

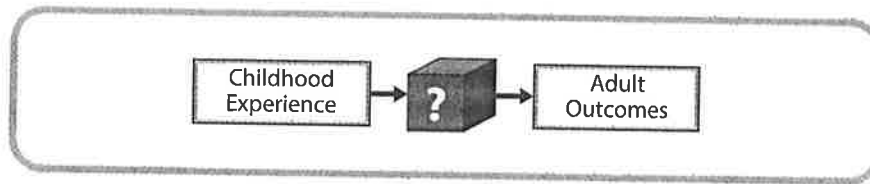
## Life Course Science and the Proverbial Black Box

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*Of a good beginning cometh a good end.*

— Chinese Proverb  
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As pediatricians, parents, teachers, and citizens, what do we wish for the children in our lives? For them to be healthy? Happy? Productive? Ultimately, we want our children to thrive, not only in childhood but across their life span. We want them to fulfill their potential, to make a difference in the world, and to positively influence generations to come. As such, we tend to measure success not in the short term but over the life course. We may worry about recurrent ear infections in a young girl because they may affect her hearing as she gets older. We might worry about a boy's early struggles in elementary school because they may diminish his ability to graduate high school or college or to get a good-paying job. We intuitively understand that what happens in childhood may not stay in childhood.

But we also understand that what happens in early childhood is not necessarily destiny. We all know examples of healthy, happy, and productive adults who overcame tremendous adversity as children, just as we know teenagers and adults who benefitted from every possible resource as children but nevertheless fared poorly over the years. The link between childhood experiences and adult outcomes is strong, but it is not perfect, and this ambiguity poses important questions: What adversities in childhood alter life course trajectories for the worse? What are the essential ingredients of *good-enough parenting* (to be discussed more in Chapter 7) that alter life course trajectories for the better? Where can differences be made in what we do as parents, pediatricians, teachers, and neighbors?



**Figure 1-1.** Defining the proverbial black box that links experiences in childhood with outcomes decades later. To advance health, educational, and economic outcomes across the life span, we need to peer inside this black box and better understand the biological mechanisms underlying these well-established associations.

In this chapter, we will briefly review the associations between experiences in childhood and outcomes in health, behavior, and economic productivity decades later. We conceptualize this process as a black box. We know what goes into the box: early childhood experiences, both *adverse* (negative, harmful, isolating) and *affiliative* (positive, affirming, inclusive). We also know what comes out of the box: childhood, adolescent, and adult outcomes. However, what goes on *inside* the box—the biological mechanisms underlying these strong but imperfect associations—has, until recently, remained poorly understood (Figure 1-1). Only by peering inside this black box and understanding the biological mechanisms at play will we be able to ensure a good beginning and set a steady course toward a good end. But here we will begin by looking at those pivotal inputs as well as the outputs of utmost concern.

## Life Course Science

Advances in life course sciences, like epidemiology and intervention science, are confirming that the link between childhood experiences and adult outcomes is quite strong. For example, the landmark Adverse Childhood Experiences (ACE) Study<sup>1,2</sup> asked more than 17,000 middle-class, middle-aged Americans if they had experienced any of the following 10 categories of adversity (Table 1-1) prior to their 18th birthday: emotional (psychological) abuse, physical abuse, sexual abuse, mother treated violently (ie, witnessing intimate partner violence), household substance abuse, household mental illness, parental separation or divorce, an incarcerated household member, emotional neglect, and physical neglect. The lead researchers of the ACE Study, Drs Vincent Felitti and Robert Anda, were astonished to see just how prevalent these ACEs were, with more than one-quarter of the participants reporting physical abuse and household substance abuse prior to their adulthood. Moreover, sexual abuse, parental separation or divorce, and household

**Table 1-1. Adverse Childhood Experiences Are Not Rare**

	Women (n = 9,367)	Men (n = 7,970)	Total (N = 17,337)
Abuse			
• Emotional	13.1	7.6	10.6
• Physical	27.0	29.9	28.3
• Sexual	24.7	16.0	20.7
Household dysfunction			
• Mother treated violently	13.7	11.5	12.7
• Household substance abuse	29.5	23.8	26.9
• Household mental illness	23.3	14.8	19.4
• Parental separation or divorce	24.5	21.8	23.3
• Incarcerated household member	5.2	4.1	4.7
Neglect <sup>a</sup>			
• Emotional	16.7	12.4	14.8
• Physical	9.2	10.7	9.9

<sup>a</sup> Wave 2 data only (n = 8,667).

Data from [www.cdc.gov/violenceprevention/acestudy](http://www.cdc.gov/violenceprevention/acestudy).

The Adverse Childhood Experiences (ACE) Study asked more than 17,000 middle-class adults to recall if they had experienced any of the 10 listed adversities prior to their 18th birthday. The percentage of participants who experienced each category of ACE is given for women and men. To determine an individual's ACE score, 1 point was given for each type of ACE recalled (for a maximum score of 10). Only 36% of the participants had an ACE score of 0, and 1 in 8 had an ACE score of 4 or more.

From Garner AS. Home visiting and the biology of toxic stress: opportunities to address early childhood adversity. *Pediatrics*. 2013;132(Suppl 2):S65–S73.

mental illness were each reported by about 1 in 5 participants during their first 18 years of life.

When these data were first published in 1998, they were met with a great deal of skepticism because the original ACE Study was conducted on a population (primarily white and well educated) that might be expected to have

experienced minimal adversity in childhood.<sup>1</sup> However, subsequent studies have confirmed that ACEs are indeed quite common, and they are even more common in underprivileged populations, like those living in poverty<sup>3</sup> or subjected to incarceration.<sup>4</sup>

To quantify this childhood adversity, the authors developed an ACE score encompassing 10 different categories of adversity. Participants were given 1 point for each category they had experienced during their childhood. Here again, the prevalence of high ACE scores was shocking, with about two-thirds (64%) having an ACE score of 1 or higher, and 1 in 8 (12.5%) having an ACE score of 4 or higher.<sup>1</sup> As disturbing as these numbers are, it is important to remember that the ACE score is actually a relatively insensitive measure of adversity for several reasons. First, because the original ACE Study was retrospective (most participants were in their 50s and were asked about experiences that had happened prior to their 18th birthday), issues with recall may lower the ACE score, as people may repress or try to forget upsetting experiences.<sup>5</sup> Second, the ACE score does not account for frequency or repetition. Whether a participant was sexually abused one time or every day for years, the participant received only 1 ACE point. Finally, redundancy is possible within the 10 categories: a participant may have had an alcoholic father and a mother who was a chronic marijuana user, but that participant would have received only 1 ACE point for the category of household substance abuse. These limitations suggest that, if anything, ACE scores underestimate the true prevalence of childhood adversity.

Despite these limitations, Felitti, Anda, and colleagues were able to demonstrate graded, dose-dependent, and statistically significant relationships between ACE scores and a wide array of outcomes (Box 1-1).<sup>1,2</sup> These outcomes included not only common diseases (eg, cancer, ischemic heart disease, chronic lung disease, liver disease) but measures of sexual health (eg, early intercourse, teen pregnancy, sexually transmitted infections, sexual dissatisfaction), mental health (eg, anxiety, depression, hallucinations, panic reactions [attacks], poor anger control), and general or social functioning (eg, relationship problems, difficulty at work, high perceived stress). The list of outcomes associated with ACEs is almost overwhelming, but this also underscores a tremendous potential for benefit. If we are able to understand the biological mechanisms underlying these associations, we are in a better position to address and, hopefully, prevent a wide array of seemingly intractable outcomes.

The opportunities for prevention are even more promising when one considers that adverse experiences in childhood were associated, in adulthood, with what we will call *the Big 5*: smoking, alcoholism, obesity, promiscuity,

### **Box 1-1. Adverse Childhood Experiences Are Associated With Numerous Measures of Poor Health**

- |                             |                                      |
|-----------------------------|--------------------------------------|
| I. Social Functioning       | e. Fetal Death                       |
| a. High Perceived Stress    | f. Sexual Dissatisfaction            |
| b. Relationship Problems    | IV. Risk Factors for Common Diseases |
| c. Married to an Alcoholic  | a. Obesity                           |
| d. Difficulty With Job      | b. Promiscuity                       |
| II. Mental Health           | c. Alcoholism                        |
| a. Anxiety                  | d. Smoking                           |
| b. Depression               | e. Illicit Drugs                     |
| c. Poor Anger Control       | f. IV Drugs                          |
| d. Panic Reactions          | g. High Perceived Risk of HIV        |
| e. Sleep Disturbances       | h. Multiple Somatic Symptoms         |
| f. Memory Disturbances      | V. Prevalent Diseases                |
| g. Hallucinations           | a. Ischemic Heart Disease            |
| III. Sexual Health          | b. Chronic Lung Disease              |
| a. Age of First Intercourse | c. Liver Disease                     |
| b. Unintended Pregnancy     | d. Cancer                            |
| c. Teen Pregnancy           | e. Skeletal Fractures                |
| d. Teen Paternity           | f. Sexual Transmitted Infections     |

Abbreviations: ACE, Adverse Childhood Experiences; HIV, human immunodeficiency virus; IV, intravenous.

All these adolescent and adult outcomes are associated with ACE scores in a dose-dependent and statistically significant manner. The higher the ACE score, the higher the risk for these measures of poor health. Note that the Big 5 (overeating [a proxy for obesity], sex, alcohol, smoking, and substance abuse) are behaviors that transiently turn off stress and that they, in turn, are associated with most of the other outcomes associated with childhood adversity. For example, overeating is associated with heart disease, promiscuity is associated with sexual health dysfunction, alcoholism is associated with liver disease and social difficulties, smoking is associated with chronic lung disease, and substance abuse is associated with social difficulties and mental health conditions.

Adapted from Centers for Disease Control and Prevention. Adverse childhood experiences (ACEs). [www.cdc.gov/violenceprevention/acestudy](http://www.cdc.gov/violenceprevention/acestudy). Updated April 1, 2016. Accessed February 27, 2018.

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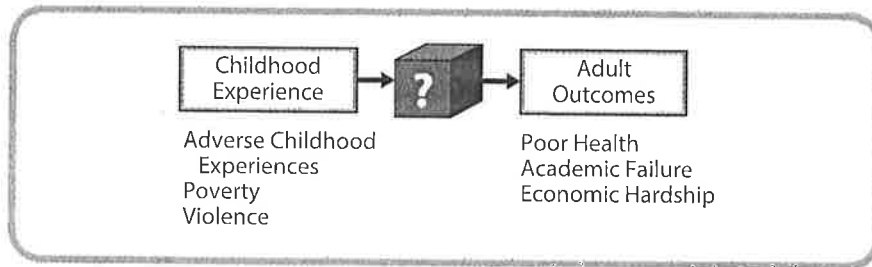
and substance abuse. Each of these is a well-established risk factor for disease. In fact, many of the other outcomes associated with ACEs are known to be related to these Big 5. For example, if you are obese, that increases your risks for hypertension, diabetes, and heart disease. If you are alcoholic, that increases your risk of having liver disease and other forms of cancer. If you are a smoker, that increases your risk of chronic lung disease and many types of

cancer. If you are promiscuous, that increases your risk of sexually transmitted infections (including HIV and hepatitis C), early parenting, and poor sexual health. Finally, substance abuse and alcoholism are associated with mental health conditions and other measures of poor general or social functioning.

## Behavioral Allostasis

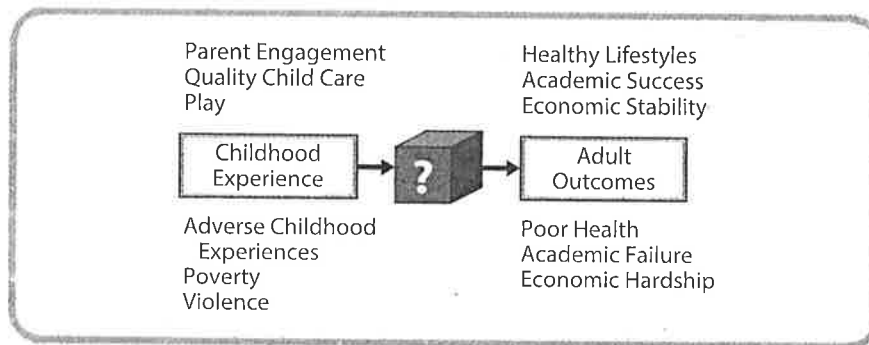
What is driving the relationship between ACE scores and the Big 5? Physiologists would point out that the Big 5 are all examples of *behavioral allostasis*.<sup>6-8</sup> The term *allostasis* refers to the active process that the body uses to get back to baseline after being altered by the environment. For example, if the body's core temperature begins to rise, allostasis is manifest on the redirection of blood flow to the skin to dissipate heat. Similarly, behavioral allostasis refers to behaviors that return the body's functioning back to baseline. In the case of the Big 5 (tobacco, alcohol, overeating [as a proxy for obesity], sex, and substance abuse), they all provide an opportunity to transiently turn off stress, allowing us to relax, if only for a moment. While it might seem intuitive that significant adversity is associated with the Big 5 and other risky behaviors (eg, compulsive gambling<sup>9</sup>) that provide a rush of positive feelings or transiently turn off stress, it may be surprising to consider that these stress-modulating behaviors are occurring decades after the original childhood adversity. Even more surprising is the fact that ACEs increase the risk of disease—*ischemic heart disease*, for example—even after controlling for the Big 5 and other traditional risk factors for disease.<sup>10</sup> This means that someone who has suffered significant childhood adversity is at a higher risk of ischemic heart disease even if he or she does not have any of the associated behavioral risk factors. This raises an intriguing question: Are ACEs getting under the skin, becoming biologically embedded and driving health, behavior, and economic outcomes over the entire life course? We will return to this question and address it more thoroughly in chapters 3 and 4.

Of course, the adversities examined in the ACE Study are not the only ones associated with poor adult outcomes. Other known risk factors for poor outcomes later in life include growing up in poverty, being bullied, witnessing violence, experiencing other forms of parental dysfunction (eg, harsh or belittling parents), or living in a violent neighborhood. While it seems intuitive that *catastrophic* adversities (eg, physical abuse, sexual abuse, witnessing violence) might be associated with poor outcomes, the retrospective ACE Study and several smaller prospective studies have demonstrated that *chronic* adversities (eg, maternal depression, poverty, emotional neglect) are also associated with poor outcomes.<sup>11-14</sup> When we explore what is going on inside the black box, we must consider catastrophic and chronic sources of adversity (Figure 1-2).<sup>15</sup>



**Figure 1-2.** Adverse experiences, both catastrophic (eg, violence) and chronic (eg, poverty), are associated with outcomes like **poor health**, academic failure, and **economic hardship** later in life. To break this association and **improve outcomes**, we need to **understand** the biological mechanisms at play inside the black box.

The good news is that childhood experiences appear to cut both ways. Although adversities are associated with poor outcomes, sources of enrichment during childhood are associated with improved outcomes in behavior, learning, and health (Figure 1-3). For example, *affiliative* childhood experiences, like engaged, attentive caregivers; access to health care; quality early education services; and even ample opportunities to play, have been associated with lifelong outcomes such as **better health**,<sup>16</sup> **higher academic achievement**, more employment, fewer divorces, less depression, and lower incarceration rates.<sup>17-19</sup>



**Figure 1-3.** Affiliative childhood experiences, like parental engagement, quality child care, and opportunities to play, are associated with outcomes like healthy lifestyles, academic success, and economic **stability** later in life. An understanding of the biological **mechanisms** working inside the box is **absolutely necessary** for **preventing** the negative outcomes associated with adverse childhood experiences, promoting the positive outcomes associated with affiliative childhood experiences, and addressing many of society's most intractable problems, like disparities in health, education, and economic productivity.

## Summary

Early childhood experiences, both affiliative and adverse, are strongly associated with important outcomes later in life. The challenge now is to begin looking into this black box to understand the biological mechanisms underlying these well-established associations and to translate this knowledge into practices and policies that will address and perhaps even prevent many of our society's most intractable problems. Understanding the biological mechanisms within the black box is requisite knowledge for pediatricians, parents, teachers, advocates, policy makers, and all others interested in fostering healthy children, resilient teens, and the next generation of productive, civic-minded adults.

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