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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{23,31}

Based on a comprehensive public health framework, primary prevention strategies are rooted in ensuring broad public awareness\textsuperscript{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.\textsuperscript{23,24,31,42,56,619} 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.\textsuperscript{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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In addition, surveillance mechanisms 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. 

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. 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. 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. 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.

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. Early detection of ACEs and other risk factors for toxic stress provide 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 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). \(^6^{34}\)

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. \(^6^{35}\)

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

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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**

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.

1986 The US Public Health Service issues its first recommendations for preventing perinatal transmission of HIV. 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. An Institute of Medicine report provides national HIV strategy recommendations, including the importance of public education.

1987 The FDA approves zidovudine, or AZT, as the first antiretroviral drug. 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.”


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

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

1991 *International Council of AIDS Service Organizations* 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. 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. CDC issues the first *guidelines* for prevention of opportunistic infections in HIV-infected persons, and a report on syringe exchange programs as a prevention
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 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. 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. 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 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, 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.


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 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.

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. HHS launches **12 Cities Project**, focusing resources on areas with the highest HIV/AIDS burden in the country.

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.”

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**

**2016** Advice on 

**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.

More than 25 options for HAART now exist.