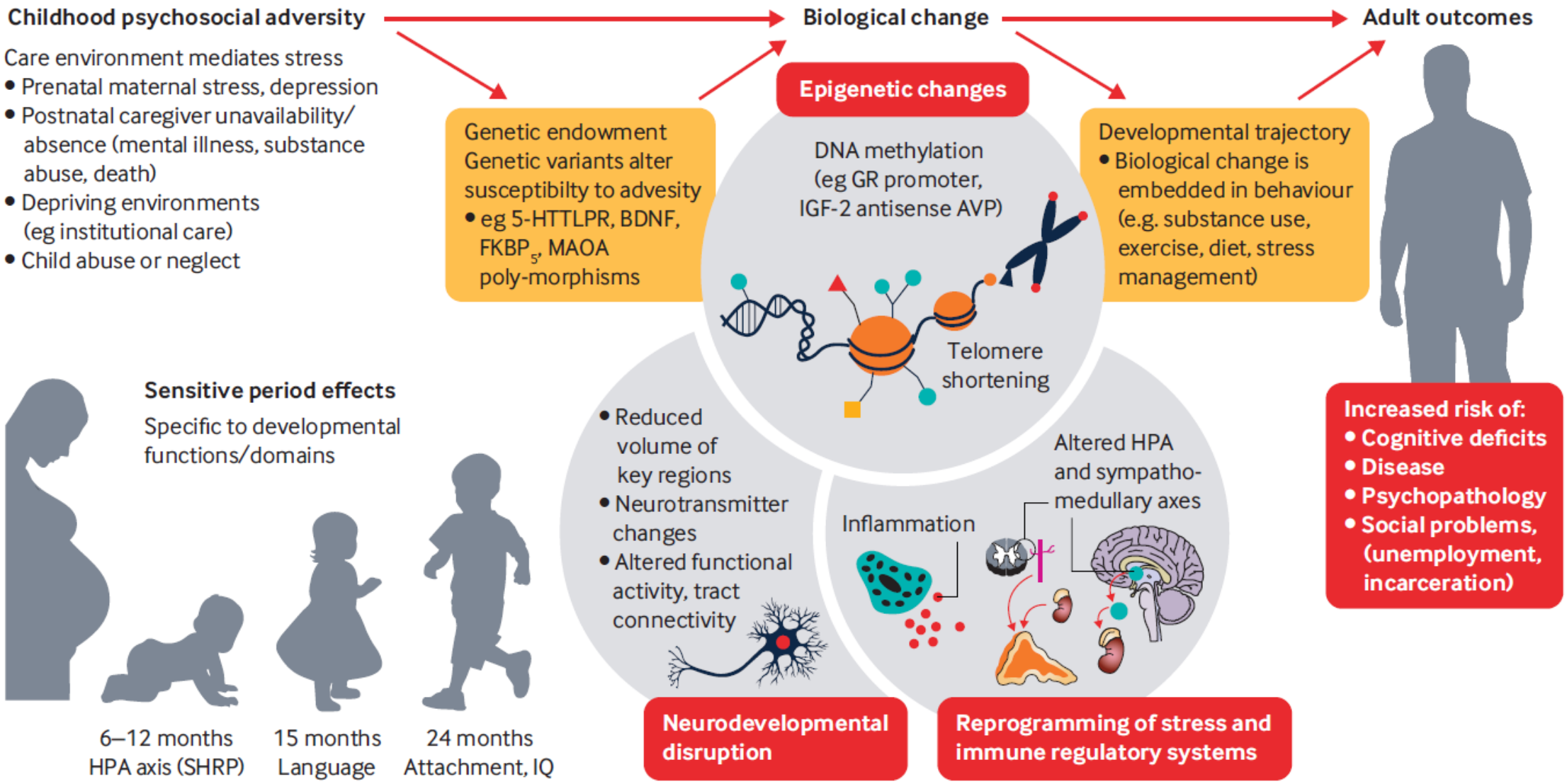
Sources: Miller TR, et al. (2020) Adult health burden and costs in California during 2013 associated with prior adverse childhood experiences. *PLoS ONE* 15(1): e0228019.; Safe & Sound. *The economics of child abuse: A study of California*: Safe & Sound, 2019.

ACEs and Toxic Stress are
A Public Health Crisis

ACEs and toxic stress are a root cause to some of the most harmful, persistent, and expensive societal and health challenges facing our world today.

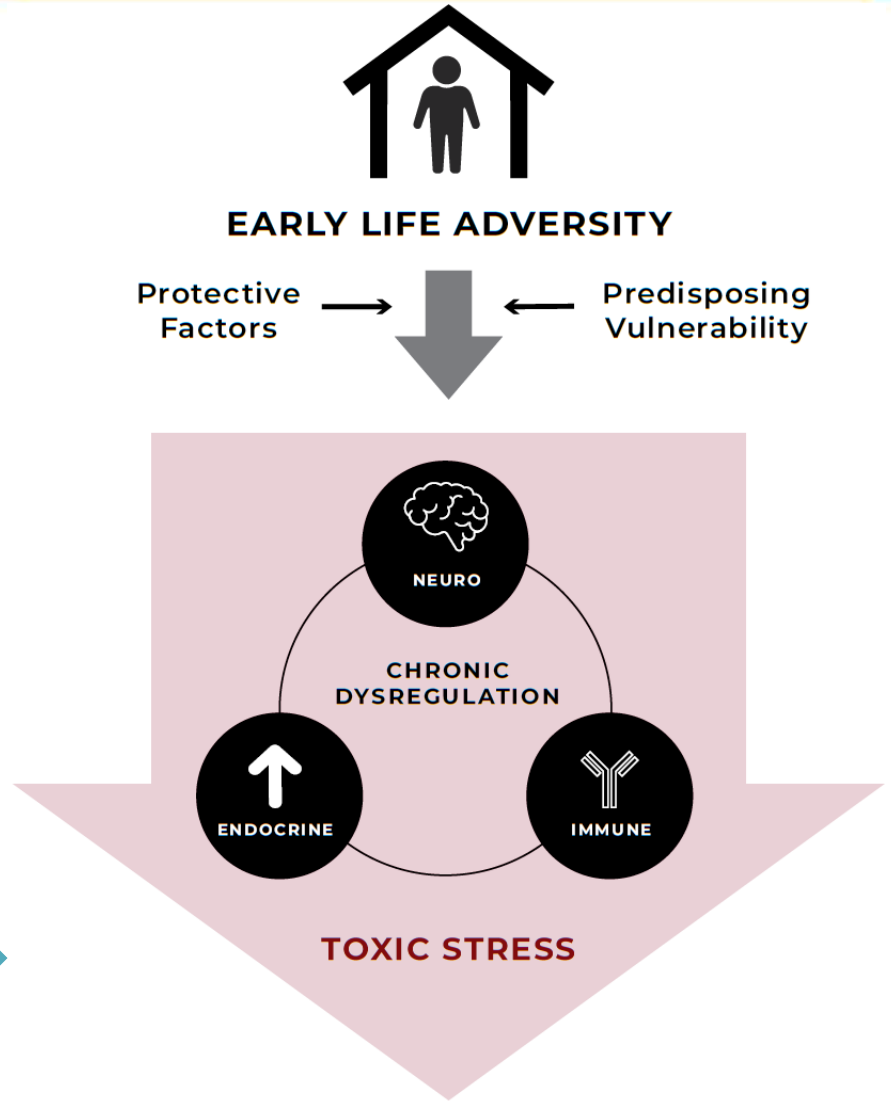
The Biology of Adversity

Childhood Adversity, Biological Changes, and Adult Outcomes



Source: 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.

Adverse Childhood Experiences can generate chronic activation of the stress response system



Toxic stress is a physiological response

CLINICAL IMPLICATIONS

Epigenetic		
Endocrine Metabolic Reproductive	Neurological Psychiatric Behavioral	Immune Inflammatory Cardiovascular

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

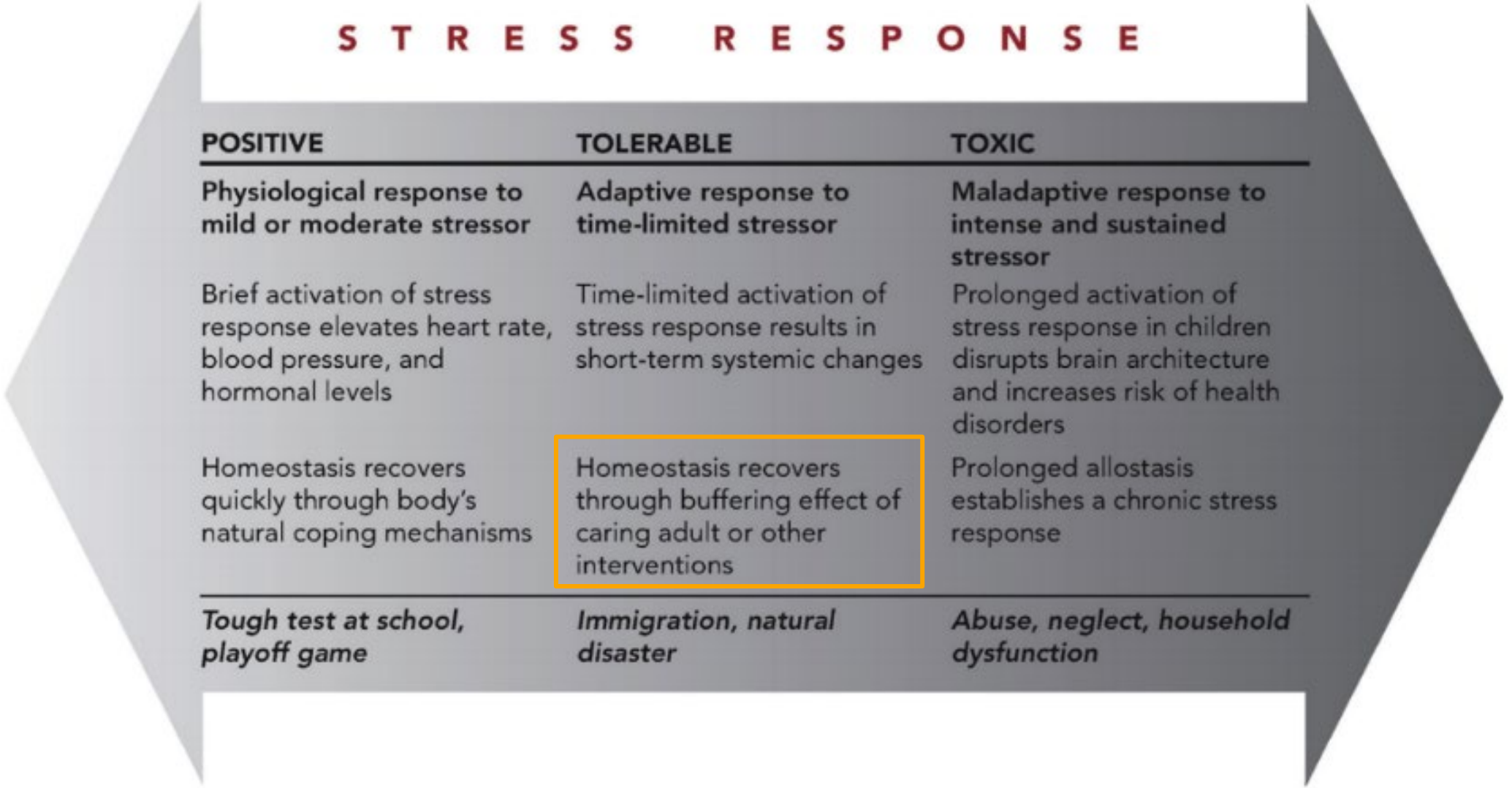
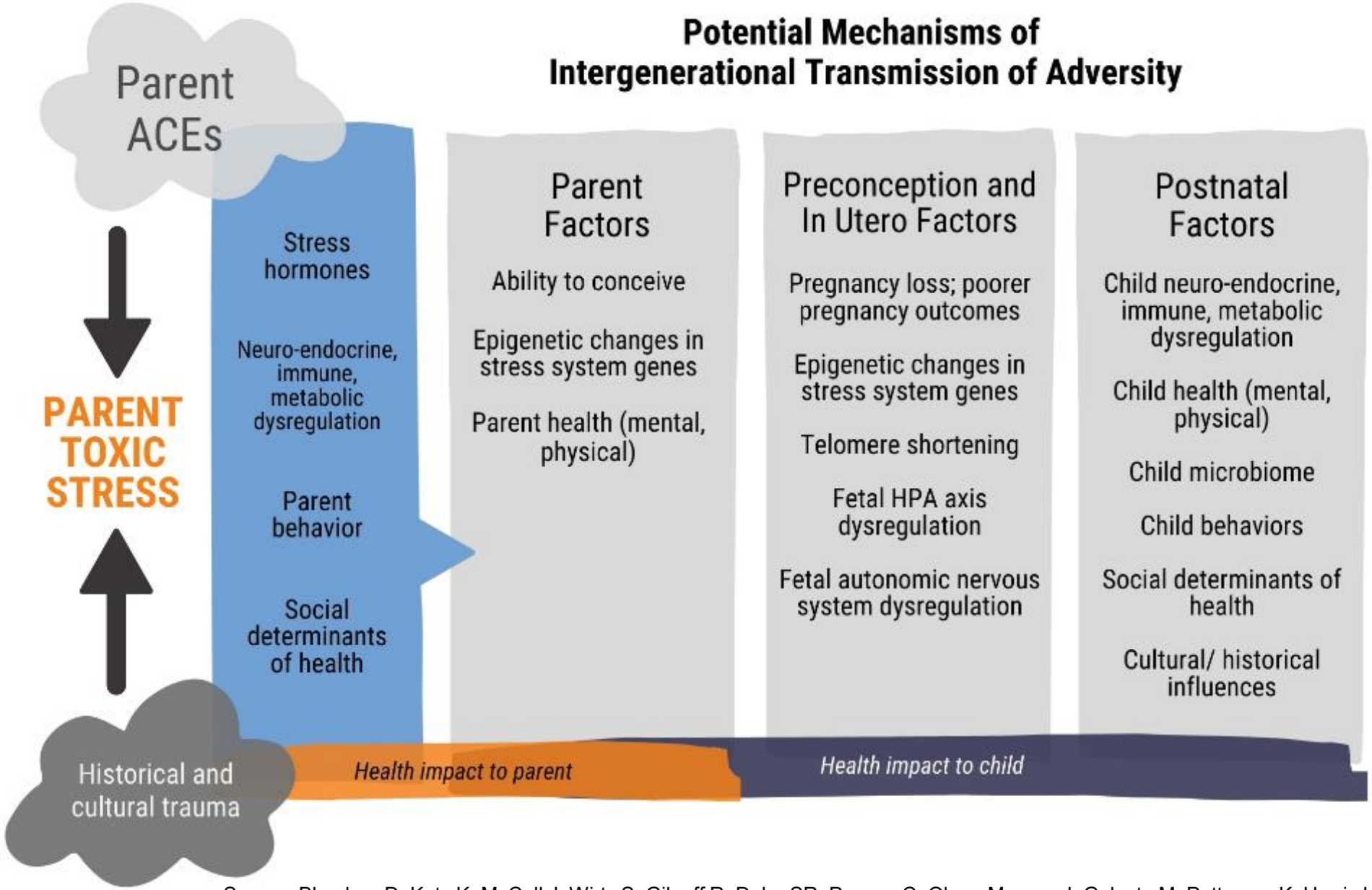


Fig. 2. Spectrum of the stress response: positive, tolerable, and toxic.

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.

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



Source: Bhushan D, Kotz K, McCall J, Wirtz S, Gilgoff R, Dube SR, Powers C, Olson-Morgan J, Galeste M, Patterson K, Harris L, Mills A, Bethell C, Burke Harris N, Office of the California Surgeon General. Roadmap for Resilience: The California Surgeon General's Report on Adverse Childhood Experiences, Toxic Stress, and Health. Office of the California Surgeon General, 2020.

California is Addressing Toxic Stress

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.

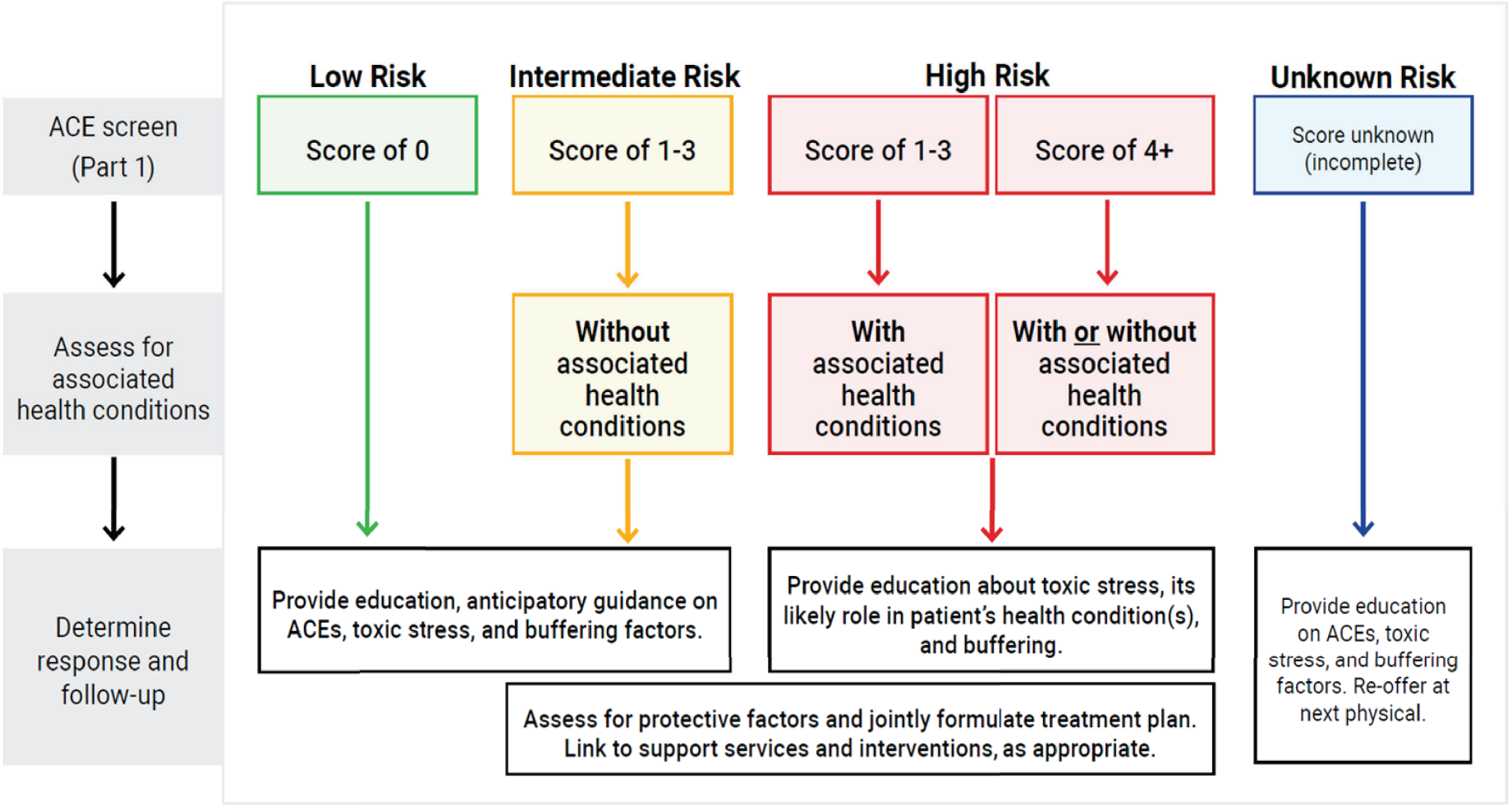
- **Early intervention** can improve brain, immune, hormonal, and genetic regulatory control of development.

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

Sources: Gilgoff et al. Adverse Childhood Experiences, outcomes, and interventions. *Pediatric Clinics* 2020; **67**(2): 259-73; Purewal Boparai et al. Ameliorating the biological impacts of childhood adversity: A review of intervention programs. *Child Abuse & Neglect* 2018; **81**: 82-105; 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. Blaisdell et al. Early adversity, child neglect, and stress neurobiology: From observations of impact to empirical evaluations of mechanisms. *International Journal of Developmental Neuroscience* 2019; **78**: 139-46. ; Jaffee et al. Safe, stable, nurturing relationships break the intergenerational cycle of abuse: A prospective nationally representative cohort of children in the United Kingdom. *Journal of Adolescent Health* 2013; **53**(4): S4-S10.

ACEs and Toxic Stress Risk Assessment Algorithm – Pediatrics

Full algorithm is available at: ACEsAware.org/clinical-assessment



ACE-Associated Health Conditions – Pediatrics

Symptom or Health Condition	For ≥ X ACEs (compared to 0)	Odds Ratio
Asthma[26, 33]	4	1.7 - 2.8
Allergies[33]	4	2.5
Dermatitis and eczema[39]	3*	2.0
Urticaria[39]	3*	2.2
Increased incidence of chronic disease, impaired management[25]	3	2.3
Any unexplained somatic symptoms[25] (eg, nausea/vomiting, dizziness, constipation, headaches)	3	9.3
Headaches[33]	4	3.0
Enuresis; encopresis[5]	--	--
Overweight and obesity[3]	4	2.0
Failure to thrive; poor growth; psychosocial dwarfism[5, 2, 41]	--	--
Poor dental health[16, 22]	4	2.8
Increased infections[39] (viral, URIs, LRTIs and pneumonia, AOM, UTIs, conjunctivitis, intestinal)	3*	1.4 - 2.4
Later menarche[40] (≥ 14 years)	2*	2.3
Sleep disturbances[5, 31]	5**	PR 3.1
Developmental delay[30]	3	1.9
Learning and/or behavior problems[3]	4	32.6
Repeating a grade[15]	4	2.8
Not completing homework[15]	4	4.0
High school absenteeism[33]	4	7.2
Graduating from high school[29]	4	0.4
Aggression; physical fighting[28]	For each additional ACE	1.9
Depression[29]	4	3.9
ADHD[42]	4	5.0
Any of: ADHD, depression, anxiety, conduct/behavior disorder[30]	3	4.5
Suicidal ideation[28]	For each additional ACE	1.9
Suicide attempts[28]		1.9 - 2.1
Self-harm[28]		1.8
First use of alcohol at < 14 years[7]	4	6.2
First use of illicit drugs at < 14 years[10]	5	9.1
Early sexual debut[21] (<15-17 y)	4	3.7
Teenage pregnancy[21]	4	4.2

*Odds ratio represents at least one ACE, but also includes other adversities

**Prevalence ratio represents at least one ACE, but also includes other adversities

Protective Factors

"Intrinsic or extrinsic conditions or attributes that mitigate risk for toxic stress"

Intrinsic Factors

- Neurologic, endocrine, metabolic, immune, genetic, and epigenetic factors
- Curiosity in learning
- Ability to pay attention
- Ability to regulate emotions

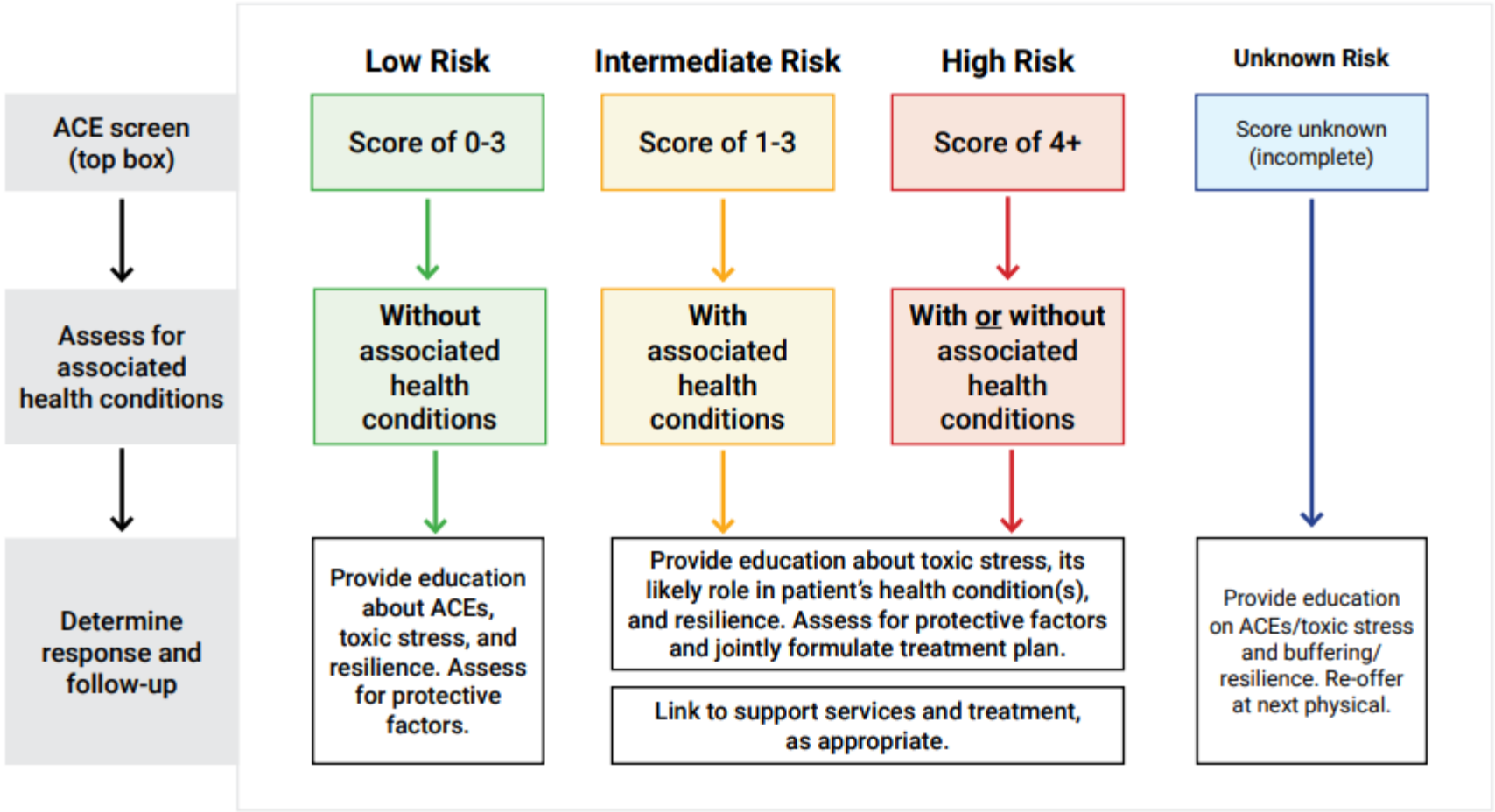
Extrinsic Factors

- Buffering relationships
- Supportive environments
- Community resources

Source: Bhushan D et al. Office of the California Surgeon General. Roadmap for Resilience: The California Surgeon General's Report on Adverse Childhood Experiences, Toxic Stress, and Health. Office of the California Surgeon General, 2020. DOI: 10.48019/PEAM8812.

ACEs and Toxic Stress Risk Assessment Algorithm – Adults

Full algorithm is available at: ACEsAware.org/clinical-assessment



ACE-Associated Health Conditions – Adults

Symptom or Health Condition	Odds Ratio (excluding outliers)
Cardiovascular disease[21] (CAD, MI, ischemic heart disease)	2.1
Tachycardia[37]	≥ 1 ACE: 1.4
Stroke[20]	2.0
Chronic obstructive pulmonary disease (emphysema, bronchitis)[21]	3.1
Asthma[43]	2.2
Diabetes[21]	1.4
Obesity[20]	2.1
Hepatitis or jaundice[1]	2.4
Cancer, any[21]	2.3
Arthritis[32, 7] (self-reported)	3 ACEs, HR: 1.5 ≥ 1 ACE: 1.3
Memory impairment[20] (all causes, including dementias)	4.9
Kidney disease[43]	1.7
Headaches[11]	≥ 5 ACEs: 2.1
Chronic pain, any[38] (using trauma z-score)	1.2
Chronic back pain[38] (using trauma z-score)	1.3
Fibromyalgia[37]	≥ 1 ACE: 1.8
Unexplained somatic symptoms, including somatic pain, headaches[20, 2]	2.0 - 2.7
Skeletal fracture[1]	1.6 - 2.6[20]
Physical disability requiring assistive equipment[23]	1.8
Depression[21]	4.7
Suicide attempts[21]	37.5
Suicidal ideation[20]	10.5
Sleep disturbance[20]	1.6
Anxiety[21]	3.7
Panic and anxiety[20]	
Post-traumatic stress disorder[37]	4.5
Illicit drug use[21] (any)	5.2
Injected drug, crack cocaine, or heroin use[21]	10.2
Alcohol use[21]	6.9
Cigarettes or e-cigarettes use[35]	6.1
Cannabis use[35]	11.0
Teen pregnancy[21]	4.2
Sexually transmitted infections, lifetime[21]	5.9
Violence victimization[21] (intimate partner violence, sexual assault)	7.5
Violence perpetration[21]	8.1

Odds ratios compare outcomes in individuals with ≥ 4 ACEs to those with 0 ACEs, except where specified

Clinical Response to ACEs and Toxic Stress

1. Applying principles of **trauma-informed care** including establishing trust, safety, and collaborative decision-making.
2. Supplementing usual care for ACE-Associated Health Conditions by providing **patient education** on toxic stress and offering **strategies to regulate the stress response** (using seven evidence-based strategies for toxic stress regulation).
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, community health workers.
5. **Follow-up** as necessary, using the presenting ACE-Associated Health Condition(s) as indicators of treatment progress.

Buffering the Toxic Stress Response

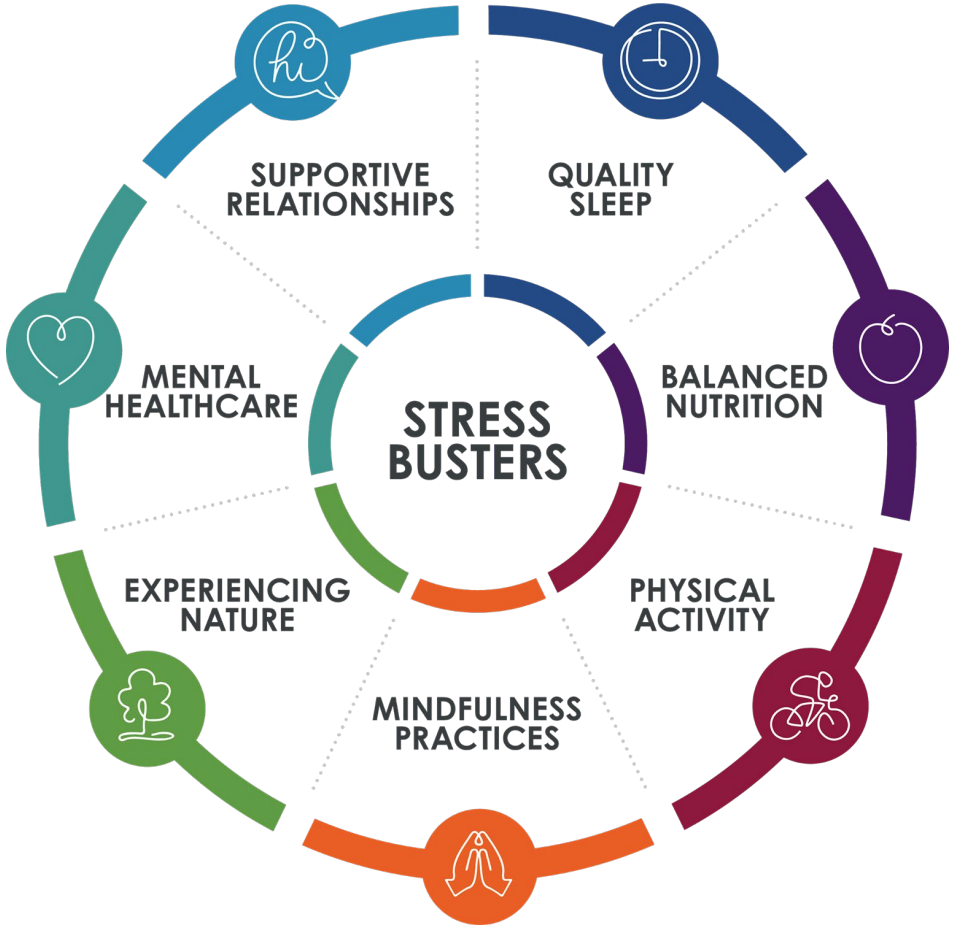
Neurologic/Neuroendocrine: MRI studies found that institutionalized children randomized to **high-quality nurturant caregiving** showed normalization of the developmental trajectory of white matter structures. **Responsive caregiving** also improves cortisol reactivity in children. **Time in nature**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

Strategies for Regulating the Toxic Stress Response



Source: Adapted from Burke Harris, Nadine. *The Deepest Well: Healing the Long-Term Effects of Childhood Adversity*. Boston: Houghton Mifflin Harcourt, 2018; Gilgoff et al. Adverse Childhood Experiences, outcomes, and interventions. *Pediatric Clinics* 2020; **67**(2): 259-73;

What can we do next?

Take the ACEs Aware Provider Training

1. **Get trained** at www.ACEsAware.org/training

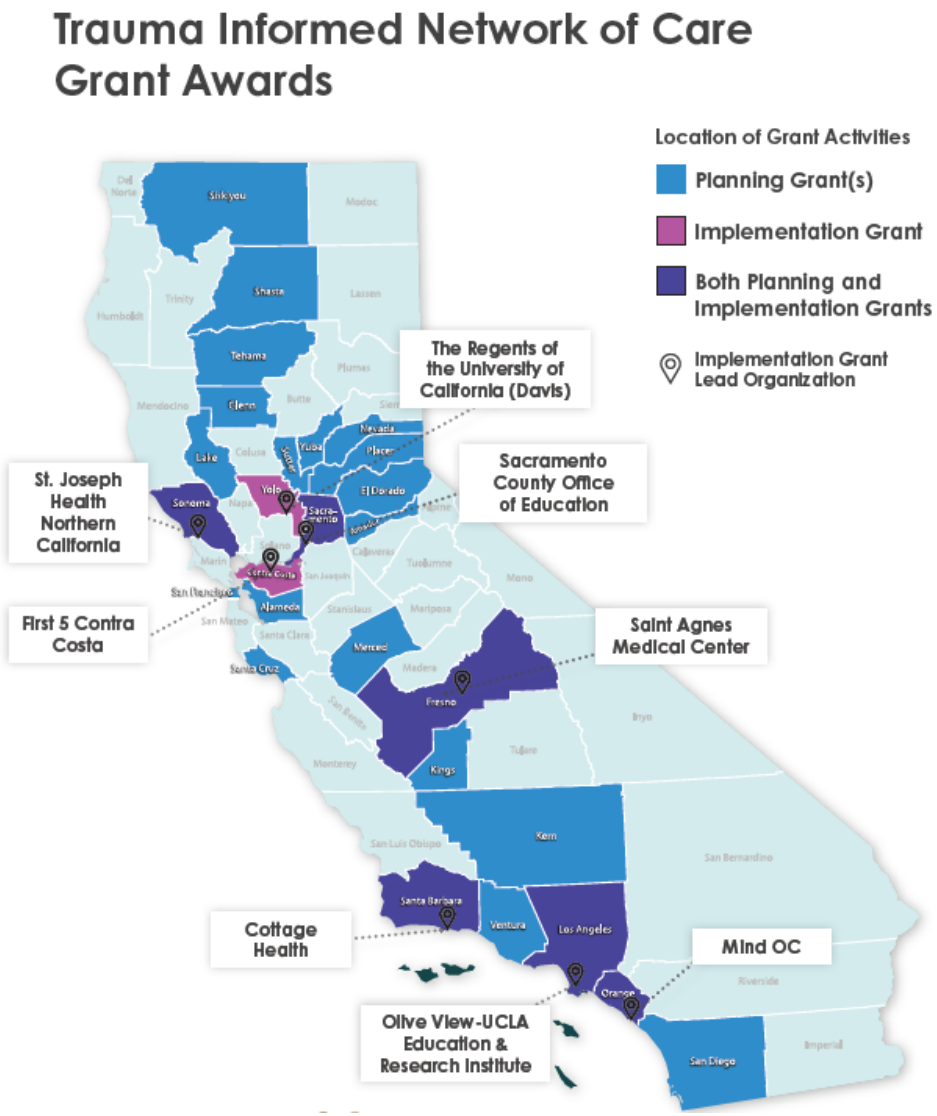
   - Free, 2-hour online course that offers CME and MOC credits

2. **Attest to completing the training** at www.Medi-Cal.ca.gov/ TSTA/TSTAattest.aspx

   - List of Medi-Cal provider types eligible to receive payment at www.ACEsAware.org/eligible-providers/

3. **Join the ACEs Aware Clinician Directory** at www.acesaware.org/provider-directory

Join a Trauma-Informed Network of Care



- A group of **interdisciplinary** health, education, and human service professionals, community members, and organizations;
- Supports families by providing access to **evidence-based "buffering" resources** and supports; and
- Helps to **prevent, treat, and heal** the harmful consequences of toxic stress.

Source: ACEs Aware Network of Care Roadmap: Draft for Public Comment. Released December 2020.
Bhushan D, et al. Office of the California Surgeon General. Roadmap for Resilience: The California Surgeon General's Report on Adverse Childhood Experiences, Toxic Stress, and Health. Office of the California Surgeon General, 2020. DOI: 10.48019/PEAM8812. (p. 79-80)

Who is in the Network of Care?

Provider Type	Examples
Primary Care Providers	Pediatricians, Family Medicine, Nurse Practitioners, SBHCs
Behavioral Health Providers	Psycologists, County Mental Health, Social Workers, FQHCs
Schools/Education	Offices of Education, Superintendents, Family Resource Centers, SBHCs, School lunch program
Early Intervention Services	Help Me Grow, Child Advocacy Centers
Social Service Programs	FRCs, CalFresh, WIC, Home Visiting
Local and County Government Programs	First 5, Black Infant Health, Child Abuse Prevention, Parks & Recreation, Adult Protective Services
Community Based Organizations	National Alliance on Mental Illness (NAMI), Culturally Specific Providers (e.g., Promotoras, LGBTQ community centers, translation services),
Tribal Organizations	Urban-Indian Health Agencies, Indian Child Welfare Act, Family Violence Prevention, Tribal Justice
Legal/Justice System	Juvenile Justice, Family Courts, Mediation/Divorce Teams, Domestic Violence Support, Family Reunification, Tribal-State-Court Forum, Medical-Legal Partnerships
Digital Health Technology Platforms	Unite Us, Aunt Bertha, FINDConnect), Service Care Coordination (e.g. Mahmee, Emilio Health), Mindfulness services, (e.g. Headspace)
Provider Networks/Managed Care Plans	IPAs, MCPs, DMC-ODS, County MH

Work toward Network of Care "Milestones"

- Build and commit to **cross-sector partnerships** and establish a formal **leadership and accountability** structure;

- Understand and document all **available resources** such as health care, community-based, and social services;
- Establish **referral and response workflows** across sectors; hold each other accountable for follow-up;

- Leverage **technology** to facilitate connections; and

- **Evaluate,** refine, and improve Network of Care activities.

See the full Network of Care Roadmap for more information.

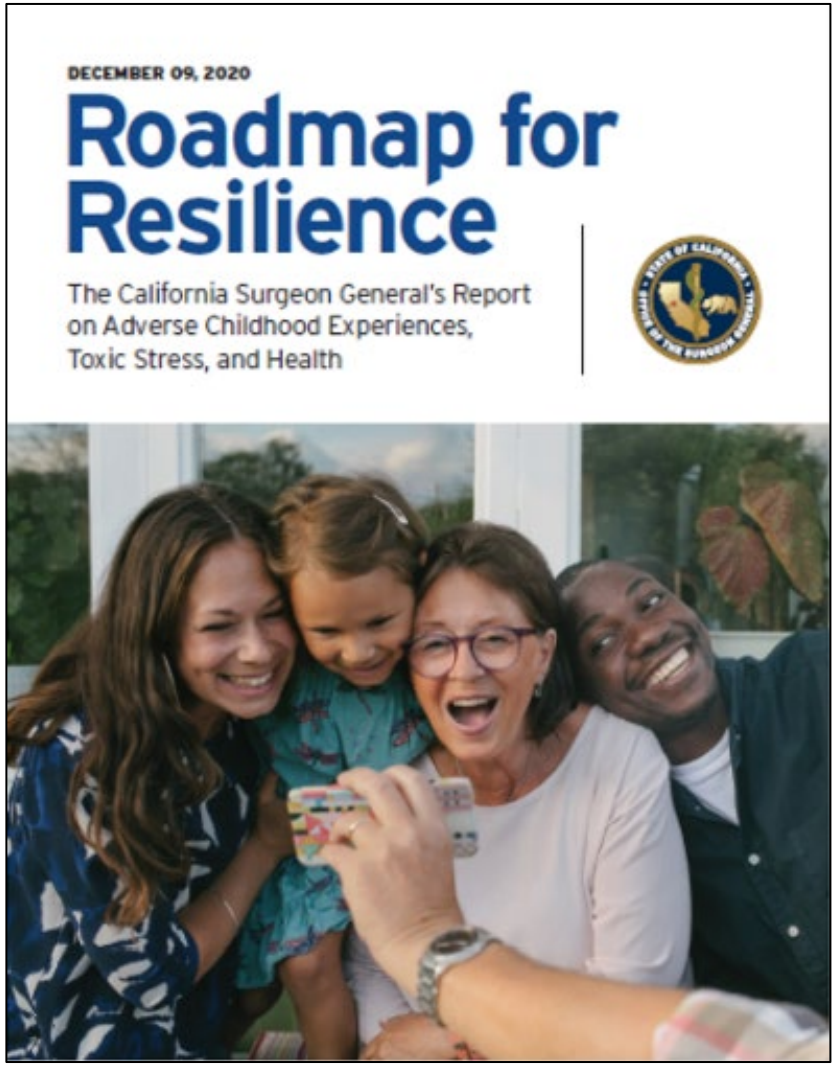
No Single Sector or Category of Prevention is Sufficient Alone

Healthcare	Public Health	Social Services	Early Childhood	Education	Justice

Check out the California Surgeon General's Report

Materials available at
https://osg.ca.gov/sg-report/

- Full 438-page report
- Executive Summary
- 12 briefs summarizing key themes, **including the Biology of Toxic Stress**
- Social Media Toolkit
- Public webinar



Join the Movement!

Nearly 10,000 Medi-Cal providers are certified to screen for ACEs, but there is more work to be done!

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NumberStory.org

Patient-facing materials now available!

Look to the Future – Governor Newsom's 2021-2022 Budget

- $4 billion children's behavioral health initiative
- ACEs Aware public education campaign
- Trauma Informed Care training for educators
- Coverage of community health workers through Medi-Cal
- Additional ACEs research grant funds through Precision Medicine Initiative