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

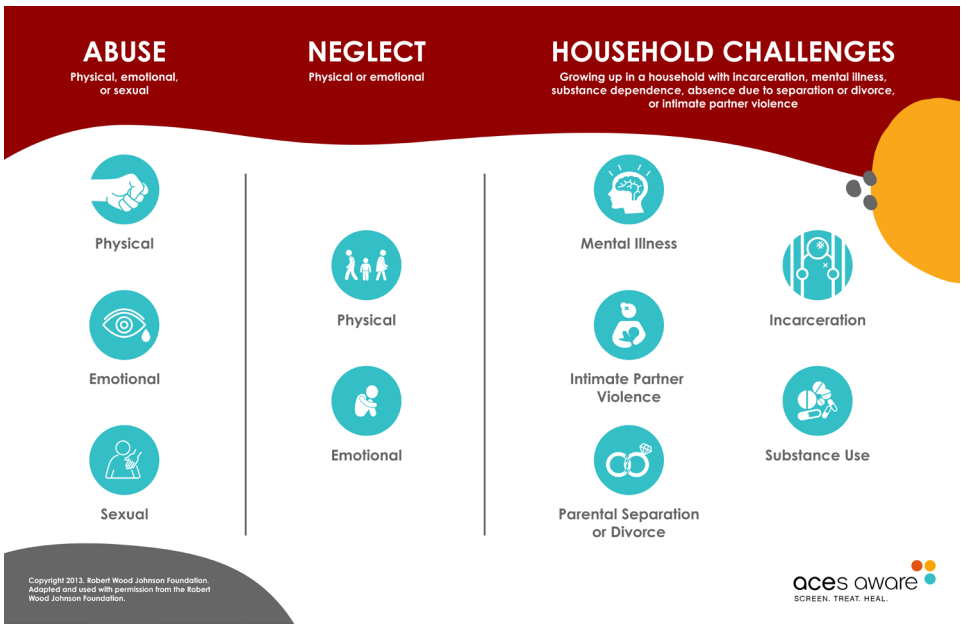

Figure 1. *The 10 ACE categories investigated in the landmark study by the CDC and Kaiser Permanente. Image reproduced with permission from ACEs Aware,[26] which adapted this with permission from the Robert Wood Johnson Foundation.*

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

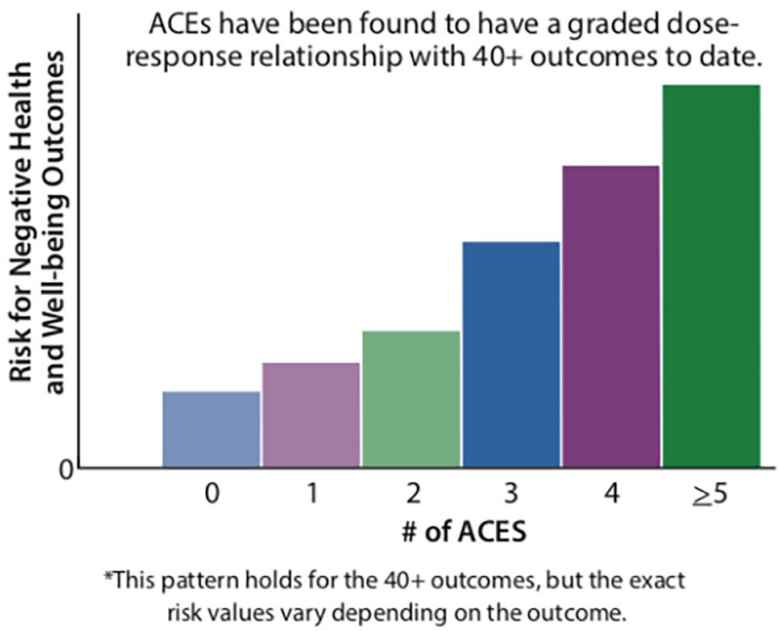

Figure 2. *There is a dose-response relationship between the number of ACE categories experienced and successively increasing risk of numerous negative health and social outcomes. Image reproduced from the CDC.*[31]

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,

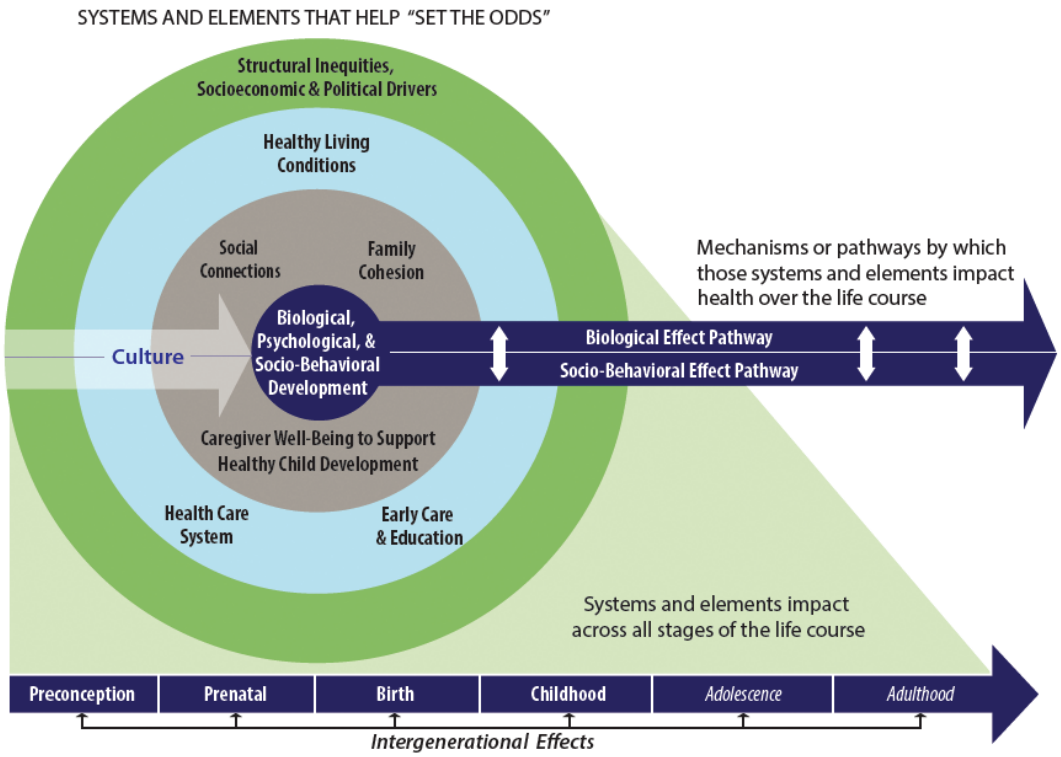

Figure 3. *Multi-layered structural and contextual factors that influence life course health. Reproduced with permission from the National Academies of Sciences, Engineering, and Medicine (NASEM, 2019), courtesy of the National Academies Press, Washington, D.C.*[23]

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.