Addiction: Neurobiology, Prevention, and Treatment
Part 1

Quantum Units Education
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CHAPTER 1.
INTRODUCTION AND OVERVIEW OF THE REPORT

Chapter 1 Preview

The United States has a serious substance misuse problem. Substance misuse is the use of alcohol or drugs in a manner, situation, amount, or frequency that could cause harm to the user or to those around them. Alcohol and drug misuse and related substance use disorders affect millions of Americans and impose enormous costs on our society. In 2015, 66.7 million people in the United States reported binge drinking in the past month and 27.1 million people were current users of illicit drugs or misused prescription drugs. The accumulated costs to the individual, the family, and the community are staggering and arise as a consequence of many direct and indirect effects, including compromised physical and mental health, increased spread of infectious disease, loss of productivity, reduced quality of life, increased crime and violence, increased motor vehicle crashes, abuse and neglect of children, and health care costs.

The most devastating consequences are seen in the tens of thousands of lives that are lost each year as a result of substance misuse. Alcohol misuse contributes to 88,000 deaths in the United States each year; 1 in 10 deaths among working adults are due to alcohol misuse. In addition, in 2014 there were 47,055 drug overdose deaths including 28,647 people who died from a drug overdose involving some type of opioid, including prescription pain relievers and heroin—more than in any previous year on record.

Even though the United States spends more than any other country on health care, it ranks 27th in life expectancy, which has plateaued or decreased for some segments of the population at a time when life expectancy continues to increase in other developed countries—and the difference is largely due to substance misuse and associated physical and mental health problems. For example, recent research has shown an unprecedented increase in mortality among middle-aged White Americans between 1999 and 2014 that was largely driven by alcohol and drug misuse and suicides, although this trend was not seen within other racial and ethnic populations such as Blacks and Hispanics. An analysis from the Centers for Disease Control and Prevention (CDC) demonstrated that alcohol and drug misuse accounted for a roughly 4-month decline in life expectancy among White Americans; no other cause of death had a larger negative impact in this population.
Substance misuse and substance use disorders also have serious economic consequences, costing more than $400 billion annually in crime, health, and lost productivity.\textsuperscript{10,11} These costs are of a similar order of magnitude to those associated with other serious health problems such as diabetes, which is estimated to cost the United States $245 billion each year.\textsuperscript{12} Alcohol misuse and alcohol use disorders alone costs the United States approximately $249 billion in lost productivity, health care expenses, law enforcement, and other criminal justice costs.\textsuperscript{10} The costs associated with drug use disorders and use of illegal drugs and non-prescribed medications were estimated to be more than $193 billion in 2007.\textsuperscript{11}

Despite decades of expense and effort focused on a criminal justice–based model for addressing substance use–related problems, substance misuse remains a national public health crisis that continues to rob the United States of its most valuable asset: its people. In fact, high annual rates of past-month illicit drug use and binge drinking among people aged 12 years and older from 2002 through 2014 (Figure 1.1) emphasize the importance of implementing evidence-based public-health–focused strategies to prevent and treat alcohol and drug problems in the United States.\textsuperscript{13} A public health approach seeks to improve the health and safety of the population by addressing underlying social, environmental, and economic determinants of substance misuse and its consequences, to improve the health, safety, and well-being of the entire population.

**Figure 1.1: Past Month Rates of Substance Use Among People Aged 12 or Older: Percentages, 2002-2014, 2014 National Survey on Drug Use and Health (NSDUH)**

Notes: The National Survey on Drug Use and Health (NSDUH) obtains information on nine categories of illicit drugs: marijuana (including hashish), cocaine (including crack), heroin, hallucinogens, and inhalants, as well as the nonmedical use of prescription-type pain relievers, tranquilizers, stimulants, and sedatives; see the section on nonmedical use of psychotherapeutic drugs for the definition of nonmedical use. Estimates of “illicit drug use” reported from NSDUH reflect the use of these nine drug categories. Difference between the Illicit Drug Use estimate for 2002-2013 and the 2014 estimate is statistically significant at the .05 level for all years against 2014. Binge drinking for NSDUH data collected in 2014 is defined as five or more drinks on the same occasion on at least one day in the past 30 days. There was no significant difference between 2002-2013 against 2014. In 2015, changes were made to the NSDUH questionnaire and data collection procedures that do not allow comparisons between 2015 and previous years for a number of outcomes.

Source: Center for Behavioral Health Statistics and Quality, (2015).\textsuperscript{13}
This Surgeon General’s Report has been created because of the important health and social problems associated with alcohol and drug misuse in America. As described in this Report, a comprehensive approach is needed to address substance use problems in the United States that includes several key components:

- Enhanced public education to improve awareness about substance use problems and demand for more effective policies and practices to address them;
- Widespread implementation of evidence-based prevention policies and programs to prevent substance misuse and related harms;
- Improved access to evidence-based treatment services, integrated with mainstream health care, for those at risk for or affected by substance use disorders;
- Recovery support services (RSS) to assist individuals in maintaining remission and preventing relapse; and
- Research-informed public policies and financing strategies to ensure that substance misuse and use disorder services are accessible, compassionate, efficient, and sustainable.

Recognizing these needs, the Report explains the neurobiological basis for substance use disorders and provides the biological, psychological, and social frameworks for improving diagnosis, prevention, and treatment of alcohol and drug misuse. It also describes evidence-based prevention strategies, such as public policies that can reduce substance misuse problems (e.g., driving under the influence [DUI]); effective treatment strategies, including medications and behavioral therapies for treating substance use disorders; and RSS for people who have completed treatment. Additionally, the Report describes recent changes in health care financing, including changes in health insurance regulations, which support the integration of clinical prevention and treatment services for substance use disorders into mainstream health care practice, and defines a research agenda for addressing alcohol and drug misuse as medical conditions.

Thus, this first Surgeon General’s Report on Alcohol, Drugs, and Health is not issued simply because of the prevalence of substance misuse or even the related devastating harms and costs, but also to help inform policymakers, health care professionals, and the general public about effective, practical, and sustainable strategies to address these problems. These strategies have the potential to substantially reduce substance misuse and related problems; promote early intervention for substance misuse and substance use disorders; and improve the availability of high-quality treatment and RSS for persons with substance use disorders.
A Public Health Model for Addressing Substance Misuse and Related Consequences

A public health systems approach to substance misuse and its consequences, including substance use disorders, aims to:

- Define the problem through the systematic collection of data on the scope, characteristics, and consequences of substance misuse;
- Identify the risk and protective factors that increase or decrease the risk for substance misuse and its consequences, and the factors that could be modified through interventions;
- Work across the public and private sector to develop and test interventions that address social, environmental, or economic determinants of substance misuse and related health consequences;
- Support broad implementation of effective prevention and treatment interventions and recovery supports in a wide range of settings; and
- Monitor the impact of these interventions on substance misuse and related problems as well as on risk and protective factors.

A healthy community is one with not just a strong health care system but also a strong public health educational system, safe streets, effective public transportation and affordable, high quality food and housing – where all individuals have opportunities to thrive. Thus, community leaders should work together to mobilize the capacities of health care organizations, social service organizations, educational systems, community-based organizations, government health agencies, religious institutions, law enforcement, local businesses, researchers, and other public, private, and voluntary entities that can contribute to the above aims. Everyone has a role to play in addressing substance misuse and its consequences and thereby improving the public health.

Substances Discussed in this Report

This Report defines a substance as a psychoactive compound with the potential to cause health and social problems, including substance use disorders (and their most severe manifestation, addiction). These substances can be divided into three major categories: Alcohol, Illicit Drugs (a category that includes prescription drugs used nonmedically), and Over-the-Counter Drugs. Some specific examples of the substances included in each of these categories are included in Table 1. Over-the-Counter Drugs are not discussed in this Report, but are included in Appendix D – Important Facts about Alcohol and Drugs.

Although different in many respects, the substances discussed in this Report share three features that make them important to public health and safety. First, many people use and misuse these substances: 66.7 million individuals in the United States aged 12 or older admitted to binge drinking in the past month and 27.1 million people aged 12 or older used an illicit drug in the past month.³
Table 1.1: Categories and Examples of Substances

<table>
<thead>
<tr>
<th>Substance Category</th>
<th>Representative Examples</th>
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<tbody>
<tr>
<td>Alcohol</td>
<td>• Beer</td>
</tr>
<tr>
<td></td>
<td>• Wine</td>
</tr>
<tr>
<td></td>
<td>• Malt liquor</td>
</tr>
<tr>
<td></td>
<td>• Distilled spirits</td>
</tr>
<tr>
<td>Illicit Drugs</td>
<td>• Cocaine, including crack</td>
</tr>
<tr>
<td></td>
<td>• Heroin</td>
</tr>
<tr>
<td></td>
<td>• Hallucinogens, including LSD, PCP, ecstasy, peyote, mescaline, psilocybin</td>
</tr>
<tr>
<td></td>
<td>• Methamphetamines, including crystal meth</td>
</tr>
<tr>
<td></td>
<td>• Marijuana, including hashish*</td>
</tr>
<tr>
<td></td>
<td>• Synthetic drugs, including K2, Spice, and “bath salts”***</td>
</tr>
<tr>
<td></td>
<td>• Prescription-type medications that are used for nonmedical purposes</td>
</tr>
<tr>
<td></td>
<td>o Pain Relievers - Synthetic, semi-synthetic, and non-synthetic opioid medications,</td>
</tr>
<tr>
<td></td>
<td>including fentanyl, codeine, oxycodone, hydrocodone, and tramadol products</td>
</tr>
<tr>
<td></td>
<td>o Tranquilizers, including benzodiazepines, meprobamate products, and muscle relaxants</td>
</tr>
<tr>
<td></td>
<td>o Stimulants and Methamphetamine, including amphetamine,</td>
</tr>
<tr>
<td></td>
<td>dextroamphetamine, and phentermine products; mazindol products; and methylphenidate</td>
</tr>
<tr>
<td></td>
<td>or dextmethylphenidate products</td>
</tr>
<tr>
<td></td>
<td>o Sedatives, including temazepam, flurazepam, or triazolam and any barbiturates</td>
</tr>
<tr>
<td>Over-the-Counter Drugs and</td>
<td>• Cough and cold medicines**</td>
</tr>
<tr>
<td>Other Substances</td>
<td>• Inhalants, including amyl nitrite, cleaning fluids, gasoline and lighter gases,</td>
</tr>
<tr>
<td></td>
<td>anesthetics, solvents, spray paint, nitrous oxide</td>
</tr>
</tbody>
</table>

Notes: The Report discusses the substances known to have a significant public health impact. These substances are also included in NSDUH. Additionally, NSDUH includes tobacco products (cigarettes, smokeless tobacco, cigars, and pipe tobacco); however, tobacco products are not discussed in this Report at length because they have been covered extensively in other Surgeon General’s Reports.14-17

* As of June 2016, 25 states and the District of Columbia have legalized medical marijuana use, four states have legalized retail marijuana sales, and the District of Columbia has legalized personal use and home cultivation (both medical and recreational). It should be noted that none of the permitted uses under state laws alter the status of marijuana and its constituent compounds as illicit drugs under Schedule I of the federal Controlled Substances Act. See the section on Marijuana: A Changing Legal and Research Environment later in this chapter for more detail on this issue.

** These substances are not included in NSDUH and are not discussed in this Report. However, important facts about these drugs are included in Appendix D - Important Facts about Alcohol and Drugs.

Second, individuals can use these substances in a manner that causes harm to the user or those around them. This is called substance misuse and often results in health or social problems, referred to in this Report as substance misuse problems. Misuse can be of low severity and temporary, but it can also result in serious, enduring, and costly consequences due to motor vehicle crashes,18,19 intimate partner and sexual violence,20 child abuse and neglect,21 suicide attempts and fatalities,22 overdose deaths,23 various forms of cancer24 (e.g., breast cancer in women),25 heart and liver diseases,26 HIV/AIDS,27 and problems related to drinking or using drugs during pregnancy, such as fetal alcohol spectrum disorders (FASDs) or neonatal abstinence syndrome (NAS).28

Third, prolonged, repeated misuse of any of these substances can produce changes to the brain that can lead to a substance use disorder, an independent illness that significantly impairs health and function and may require speciality treatment. Disorders can range from mild to severe. Severe and chronic substance use disorders are commonly referred to as addictions.
Key Terms Used in the Report

Addiction: The most severe form of substance use disorder, associated with compulsive or uncontrolled use of one or more substances. Addiction is a chronic brain disease that has the potential for both recurrence (relapse) and recovery.

Substance: A psychoactive compound with the potential to cause health and social problems, including substance use disorders (and their most severe manifestation, addiction). For a list of substance categories included in this Report see Table 1.1. Note: Cigarettes and other tobacco products are only briefly discussed here due to extensive coverage in prior Surgeon General’s Reports.14-17

Substance Use: The use—even one time—of any of the substances in this Report.

Substance Misuse: The use of any substance in a manner, situation, amount, or frequency that can cause harm to users or to those around them. For some substances or individuals, any use would constitute misuse (e.g., underage drinking, injection drug use).

Binge Drinking: Binge drinking for men is drinking 5 or more standard alcoholic drinks, and for women, 4 or more standard alcoholic drinks on the same occasion on at least 1 day in the past 30 days.

Heavy Drinking: Defined by the CDC as consuming 8 or more drinks per week for women, and 15 or more drinks per week for men, and by the Substance Abuse and Mental Health Services Administration (SAMHSA), for research purposes, as binge drinking on 5 or more days in the past 30 days.

Standard Drink: Based on the 2015-2020 Dietary Guidelines for Americans, a standard drink is defined as shown in the graphic below. All of these drinks contain 14 grams (0.6 ounces) of pure alcohol.

![Standard Drink Graphic]


Substance Misuse Problems or Consequences: Any health or social problem that results from substance misuse. Substance misuse problems or consequences may affect the substance user or those around them, and they may be acute (e.g., an argument or fight, a motor vehicle crash, an overdose) or chronic (e.g., a long-term substance-related medical, family, or employment problem, or chronic medical condition, such as various cancers, heart disease, and liver disease). These problems may occur at any age and are more likely to occur with greater frequency of substance misuse.

Substance Use Disorder: A medical illness caused by repeated misuse of a substance or substances. According to the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5),30 substance use disorders are characterized by clinically significant impairments in health, social function, and impaired control over substance use and are diagnosed through assessing cognitive, behavioral, and psychological symptoms. Substance use disorders range from mild to severe and from temporary to chronic. They typically develop gradually over time with repeated misuse, leading to changes in brain circuits governing incentive salience (the
ability of substance-associated cues to trigger substance seeking), reward, stress, and executive functions like decision making and self-control. Multiple factors influence whether and how rapidly a person will develop a substance use disorder. These factors include the substance itself; the genetic vulnerability of the user; and the amount, frequency, and duration of the misuse. Note: A severe substance use disorder is commonly called an addiction.

**Relapse:** The return to drug use after a significant period of abstinence.

**Recovery:** A process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential. Even individuals with severe and chronic substance use disorders can, with help, overcome their substance use disorder and regain health and social function. This is called remission. When those positive changes and values become part of a voluntarily adopted lifestyle, that is called “being in recovery.” Although abstinence from all substance misuse is a cardinal feature of a recovery lifestyle, it is not the only healthy, pro-social feature.

## Prevalence of Substance Use, Misuse Problems, and Disorders

How widespread are substance use, misuse, and substance use disorders in the United States? The annual *National Survey on Drug Use and Health* (NSDUH) gathers data on the scope and prevalence of substance use, misuse, and related disorders, as well as utilization of substance use disorder treatment, among Americans aged 12 and older, representing more than 265 million people. Table 1.2 provides selected findings from the 2015 NSDUH. The table provides only general statistics for the United States as a whole; readers are urged to consult NSDUH's detailed tables for subpopulation estimates.

Over 175 million persons aged 12 and older (65.7 percent of this population) reported alcohol use in the past year, with over 66 million (24.9 percent) reporting binge drinking in the past month (Table 1.2). More than 36 million (13.5 percent) reported using marijuana in the past year, 12.5 million reported misusing prescription pain relievers, and over 300,000 reported using heroin in the past year. Almost 8 percent of the population met diagnostic criteria for a substance use disorder for alcohol or illicit drugs, and another 1 percent met diagnostic criteria for both an alcohol and illicit drug use disorder. Although 20.8 million people (7.8 percent of the population) met the diagnostic criteria for a substance use disorder in 2015, only 2.2 million individuals (10.4 percent) received any type of treatment. Of those treated, 63.7 percent received treatment in specialty substance use disorder treatment programs.
Several specific findings shown in Table 1.2 bear emphasis. Past year misuse of prescription psychotherapeutic drugs was reported by 18.9 million individuals in 2015 (7.1 percent of the population). Within this category, prescribed opioid pain relievers (e.g., OxyContin®, Vicodin®, Lortab®) accounted for 12.5 million people, followed by tranquilizers, such as Xanax®, reported by 6.1 million people; stimulants, such as Adderall® or Ritalin®, reported by 5.3 million people; and sedatives, such as Valium®, reported by 1.5 million people.

Substance Use Disorder Treatment Programs

Historically, treatment services were designed for people with severe substance use disorders (addictions), and programs were generally referred to as “specialty addiction treatment programs.” Today, individuals with mild to severe substance use disorders may receive treatment. These treatments are delivered by specialty programs, as well as by more generalist providers (e.g., primary care and general mental health providers). Not everyone with a substance use disorder will need ongoing treatment; many will require only a brief intervention and monitoring. Because treatments vary substantially in level of specialization, content, duration, and setting, and because those receiving services may differ substantially in the severity, duration, and complexity of their substance use disorder, this Report uses the phrase “substance use disorder treatment” as the generic term to capture the broad spectrum of advice, therapies, services, and monitoring provided to the group of individuals with mild to severe substance use disorders. The programs and services that provide specialty treatment are referred to as “substance use disorder treatment programs or services.”

The prevalence of past 30-day use of “any illicit drugs” (a broad category including marijuana/hashish, cocaine/crack, heroin, hallucinogens, inhalants, and prescription psychotherapeutic medications used nonmedically) rose from 9.4 percent in 2013 to 10.2 percent in 2014 among persons aged 12 and older (Figure 1.2). This 2014 prevalence rate for illicit drugs is significantly higher than it was in any year from 2002 to 2013. However, no significant changes were observed that year specifically in the use of prescription psychotherapeutic drugs, cocaine, or hallucinogens, suggesting that the observed increase was primarily related to increased use of marijuana. Marijuana was the most frequently used illicit drug (35.1 million past year users). The rate for past month marijuana use in 2014 was significantly higher than it was in any year from 2002 to 2013, with the prevalence of past 30-day marijuana use rising from 7.5 percent in 2013 to 8.4 percent in 2014. (Note: In 2015, changes were made to the NSDUH questionnaire and data collection procedures that do not allow for the presentation of trend data beyond 2014. For more information, see Summary of the Effects of the 2015 NSDUH Questionnaire Redesign: Implications for Data Users.)

Demographics of Substance Use

Table 1.3 and Table 1.4 show substance use by demographic characteristics. Prevalence of substance misuse and substance use disorders differs by race and ethnicity and gender, and these factors can also influence access to health care and substance use disorder treatment. Past year alcohol use for men was 68.6 percent and for women it was 62.9 percent. Past month binge alcohol use was 29.6 percent for men and 20.5 percent for women. The prevalence of past month binge alcohol use was 24.1 percent for American Indians or Alaska Natives, 25.7 percent for Hispanics or Latinos, and 26.0 for Whites. Prevalence of an alcohol use disorder was 7.8 percent for men and 4.1 percent for women. The prevalence of an illicit drug use disorder was 3.8 percent for men and 2.0 percent for women.
### Table 1.2: Past Year Substance Use, Past Year Initiation of Substance Use, and Met Diagnostic Criteria for a Substance Use Disorder in the Past Year Among Persons Aged 12 Years or Older for Specific Substances: Numbers in Millions and Percentages, 2015 National Survey on Drug Use and Health (NSDUH)

<table>
<thead>
<tr>
<th>Substance</th>
<th>Past Year Use or Misuse&lt;sup&gt;v&lt;/sup&gt;</th>
<th>Past Year Initiation Among Total Population&lt;sup&gt;x&lt;/sup&gt;</th>
<th>Met Diagnostic Criteria for a Substance Use Disorder&lt;sup&gt;x,vii&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>#</td>
<td>%</td>
<td>#</td>
<td>%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>175.8</td>
<td>65.7</td>
<td>4.8</td>
</tr>
<tr>
<td>Drinking Pattern</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Binge Drinking&lt;sup&gt;i&lt;/sup&gt;</td>
<td>66.7</td>
<td>24.9</td>
<td>da</td>
</tr>
<tr>
<td>Heavy Drinking&lt;sup&gt;i&lt;/sup&gt;</td>
<td>7.3</td>
<td>6.5</td>
<td>da</td>
</tr>
<tr>
<td>Any Illicit Drug&lt;sup&gt;ii&lt;/sup&gt;</td>
<td>47.7</td>
<td>17.8</td>
<td>nr</td>
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<tr>
<td>Cocaine/Crack</td>
<td>36.0</td>
<td>1.8</td>
<td>1.0</td>
</tr>
<tr>
<td>Heroin</td>
<td>0.8</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>Hallucinogens</td>
<td>4.7</td>
<td>1.8</td>
<td>1.2</td>
</tr>
<tr>
<td>Marijuana&lt;sup&gt;iii&lt;/sup&gt;</td>
<td>36.0</td>
<td>13.5</td>
<td>2.6</td>
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<tr>
<td>Inhalants</td>
<td>1.8</td>
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<tr>
<td>Misuse of Psychotherapeutics&lt;sup&gt;iv&lt;/sup&gt;</td>
<td>18.9</td>
<td>7.1</td>
<td>nr</td>
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<tr>
<td>Pain Relievers</td>
<td>12.5</td>
<td>4.7</td>
<td>2.1</td>
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<td>Tranquilizers</td>
<td>6.1</td>
<td>2.3</td>
<td>1.4</td>
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<td>Stimulants</td>
<td>5.3</td>
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<td>1.3</td>
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<td>Sedatives</td>
<td>1.5</td>
<td>0.6</td>
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<tr>
<td>Alcohol or Any Illicit Drugs&lt;sup&gt;iii&lt;/sup&gt;</td>
<td>182.3</td>
<td>68.1</td>
<td>nr</td>
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<tr>
<td>Alcohol and Any Illicit Drugs&lt;sup&gt;iv&lt;/sup&gt;</td>
<td>41.3</td>
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</tbody>
</table>

Notes: Past year initiates are defined as persons who used the substance(s) for the first time in the 12 months before the date of interview. The “nr = not reported due to measurement issues” notation indicates that the estimate could be calculated based on available data but is not calculated due to potential measurement issues. The “da” indication means does not apply.

i. Binge and heavy drinking, as defined by SAMHSA, are reported only for the period of 30 days before the interview date. SAMHSA defines binge use of alcohol for males and females as “drinking five (males)/four (females) or more drinks on the same occasion (i.e., at the same time or within a couple of hours of each other) on at least 1 day in the past 30 days” and heavy use of alcohol for both males and females as “binge drinking on each of 5 or more days in the past 30 days.”

ii. Illicit drug use includes the misuse of prescription psychotherapeutics or the use of marijuana, cocaine (including crack), heroin, hallucinogens, inhalants, or methamphetamine.

iii. As of June 2016, 25 states and the District of Columbia have legalized medical marijuana use. Four states have legalized retail marijuana sales; the District of Columbia has legalized personal use and home cultivation (both medical and recreational). It should be noted that none of the permitted uses under state laws alter the status of marijuana and its constituent compounds as illicit drugs under Schedule I of the federal Controlled Substances Act.

iv. Misuse of prescription-type psychotherapeutics includes the nonmedical use of pain relievers, tranquilizers, stimulants, or sedatives and does not include over-the-counter drugs.

v. Estimates of misuse of psychotherapeutics and stimulants include data from new methamphetamine items added in 2005 and 2006 and are not comparable with estimates presented in NSDUH reports before 2007. See Section B.4.8 in Appendix B of the Results from the 2008 NSDUH.

vi. Estimates of misuse of psychotherapeutics and stimulants do not include data from new methamphetamine items added in 2005 and 2006.

vii. Diagnostic criteria for a substance use disorder is based on definitions found in the Fourth Edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV).

Source: Center for Behavioral Health Statistics and Quality, (2016).
Relevance of Substance Use and Misuse

It is sometimes thought that concern over substance use and misuse should be secondary to the real issue of substance use disorders and especially their severest manifestation, addiction, which has captured media headlines and has been linked to many health and social problems. This is an important misconception. Individuals with substance use disorders have elevated rates of substance misuse–related health and social problems and costs, but as shown in the last columns of Table 1.2, Table 1.3, and Table 1.4, many people who misuse substances do not meet the diagnostic criteria for a substance use disorder. For example, binge drinking at least once during the past month was self-reported by over 66 million individuals. By definition, those episodes have the potential for producing harm to the user and/or to those around them, through increases in motor vehicle crashes, violence, and alcohol-poisonings. Similarly, in 2015, 12.5 million individuals misused a pain reliever in the past year—setting the stage for a potential overdose—but only 2.9 million met diagnostic criteria for a prescription medication disorder.
**Table 1.3: Past Year Alcohol Use, Past Month Binge Alcohol Use, and Met Diagnostic Criteria for a Substance Use Disorder in the Past Year Among Persons Aged 12 Years or Older: Numbers in Millions and Percentages, 2015 National Survey on Drug Use and Health (NSDUH)**

<table>
<thead>
<tr>
<th>Demographic Group</th>
<th>Past Year Alcohol Use</th>
<th>Past Month Binge Alcohol Use&lt;sup&gt;i&lt;/sup&gt;</th>
<th>Met Diagnostic Criteria for a Substance Use Disorder in Past Year&lt;sup&gt;i&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>#</td>
<td>%</td>
<td>#</td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>89.0</td>
<td>68.6</td>
<td>38.4</td>
</tr>
<tr>
<td>Female</td>
<td>86.9</td>
<td>62.9</td>
<td>28.3</td>
</tr>
<tr>
<td>White</td>
<td>119.9</td>
<td>70.3</td>
<td>44.4</td>
</tr>
<tr>
<td>Black or African American</td>
<td>18.6</td>
<td>58.0</td>
<td>7.5</td>
</tr>
<tr>
<td>American Indian or Alaska Native</td>
<td>0.7</td>
<td>51.4</td>
<td>0.3</td>
</tr>
<tr>
<td>Native Hawaiian or Other Pacific Islander</td>
<td>0.4</td>
<td>51.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Asian</td>
<td>7.8</td>
<td>53.1</td>
<td>2.1</td>
</tr>
<tr>
<td>Two or More Races</td>
<td>2.7</td>
<td>57.8</td>
<td>1.1</td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>25.7</td>
<td>59.0</td>
<td>11.2</td>
</tr>
</tbody>
</table>

**Table 1.4: Past Year Substance Use, Past 30-Day Illicit Drug Use, and Met Diagnostic Criteria for a Substance Use Disorder in the Past Year Among Persons Aged 12 Years or Older: Numbers in Millions and Percentages, 2015 National Survey on Drug Use and Health (NSDUH)**

<table>
<thead>
<tr>
<th>Demographic Group</th>
<th>Past Year Use</th>
<th>Past 30-Day Illicit Drug Use</th>
<th>Met Diagnostic Criteria for a Substance Use Disorder in Past Year&lt;sup&gt;i&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>#</td>
<td>%</td>
<td>#</td>
</tr>
<tr>
<td>Any Illicit Drug&lt;sup&gt;i&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26.6</td>
<td>20.5</td>
<td>16.2</td>
</tr>
<tr>
<td>Female</td>
<td>21.2</td>
<td>15.3</td>
<td>10.9</td>
</tr>
<tr>
<td>White</td>
<td>30.5</td>
<td>17.9</td>
<td>17.4</td>
</tr>
<tr>
<td>Black or African American</td>
<td>6.6</td>
<td>20.7</td>
<td>4.0</td>
</tr>
<tr>
<td>American Indian or Alaska Native</td>
<td>0.3</td>
<td>22.9</td>
<td>0.2</td>
</tr>
<tr>
<td>Native Hawaiian or Other Pacific Islander</td>
<td>0.1</td>
<td>20.5</td>
<td>0.07</td>
</tr>
<tr>
<td>Asian</td>
<td>1.4</td>
<td>9.2</td>
<td>0.6</td>
</tr>
<tr>
<td>Two or More Races</td>
<td>1.3</td>
<td>27.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>7.4</td>
<td>17.2</td>
<td>4.0</td>
</tr>
</tbody>
</table>

<sup>i</sup> Diagnostic criteria for a substance use disorder is based on definitions found in the Fourth Edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV).

<sup>ii</sup> Binge drinking, as defined by SAMHSA, are reported only for the period of 30 days before the interview date. SAMHSA defines binge use of alcohol for males and females as “drinking five (males)/four (females) or more drinks on the same occasion (i.e., at the same time or within a couple of hours of each other) on at least 1 day in the past 30 days.”

<sup>iii</sup> Illicit drugs include marijuana/hashish, cocaine (including crack), heroin, hallucinogens, inhalants, or misuse of prescription-type psychotherapeutics, including data from original methamphetamine questions but not including new methamphetamine items added in 2005 and 2006.

Source: Center for Behavioral Health Statistics and Quality, (2016).3
The clear implications of these data are that a comprehensive approach to reducing the misuse of alcohol and drugs—one that includes the implementation of effective prevention programs and policy strategies as well as high-quality treatment services—is needed to reduce the problems and costs of substance misuse in the United States. In fact, greater impact is likely to be achieved by reducing substance misuse in the general population—that is, among people who are not addicted—than among those with severe substance use problems. Of course, efforts to reduce general population rates of substance use and misuse are also likely to reduce rates of substance use disorders, because substance use disorders typically develop over time following repeated episodes of misuse (often at escalating rates) that result in the progressive changes to brain circuitry that underlie addiction.

## Costs and Impact of Substance Use and Misuse

Alcohol misuse, illicit drug use, misuse of medications, and substance use disorders are estimated to cost the United States more than $400 billion in lost workplace productivity (in part, due to premature mortality), health care expenses, law enforcement and other criminal justice costs (e.g., drug-related crimes), and losses from motor vehicle crashes.\(^{10,11}\) Furthermore, about three quarters of the costs associated with alcohol use were due to binge drinking, and about 40 percent of those costs were paid by government, emphasizing the huge cost of alcohol misuse to taxpayers.\(^{34}\)

These costs are not unique to the United States. A 2010 study examined the global burden of disability attributable to substance misuse problems and disorders, focusing particularly on lost ability to work and years of life lost to premature mortality. Costs were calculated for 20 age groups and both sexes in 187 countries.\(^{35}\) Mental and substance use disorders were the leading causes of years lived with disability worldwide, largely because these problems strike individuals early in their lives and can continue—especially if untreated—for long periods.

In addition to the costs to society, substance misuse can have many direct and indirect health and personal consequences for individuals. The direct effects on the user depend on the specific substances used, how much and how often they are used, how they are taken (e.g., orally vs. injected), and other factors. Acute effects can range from changes in mood and basic body functions, such as heart rate or blood pressure, to overdose and death. Alcohol misuse and drug use can also have long-term effects on physical and mental health and can lead to substance use disorders. For example, drug use is associated with chronic pain conditions and cardiovascular and cardiopulmonary diseases.\(^{36,37}\) Alcohol misuse is associated with liver and pancreatic diseases, hypertension, reproductive system disorders, trauma, stroke, FASD, and cancers of the oral cavity, esophagus, larynx, pharynx, liver, colon, and rectum.\(^{26,28}\) For breast cancer, studies have shown that even moderate drinking may increase the risk.\(^{25}\) Although alcohol consumption is associated with adverse health effects as noted above, the 2015-2020 Dietary Guidelines for
Americans indicate that moderate alcohol use can be part of a healthy diet, but only when used by adults of legal drinking age.\(^1\)

In addition, alcohol and drug use by pregnant women can have profound effects on the developing fetus. Alcohol use during pregnancy can lead to a wide range of disabilities in children, the most severe of which is FASD, characterized by intellectual disabilities, speech and language delays, poor social skills, and sometimes facial deformities. Use of drugs, such as opioids during pregnancy, can result in NAS, a drug-withdrawal syndrome requiring medical intervention and extended hospital stay for newborns. Use of some drugs, such as cocaine, during pregnancy may also lead to premature birth or miscarriage. In addition, substance use during pregnancy may interfere with a child’s brain development and result in later consequences for mental functioning and behavior.

Substance misuse also can affect a user’s nutrition and sleep, as well as increase the risk for trauma, violence, injury, and contraction of communicable diseases, such as HIV/AIDS and Hepatitis C. These consequences can all contribute to the spectrum of public health consequences of substance misuse and need to be considered both independently and collectively when developing and implementing clinical and public health interventions.

Substance misuse problems can also result in other serious and sometimes fatal health problems and extraordinary costs; they may also lead to unexpected death from other causes. Three examples of these serious, sometimes lethal, problems related to substance misuse are highlighted below.

Driving Under the Influence

In 2014, 9,967 people were killed in motor vehicle crashes while driving under the influence of alcohol, representing nearly one third (31 percent) of all traffic-related fatalities in the United States.\(^3\) DUI continues to be among the most frequent causes for arrests every year.\(^4\) But at approximately 1.3 million per year, these arrests represent only about 1 percent of the actual alcohol-impaired driving incidents reported in national surveys, suggesting that there are many more people who drive while impaired that have not been arrested, putting themselves and others at high risk of being harmed.\(^5\)

In addition to the deaths that result from DUI, the National Highway Traffic Safety Administration (NHTSA) estimates that DUI costs the United States more than $44 billion each year in prosecution, higher insurance rates, higher taxes, medical claims, and property damage.\(^6\)

As important as they are, these statistics account for only alcohol-related driving impairment and fail to measure other impairing substances. A study by NHTSA tested oral fluid and blood specimens from a random sample of drivers at the roadside (during daytime on Friday or nighttime Friday to Sunday) and

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\(^1\) Moderate alcohol use is defined by the 2015-2020 Dietary Guidelines for Americans as up to 1 drink per day for women and up to 2 drinks per day for men—and only by adults of legal drinking age. Many individuals should not consume alcohol, including individuals who are taking certain over-the-counter or prescription medications or who have certain medical conditions, those who are recovering from an alcohol use disorder or are unable to control the amount they drink, and anyone younger than age 21 years. In addition, drinking during pregnancy may result in negative behavioral or neurological consequences in the offspring.
found 12 to 15 percent had used one or more illegal substances.\(^{42}\) Drivers tested positive for drugs in approximately 16 percent of all motor vehicle crashes.\(^{43}\)

### Overdose Deaths

Overdose deaths are typically caused by consuming substances at high intensity and/or by consuming combinations of substances such as alcohol, sedatives, tranquilizers, and opioid pain relievers to the point where critical areas in the brain that control breathing, heart rate, and body temperature stop functioning.

**Alcohol Overdose (Alcohol Poisoning)**

The CDC reports more than 2,200 alcohol overdose deaths in the United States each year—an average of six deaths every day.\(^{44}\) More than three quarters (76 percent) of alcohol overdose deaths occur among adults between ages 35 and 64, and 76 percent of those who die from alcohol overdose are men.

**Drug Overdose (Illicit and Prescription Drugs)**

Opioid analgesic pain relievers are now the most prescribed class of medications in the United States, with more than 289 million prescriptions written each year.\(^{35,46}\) The increase in prescriptions of opioid pain relievers has been accompanied by dramatic increases in misuse (\textit{Table 1}) and by a more than 200 percent increase in the number of emergency department visits from 2005 to 2011.\(^{47}\) In 2014, 47,055 drug overdose deaths occurred in the United States, and 61 percent of these deaths were the result of opioid use, including prescription opioids and heroin.\(^{7}\) Heroin overdoses have more than tripled from 2010 to 2014.\(^{7}\) Heroin overdoses were more than five times higher in 2014 (10,574) then ten years before in 2004 (1,878). Additionally, rates of cocaine overdose were higher in 2014 than in the previous six years (5,415 deaths from cocaine overdose). In 2014, there were 17,465 overdoses from illicit drugs and 25,760 overdoses from prescription drugs.\(^{48}\) Drug overdose deaths also occur as a result of the illicit manufacturing and distribution of synthetic opioids, such as fentanyl, and the illegal diversion of prescription opioids. Illicit fentanyl, for example, is often combined with heroin or counterfeit prescription drugs or sold as heroin, and may be contributing to recent increases in drug overdose deaths.\(^{7,49}\)

### Intimate Partner Violence, Sexual Assault, and Rape

Intimate partner violence, sexual assault, and rape are crimes with long-lasting effects on victims and great cost to society.\(^{50,51}\) These crimes happen to both women and men and are often associated with substance use. A recent national survey found that 22 percent of women and 14 percent of men reported experiencing severe physical violence from an intimate partner in their lifetimes.\(^{52}\) In this survey, 19.3 percent of women and 1.7 percent of men reported being raped in their lifetimes, while 43.9 percent of women and 23.4 percent of men reported some other form of sexual violence in their lifetimes.\(^{52}\) Substance misuse is often related to these crimes.
Numerous studies have found a high correlation between substance use and intimate partner violence, although this does not mean that substance use causes intimate partner violence. In addition to evidence from the criminal justice arena, recent systematic reviews have found that substance use is both a risk factor for and a consequence of intimate partner violence.

A recent survey of sexual assault and sexual misconduct on college campuses found that use of alcohol and drugs are important risk factors for nonconsensual sexual contact among undergraduate, graduate, and professional students. It is clear that substance use and intimate partner violence and sexual assault are closely linked; however, more research is needed on the nature of the relationship between substance use and these forms of violence to determine how substance use contributes to the perpetration of violence and victimization and how violence contributes to subsequent substance use among both perpetrators and victims.

Vulnerability to Substance Misuse Problems and Disorders

Risk and Protective Factors: Keys to Vulnerability

Substance misuse problems and substance use disorders are not inevitable. An individual’s vulnerability may be partly predicted by assessing the nature and number of their community, caregiver/family, and individual-level risk and protective factors.

Significant community-level risk factors for substance misuse and use disorders include easy access to inexpensive alcohol and other substances. Caregiver/family-level risk factors include low parental monitoring, a family history of substance use or mental disorders, and high levels of family conflict or violence. At the individual level, major risk factors include current mental disorders, low involvement in school, a history of abuse and neglect, and a history of substance use during adolescence, among others.

Community-level protective factors include higher cost for alcohol and other drugs (often achieved by increasing taxes on these products); regulating the number and concentration of retailers selling various substances (e.g., density of alcohol outlets or marijuana dispensaries); preventing illegal alcohol and other drug sales by enforcing existing laws and holding retailers accountable for harms caused by illegal sales (e.g., commercial host [dram shop] liability); availability of healthy recreational and social activities; and other population-level policies and their enforcement. Caregiver/family-level protective factors include support and regular monitoring by parents. Some important individual-level protective factors include involvement in school, engagement in healthy recreational and social activities, and good coping skills.

Three important points about vulnerability should be highlighted. First, no single individual or community-level factor determines whether an individual will develop a substance misuse problem or disorder. Second, most risk and protective factors can be modified through preventive programs and
policies to reduce vulnerability. Third, although substance misuse problems and disorders may occur at any age, adolescence and young adulthood are particularly critical at-risk periods. Research now indicates that the majority of those who meet criteria for a substance use disorder in their lifetime started using substances during adolescence and met the criteria by age 20 to 25.\textsuperscript{62-64} One likely reason for this vulnerability in adolescence and young adulthood is that alcohol and other substances have particularly potent effects on developing brain circuits, and recent scientific findings indicate that brain development is not complete until approximately age 21 to 23 in women and 23 to 25 in men.\textsuperscript{65-67} Among the last brain regions to reach maturity is the prefrontal cortex, the brain region primarily responsible for “adult” abilities, such as delay of reward, extended reasoning, and impulse control. This area of the brain is one of the most affected regions in a substance use disorder.

Substance misuse can begin at any age. Therefore, it is important to focus on prevention of substance misuse across the lifespan as well as the prevention of substance use disorders.

### Diagnosing a Substance Use Disorder

#### Changes in Understanding and Diagnosis of Substance Use Disorders

Repeated, regular misuse of any of the substances listed in Figure 1.2 may lead to the development of a substance use disorder. Severe substance use disorders are characterized by compulsive use of substance(s) and impaired control of substance use. Substance use disorder diagnoses are based on criteria specified in the American Psychiatric Association’s \textit{Diagnostic and Statistical Manual of Mental Disorders} (DSM). Much of the substance use disorder data included in this \textit{Report} is based on definitions included in the DSM-IV, which described two distinct disorders: substance abuse and substance dependence, with specific diagnostic criteria for each. Anyone meeting one or more of the abuse criteria—which focused largely on the negative consequences associated with substance misuse, such as being unable to fulfill family or work obligations, experiencing legal trouble, or engaging in hazardous behavior as a result of drug use—would receive the “abuse” diagnosis. Anyone with three or more of the dependence criteria, which included symptoms of drug tolerance, withdrawal, escalating and uncontrolled substance use, and the use of the substance to the exclusion of other activities, would receive the “dependence” diagnosis. Notably, addiction is not listed as a formal diagnosis in the DSM. However, substance
dependence was often used interchangeably with addiction, and tolerance and withdrawal were considered, by many, cardinal features of addiction.

The DSM-5, which is the fifth and current version of the DSM, integrates the two DSM-IV disorders, substance abuse and substance dependence, into a single disorder called substance use disorder with mild, moderate, and severe sub-classifications. Individuals are evaluated for a substance use disorder based on 10 or 11 (depending on the substance) equally weighted diagnostic criteria (Table 1.5). Most of these overlap with those used to diagnose DSM-IV dependence and abuse. Individuals exhibiting fewer than two of the symptoms are not considered to have a substance use disorder. Those exhibiting two or three symptoms are considered to have a “mild” disorder, four or five symptoms constitutes a “moderate” disorder, and six or more symptoms is considered a “severe” substance use disorder.30 In this Report, addiction is used to refer to substance use disorders at the severe end of the spectrum and are characterized by compulsive substance use and impaired control over use.

<table>
<thead>
<tr>
<th>Table 1.5: Criteria for Diagnosing Substance Use Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic Criteria for Substance Use Disorders</td>
</tr>
<tr>
<td>Using in larger amounts or for longer than intended</td>
</tr>
<tr>
<td>Wanting to cut down or stop using, but not managing to</td>
</tr>
<tr>
<td>Spending a lot of time to get, use, or recover from use</td>
</tr>
<tr>
<td>Craving</td>
</tr>
<tr>
<td>Inability to manage commitments due to use</td>
</tr>
<tr>
<td>Continuing to use, even when it causes problems in relationships</td>
</tr>
<tr>
<td>Giving up important activities because of use</td>
</tr>
<tr>
<td>Continuing to use, even when it puts you in danger</td>
</tr>
<tr>
<td>Continuing to use, even when physical or psychological problems may be made worse by use</td>
</tr>
<tr>
<td>Increasing tolerance</td>
</tr>
<tr>
<td>Withdrawal symptoms</td>
</tr>
</tbody>
</table>

Notes: Fewer than 2 symptoms = no disorder; 2-3 = mild disorder; 4-5 = moderate disorder; 6 or more = severe disorder.

Implications of the New Diagnostic Criteria
The new diagnostic criteria are likely to reduce the “all or nothing” thinking that has characterized the substance use field. Tolerance and withdrawal remain major clinical symptoms, but they are no longer the deciding factor in whether an individual “has an addiction.” Substance use disorders, including addiction, can occur with all substances listed in Table 1.1, not just those that are able to produce
What is an Intervention?

Intervention here and throughout this Report means a professionally delivered program, service, or policy designed to prevent substance misuse or treat an individual’s substance use disorder. It does not refer to an arranged meeting or confrontation intended to persuade a friend or loved one to quit their substance misuse or enter treatment—the type of “intervention” sometimes depicted on television. Planned surprise confrontations of the latter variety—a model developed in the 1960s, sometimes called the “Johnson Intervention”—have not been demonstrated to be an effective way to engage people in treatment. Confrontational approaches in general, though once the norm even in many behavioral treatment settings, have not been found effective and may backfire by heightening resistance and diminishing self-esteem on the part of the targeted individual.

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This type of proactive clinical monitoring and management is already done within general health care settings to address other potentially progressive illnesses that are brought about by unhealthy behaviors. For example, patients with high blood pressure may be told to adjust their activity and stress in order to reduce the progression of hypertension. Typically, these individuals are also clinically monitored for key symptoms to ensure that symptoms do not worsen.

There are compelling reasons to apply similar procedures in emerging cases of substance misuse. Routine screening for alcohol and other substance use should be conducted in primary care settings to identify early symptoms of a substance use disorder (especially among those with known risk and few protective factors). This should be followed by informed clinical guidance on reducing the frequency and amount of substance use, family education to support lifestyle changes, and regular monitoring.

Research has shown that substance use disorders are similar in course, management, and outcome to other chronic illnesses, such as hypertension, diabetes, and asthma. Unfortunately, substance use disorders have not been treated, monitored, or managed like other chronic illnesses, nor has care for these conditions been covered by insurance to the same degree. Nonetheless, it is possible to adopt the same type of chronic care management approach to the treatment of substance use disorders as is now used to manage most other chronic illnesses. Evidence-based behavioral interventions, medications, social support services, clinical monitoring, and RSS make this type of chronic care management possible, often by the same health care teams that currently treat other chronic illnesses.
Evidence also shows that such an approach will improve the effectiveness of treatments for substance use disorders. Remission of substance use and even full recovery can now be achieved if evidence-based care is provided for adequate periods of time, by properly trained health care professionals, and augmented by supportive monitoring, RSS, and social services. This fact is supported by a national survey showing that there are more than 25 million individuals who once had a problem with alcohol or drugs who no longer do.\textsuperscript{73}

The Separation of Substance Use Treatment and General Health Care

Until quite recently, substance misuse problems and substance use disorders were viewed as social problems, best managed at the individual and family levels, and sometimes through the existing social infrastructure—such as schools and places of worship, and, when necessary, through civil and criminal justice interventions.\textsuperscript{74} In the 1970s, when rates of substance misuse increased, including by college students and Vietnam War veterans, most families and traditional social services were not prepared to handle this problem.\textsuperscript{75} Despite a compelling national need for treatment, the existing health care system was neither trained to care for nor especially eager to accept patients with substance use disorders.

For these reasons, a new system of substance use disorder treatment programs was created, but with administration, regulation, and financing placed outside mainstream health care.\textsuperscript{74,75} This meant that with the exception of detoxification in hospital-based settings, virtually all treatment was delivered by programs that were geographically, financially, culturally, and organizationally separate from mainstream health care. Of equal historical importance was the decision to focus treatment only on addiction. This left few provisions for detecting or intervening clinically with the far more prevalent cases of early-onset, mild, or moderate substance use disorders.

Creating this system of substance use disorder treatment programs was a critical element in addressing the burgeoning substance use disorder problems in our nation. However, that separation also created unintended and enduring impediments to the quality and range of care options. For example, separate systems for substance use disorder treatment and other health care needs may have exacerbated the negative public attitudes toward people with substance use disorders. Additionally, the pharmaceutical industry was hesitant to invest in the development of new medications for individuals with substance use disorders, because they were not convinced that a market for these medications existed. Consequently, until the 1990s, few U.S. Food and Drug Administration (FDA) approved medications were available to treat addictions.\textsuperscript{76,77}

Meanwhile, despite numerous research studies documenting high prevalence rates of substance use disorders among patients in emergency departments, hospitals, and general medical care settings, mainstream health care generally failed to recognize or address substance use disorders.\textsuperscript{78} In fact, a recent study by the CDC found that in 2011, only 1 in 6 United States adults and 1 in 4 binge drinkers had \textit{ever} been asked by a health professional about their drinking behavior.\textsuperscript{79} Furthermore, the percent of adult binge drinkers who had been asked about their drinking had not changed since 1997, reflecting the challenges involved in fostering implementation of screening and counseling services for alcohol
misuse in clinical settings. This has been a costly mistake, with often deadly consequences. A recent study showed that the presence of a substance use disorder often doubles the odds for the subsequent development of chronic and expensive medical illnesses, such as arthritis, chronic pain, heart disease, stroke, hypertension, diabetes, and asthma.\(^8^0\)

In this regard, fatal medication errors due to unforeseen interactions between a prescribed medication for a diagnosed medical condition and unscreened, unaddressed patient substance use increased tenfold over the past 20 years.\(^8^1\) To address this problem, researchers suggested “…(1) screening patients for use…of alcohol and/or street drugs; (2) taking extra precautions when prescribing medicines with known dangerous interactions with alcohol and/or street drugs; and (3) teaching the patient the risks of mixing medicines with alcohol and/or street drugs.”\(^8^1\) Similar recommendations focusing on prescribed opioids have been issued by the CDC to curb the rise in opioid overdose deaths.\(^8^2\) Again, screening for substance use and substance use disorders before and during the course of opioid prescribing, combined with patient education, are recommended.\(^8^2\)

Yet despite these and other indications of extreme threats to health care quality, safety, effectiveness, and cost containment, as of this writing, few general health care organizations screen for, or offer services for, the early identification and treatment of substance use disorders. Moreover, few medical, nursing, dental, or pharmacy schools teach their students about substance use disorders;\(^8^3\)-\(^8^6\) and, until recently, few insurers offered adequate reimbursement for treatment of substance use disorders.\(^8^7\),\(^8^8\)

### Recent Changes in Health Care Policy and Law

The longstanding separation of substance use disorders from the rest of health care began to change with enactment of the Paul Wellstone and Pete Domenici Mental Health Parity and Addiction Equity Act of 2008 (MHPAEA) and the Affordable Care Act in 2010.\(^8^9\),\(^9^0\) MHPAEA requires that the financial requirements and treatment limitations imposed by health plans and insurers for substance use disorders be no more restrictive than the financial requirements and treatment limitations they impose for medical and surgical conditions. The Affordable Care Act requires the majority of United States health plans and insurers to offer prevention, screening, brief interventions, and other forms of treatment for substance use disorders.\(^8^9\)

It is difficult to overstate the importance of these two Acts for creating a public health-oriented approach to reducing substance misuse and related disorders. These laws and related changes in health care financing are creating incentives for health care organizations to integrate substance use disorder treatment with general health care. Many questions remain, but those questions are no longer \textit{whether} but \textit{how} this much-needed integration will occur. These changes combine to create a new, challenging but exceptionally promising era for the prevention and treatment of substance use disorders and set the context for this \textit{Report}. 

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\(^8^0\) See Chapter 6 - Health Care Systems and Substance Use Disorders.
Marijuana: A Changing Legal and Research Environment

Although this Report does not examine the issue of marijuana legalization, its continually evolving legal status is worth mentioning because of implications for both research and policy. As mentioned elsewhere, marijuana is the most commonly used illicit drug in the United States, with 22.2 million people aged 12 or older using it in the past year. In recent years marijuana use has become more socially acceptable among both adults and youth, while perceptions of risk among adolescents of the drug’s harms have been declining over the past 13 years.91

As use of marijuana and its constituent components and derivatives becomes more widely accepted, it is critical to strengthen understanding of the effects and consequences for individual users and for public health and safety. Conducting such research can be complex as laws and policies vary significantly from state to state. For example, some states use a decriminalization model, which means production and sale of marijuana are still illegal and no legal marijuana farms, distributors, companies, stores, or advertising are permitted. Through ballot initiatives, other states have “legalized” marijuana use, which means they allow the production and sales of marijuana for personal use. Additionally, some states have legalized marijuana for medical purposes, and this group includes a wide variety of different models dictating how therapeutic marijuana is dispensed. The impacts of state laws regarding therapeutic and recreational marijuana are still being evaluated, although the differences make comparisons between states challenging.92

As of June 2016, 25 states and the District of Columbia have legalized medical marijuana use. Four states have legalized retail sales; the District of Columbia has legalized personal use and home cultivation (both medical and recreational), with more states expecting to do so. None of the permitted uses under state laws alters the status of marijuana and its constituent compounds as illicit drugs under Schedule I of the federal Controlled Substances Act.93 It should also be noted that use for recreational purposes has not been legalized by any jurisdiction for people under age 21, and few jurisdictions have legalized medical marijuana for young people. While laws are changing, so too is the drug itself with average potency more than doubling over the past decade (1998 to 2008).94 The ways marijuana is used are also changing – in addition to smoking, consuming edible forms like baked goods and candies, using vaporizing devices, and using high-potency extracts and oils (e.g., “dabbing”) are becoming increasingly common.95 Because these products and methods are unregulated even in states that have legalized marijuana use, users may not have accurate information about dosage or potency, which can lead and has led to serious consequences such as hospitalizations for psychosis and other overdose-related symptoms.95 Marijuana use can also impair driving skills and, while estimates vary, is linked to a roughly two-fold increase in accident risk.96-98 The risk is compounded when marijuana is used with alcohol.96,99

There is a growing body of research suggesting the potential therapeutic value of marijuana’s constituent cannabinoid chemicals in numerous health conditions including pain, nausea, epilepsy, obesity, wasting disease, addiction, autoimmune disorders, and other conditions. Given the possibilities around therapeutic use, it is necessary to continue to explore ways of easing existing barriers to research. Marijuana has more than 100 constituent cannabinoid compounds, with cannabidiol (CBD) and tetrahydrocannabinol (THC, the chemical responsible for most of marijuana’s intoxicating effects) being the most well-studied. Evidence collected so far in clinical investigations of the marijuana plant is still insufficient to meet
FDA standards for a finding of safety and efficacy for any therapeutic indications. However, the FDA has approved three medications containing synthetically derived cannabinoids: Marinol capsules and Syndros oral solution (both containing dronabinol, which is identical in chemical structure to THC), and Cesamet capsules (containing nabilone, which is similar in structure to THC) for severe nausea and wasting in certain circumstances, for instance in AIDS patients. Recognizing the potential therapeutic importance of compounds found in marijuana, the FDA has granted Fast Track designation to four development programs of products that contain marijuana constituents or their synthetic equivalents. The therapeutic areas in which products are being developed granted Fast Track by FDA include the treatment of pain in patients with advanced cancer; treatment of Dravet syndrome (two programs), a rare and catastrophic treatment-resistant form of childhood epilepsy; and treatment of neonatal hypoxic ischemic encephalopathy, brain injury resulting from oxygen deprivation during birth.

Additionally, there are clinical investigations for the treatment of refractory seizure syndromes, including Lennox Gastaut Syndrome, and for treatment of post-traumatic stress disorder (PTSD). However, further exploration of these issues always requires consideration of the serious health and safety risks associated with marijuana use. Research shows that risks can include respiratory illnesses, dependence, mental health-related problems, and other issues affecting public health such as impaired driving. Within this context of changing marijuana policies at the state level, research is needed on the impact of different models of legalization and how to minimize harm based on what has been learned from legal substances subject to misuse, such as alcohol and tobacco. Continued assessment of barriers to research and surveillance will help build the best scientific foundation to support good public policy while also protecting the public health.

**Purpose, Focus, and Format of the Report**

**The Audience**

This Report is intended for individuals, families, community members, educators, health care professionals, public health practitioners, advocates, public policymakers, and researchers who are looking for effective, sustainable solutions to the problems created by alcohol and other substances. To meet those needs, the Report reviews and synthesizes the most important and reliable scientific findings in key topic areas and distills those findings into recommendations for:

- Improving public awareness of substance misuse and related problems;
- Reducing negative attitudes related to substance use disorders;
- Closing the gap between what is known to reduce substance misuse at the population level and within specific subgroups, and the implementation of these effective programs, policies, and environmental strategies at the federal, state, and community levels;
- Understanding the need for and effectiveness of programs for high-risk populations;
- Expanding the capacity of health care systems to deliver evidence-based substance use disorder treatment;
- Integrating financing and health care system models to facilitate access and affordability of care for substance use disorders;
• Continuing to build the science base of effective prevention, treatment, and recovery practices and policies; and
• Engaging stakeholders in reducing substance use and misuse problems and protecting the health of all individuals across the lifespan.

Because of the broad audience, the Report is purposely written in accessible language without excessive scientific jargon. The Report also focuses on current issues and practical questions that trouble so many people:

• What are the health and social impacts of alcohol and drug use and misuse in the United States? What key factors influence these behaviors?
• What are the major substance misuse problems facing the United States?
• What causes substance use disorders and why do they change people so dramatically?
• Can substance misuse problems and disorders be prevented? How?
• What constitutes effective treatment?
• Can addicted individuals recover? What will it take to manage their disorders and sustain recovery?

Topics Covered in the Report

Individual chapters in the Report review the science associated with the major substance use, misuse, and disorder issues for specific topics. Tobacco, also an addictive substance, is mentioned only briefly, because problems associated with tobacco use and nicotine addiction have been covered extensively in other Surgeon General’s Reports.  

Because of the broad audience and the practical emphasis, the Report is intentionally selective rather than exhaustive, emphasizing findings that have the potential for the greatest public health impact and the greatest potential for action. For readers wanting greater scientific detail or more specific information, detailed research reports, as well as supplemental resource materials, are supplied in references, in the Appendices, and in special emphasis boxes throughout the Report.

Scientific Standards Used to Develop the Report

Findings cited in all of the chapters came from electronic database searches of research articles published in English. Within those searches, priority was given to systematic literature reviews and to findings that were replicated by multiple controlled trials. However, many important issues in prevention, treatment, recovery, and health care systems have not yet been examined in rigorous controlled trials, or are not appropriate for such research designs. In these cases, the best available evidence was cited and labeled according to the reporting conventions published by the CDC:

• Well-supported: Evidence derived from multiple controlled trials or large-scale population studies.
• Supported: Evidence derived from rigorous but fewer or smaller trials or restricted samples.
• Promising: Findings that do not derive from rigorously controlled studies but that nonetheless make practical or clinical sense and are widely practiced.
In cases in which evidence was based on findings of neurobiological research, the CDC standards were adapted.

A summary of the key findings appears at the beginning of each chapter. The key findings highlight what is currently known from available research about the chapter topic, as well as the strength of the evidence. As with the rest of the Report, the key findings are not intended to be exhaustive, but are instead considered the important “take-aways” from each chapter. Readers interested in a fuller discussion of the topics are encouraged to read the chapters in their entirety.

**Addressing Substance Use in Specific Populations**

As indicated, the chapters are designed to prioritize best available research findings that apply most broadly across different substances and across various subgroups, while also identifying program and policy interventions that have strong evidence for particular substances (e.g., alcohol), when available. The rationale for this decision is that the available research suggests that the genetic, neurobiological, and environmental processes underlying substance use, misuse, and disorders are largely similar across most known substances and unrelated to the age, sex, race and ethnicity, gender identity, or culture of the individual. The available research also clearly indicates that many of the interventions, including population-level policies, focused programs, behavioral therapies, medications, and social services shown to be effective in one subgroup are generally effective for other subgroups. Put differently, it is reasonable to assume that the findings presented in this Report are relevant for many substance use types and patterns; for most age, gender, racial and ethnic, and cultural subgroups; and for many special needs subgroups (e.g., those with co-occurring mental or physical illnesses; those involved with the criminal justice system).

However, this general statement has some important caveats. First, the statement depends heavily on the phrase “available research.” There is insufficient research examining subgroup differences in the neurobiology of substance use disorders and in interventions aimed at preventing, treating, and promoting recovery from substance use disorders. Additional research designed to examine these differences and to test interventions in specific populations is needed.

A second caveat is that individual variability in response to standard prevention, treatment, and recovery support interventions is common throughout health care. Individuals with the same disease often react quite differently to the same medicine or behavioral intervention. Accordingly, general health care has moved toward “personalized medicine,” an individualized treatment regimen derived from specific information about the individual’s genetics and stage of illness, as well as lifestyle, language, culture, and personal preferences. Personalized care is not common in the substance use disorder field because many prevention, treatment, and recovery regimens were created as standardized “programs” rather than individualized protocols.

The third caveat to the statement on general research findings is that even if research has shown that certain medications, therapies, or recovery support services are likely to be effective, this does not mean that they will be adequate, especially for groups with specific needs. For example, a medication that is effective in blocking the rewarding effects of opioid use will not fully address the multiple, complex problems of those with opioid use disorders, nor address any co-occurring health conditions such as depression or HIV/AIDS.
Recognizing these limitations to the generalizability of research findings, each chapter has a dedicated section on Specific Populations that focuses particularly on age, racial and ethnic subgroups, and individuals with co-occurring mental and physical illnesses. Findings relevant to other important groups (e.g., military veterans; lesbian, gay, bisexual, and transgender [LGBT] populations; those with criminal justice involvement; those in rural areas) are referred to throughout the Report when available.

The Organization of the Report

This Report is divided into Chapters, highlighting the key issues and most important research findings in those topics. The final chapter concludes with recommendations for key stakeholders, including implications for practice and policy.

This Chapter 1 - Introduction and Overview describes the overall rationale for the Report, defines key terms used throughout the Report, introduces the major issues covered in the topical chapters, and describes the organization, format, and the scientific standards that dictated content and emphasis within the Report.

Chapter 2 - The Neurobiology of Substance Use, Misuse, and Addiction reviews brain research on the neurobiological processes that turn casual substance use into a compulsive disorder.

Chapter 3 - Prevention Program and Policies reviews the scientific evidence on preventing substance misuse, substance use-related problems, and substance use disorders.

Chapter 4 - Early Intervention, Treatment, and Management of Substance Use Disorders describes the goals, settings, and stages of treatment, and reviews the effectiveness of the major components of early intervention and treatment approaches, including behavioral therapies, medications, and social services.

Chapter 5 - Recovery: The Many Paths to Wellness discusses perspectives on remission and recovery from substance use disorders and reviews the types and effectiveness of RSS.

Chapter 6 - Health Care Systems and Substance Use Disorders reviews ongoing changes in organization, delivery, and financing of care for substance use disorders in both specialty treatment programs and in mainstream health care settings.

Chapter 7 - Vision for the Future: A Public Health Approach presents a realistic vision for a comprehensive, effective, and humane public health approach to addressing substance misuse and substance use disorders in our country, including actionable recommendations for parents, families, communities, health care organizations, educators, researchers, and policymakers.

The Appendices provide additional detail about the topics covered in this Report. Appendix A - Review Process for Prevention Programs details the review process for the prevention programs included in Chapter 3 and the evidence on these programs; Appendix B - Evidence-Based Prevention Programs and Policies provides detail on scientific evidence grounding the programs and policies discussed in Chapter 3; Appendix C - Resource Guide provides resources specific to those seeking information on preventing and treating substance misuse or substance use disorders; and Appendix D - Important Facts about Alcohol and Drugs contains facts about alcohol and specific drugs, including descriptions, uses and possible health effects, treatment options, and statistics as of 2015.
CHAPTER 2.
THE NEUROBIOLOGY OF SUBSTANCE USE, MISUSE, AND ADDICTION

Chapter 2 Preview
A substantial body of research has accumulated over several decades and transformed our understanding of substance use and its effects on the brain. This knowledge has opened the door to new ways of thinking about prevention and treatment of substance use disorders.

This chapter describes the neurobiological framework underlying substance use and why some people transition from using or misusing alcohol or drugs to a substance use disorder—including its most severe form, addiction. The chapter explains how these substances produce changes in brain structure and function that promote and sustain addiction and contribute to relapse. The chapter also addresses similarities and differences in how the various classes of addictive substances affect the brain and behavior and provides a brief overview of key factors that influence risk for substance use disorders.

An Evolving Understanding of Substance Use Disorders
Scientific breakthroughs have revolutionized the understanding of substance use disorders. For example, severe substance use disorders, commonly called addictions, were once viewed largely as a moral failing or character flaw, but are now understood to be chronic illnesses characterized by clinically significant impairments in health, social function, and voluntary control over substance use. Although the mechanisms may be different, addiction has many features in common with disorders such as diabetes, asthma, and hypertension. All of these disorders are chronic, subject to relapse, and influenced by genetic, developmental, behavioral, social, and environmental factors. In all of these disorders, affected individuals may have difficulty in complying with the prescribed treatment.

This evolving understanding of substance use disorders as medical conditions has had important implications for prevention and treatment. Research demonstrating that addiction is driven by changes in the brain has helped to reduce the negative attitudes associated with substance use disorders and provided support for integrating treatment for substance use disorders into mainstream health care. Moreover, research on the basic neurobiology of addiction has already resulted in several effective
medications for the treatment of alcohol, opioid, and nicotine use disorders, and clinical trials are ongoing to test other potential new treatments.\(^5\)

All addictive substances have powerful effects on the brain. These effects account for the euphoric or intensely pleasurable feelings that people experience during their initial use of alcohol or other substances, and these feelings motivate people to use those substances again and again, despite the risks for significant harms.

As individuals continue to misuse alcohol or other substances, progressive changes, called neuroadaptations, occur in the structure and function of the brain. These neuroadaptations compromise brain function and also drive the transition from controlled, occasional substance use to chronic misuse, which can be difficult to control. Moreover, these brain changes endure long after an individual stops using substances. They may produce continued, periodic craving for the substance that can lead to relapse: More than 60 percent of people treated for a substance use disorder experience relapse within the first year after they are discharged from treatment,\(^4,6\) and a person can remain at increased risk of relapse for many years.\(^7,8\)

However, addiction is not an inevitable consequence of substance use. Whether an individual ever uses alcohol or another substance, and whether that initial use progresses to a substance use disorder of any severity, depends on a number of factors. These include: a person’s genetic makeup and other individual
biological factors; the age when use begins; psychological factors related to a person’s unique history and personality; and environmental factors, such as the availability of drugs, family and peer dynamics, financial resources, cultural norms, exposure to stress, and access to social support. Some of these factors increase risk for substance use, misuse, and use disorders, whereas other factors provide buffers against those risks. Nonetheless, specific combinations of factors can drive the emergence and continuation of substance misuse and the progression to a disorder or an addiction.

Conducting Research on the Neurobiology of Substance Use, Misuse, and Addiction

Until recently, much of our knowledge about the neurobiology of substance use, misuse, and addiction came from the study of laboratory animals. Although no animal model fully reflects the human experience, animal studies let researchers investigate addiction under highly controlled conditions that may not be possible or ethical to replicate in humans. These types of studies have greatly helped to answer questions about how particular genes, developmental processes, and environmental factors, such as stressors, affect substance-taking behavior.

Neurobiology studies in animals have historically focused on what happens in the brain right after taking an addictive substance (this is called the acute impact), but research has shifted to the study of how ongoing, long-term (or chronic) substance use changes the brain. One of the main goals of this research is to understand at the most basic level the mechanisms through which substance use alters brain structure and function and drives the transition from occasional use to misuse, addiction, and relapse.

A growing body of substance use research conducted with humans is complementing the work in animals. For example, human studies have benefited greatly from the use of brain-imaging technologies, such as magnetic resonance imaging (MRI) and positron emission tomography (PET) scans. These technologies allow researchers to “see” inside the living human brain so that they can investigate and characterize the biochemical, functional, and structural changes in the brain that result from alcohol and drug use. The technologies also allow them to understand how differences in brain structure and function may contribute to substance use, misuse, and addiction.

Animal and human studies build on and inform each other, and in combination provide a more complete picture of the neurobiology of addiction. The rest of this chapter weaves together the most compelling data from both types of studies to describe a neurobiological framework for addiction.
A Basic Primer on the Human Brain

To understand how addictive substances affect the brain, it is important to first understand the basic biology of healthy brain function. The brain is an amazingly complex organ that is constantly at work. Within the brain, a mix of chemical and electrical processes controls the body’s most basic functions, like breathing and digestion. These processes also control how people react to the multitudes of sounds, smells, and other sensory stimuli around them, and they organize and direct individuals’ highest thinking and emotive powers so that they can interact with other people, carry out daily activities, and make complex decisions.

The brain is made of an estimated 86 billion nerve cells—called neurons—as well as other cell types. Each neuron has a cell body, an axon, and dendrites (Figure 2.1). The cell body and its nucleus control the neuron’s activities. The axon extends out from the cell body and transmits messages to other neurons. Dendrites branch out from the cell body and receive messages from the axons of other neurons.

Neurons communicate with one another through chemical messengers called neurotransmitters. The neurotransmitters cross a tiny gap, or synapse, between neurons and attach to receptors on the receiving neuron. Some neurotransmitters are inhibitory—they make it less likely that the receiving neuron will carry out some action. Others are excitatory, meaning that they stimulate neuronal function, priming it to send signals to other neurons.

Neurons are organized in clusters that perform specific functions (described as networks or circuits). For example, some networks are involved with thinking, learning, emotions, and memory. Other networks communicate with muscles, stimulating them into action. Still others receive and interpret stimuli from the sensory organs, such as the eyes and ears, or the skin. The addiction cycle disrupts the normal functions of some of these neuronal networks.

Figure 2.1: A Neuron and its Parts
The Primary Brain Regions Involved in Substance Use Disorders

The brain has many regions that are interconnected with one another, forming dynamic networks that are responsible for specific functions, such as attention, self-regulation, perception, language, reward, emotion, and movement, along with many other functions. This chapter focuses on three regions that are the key components of networks that are intimately involved in the development and persistence of substance use disorders: the **basal ganglia**, the **extended amygdala**, and the **prefrontal cortex** (Figure 2.2). The basal ganglia control the rewarding, or pleasurable, effects of substance use and are also responsible for the formation of habitual substance taking. The extended amygdala is involved in stress and the feelings of unease, anxiety, and irritability that typically accompany substance withdrawal. The prefrontal cortex is involved in executive function (i.e., the ability to organize thoughts and activities, prioritize tasks, manage time, and make decisions), including exerting control over substance taking.

These brain areas and their associated networks are not solely involved in substance use disorders. Indeed, these systems are broadly integrated and serve many critical roles in helping humans and other animals survive. For example, when people engage in certain activities, such as consuming food or having sex, chemicals within the basal ganglia produce feelings of pleasure. This reward motivates individuals to continue to engage in these activities, thereby ensuring the survival of the species. Likewise, in the face of danger, activation of the brain’s stress systems within the extended amygdala drives “fight or flight” responses. These responses, too, are critical for survival. As described in more detail below, these and other survival systems are “hijacked” by addictive substances.

**Figure 2.2: Areas of the Human Brain that Are Especially Important in Addiction**
The Basal Ganglia

The basal ganglia are a group of structures located deep within the brain that play an important role in keeping body movements smooth and coordinated. They are also involved in learning routine behaviors and forming habits. Two sub-regions of the basal ganglia are particularly important in substance use disorders:

- The nucleus accumbens, which is involved in motivation and the experience of reward, and
- The dorsal striatum, which is involved in forming habits and other routine behaviors.\(^\text{11}\)

The Extended Amygdala

The extended amygdala and its sub-regions, located beneath the basal ganglia, regulate the brain’s reactions to stress—including behavioral responses like “fight or flight” and negative emotions like unease, anxiety, and irritability. This region also interacts with the hypothalamus, an area of the brain that controls activity of multiple hormone-producing glands, such as the pituitary gland at the base of the brain and the adrenal glands at the top of each kidney. These glands, in turn, control reactions to stress and regulate many other bodily processes.\(^\text{12}\)

The Prefrontal Cortex

The prefrontal cortex is located at the very front of the brain, over the eyes, and is responsible for complex cognitive processes described as “executive function.” Executive function is the ability to organize thoughts and activities, prioritize tasks, manage time, make decisions, and regulate one’s actions, emotions, and impulses.\(^\text{13}\)

The Addiction Cycle

Addiction can be described as a repeating cycle with three stages. Each stage is particularly associated with one of the brain regions described above—basal ganglia, extended amygdala, and prefrontal cortex (Figure 2.3).\(^\text{10}\) This three-stage model draws on decades of human and animal research and provides a useful way to understand the symptoms of addiction, how it can be prevented and treated, and how people can recover from it.\(^\text{14}\) The three stages of addiction are:

- **Binge/Intoxication**, the stage at which an individual consumes an intoxicating substance and experiences its rewarding or pleasurable effects;
- **Withdrawal/Negative Affect**, the stage at which an individual experiences a negative emotional state in the absence of the substance; and
- **Preoccupation/Anticipation**, the stage at which one seeks substances again after a period of abstinence.
The three stages are linked to and feed on each other, but they also involve different brain regions, circuits (or networks), and neurotransmitters and result in specific kinds of changes in the brain. A person may go through this three-stage cycle over the course of weeks or months or progress through it several times in a day. There may be variation in how people progress through the cycle and the intensity with which they experience each of the stages. Nonetheless, the addiction cycle tends to intensify over time, leading to greater physical and psychological harm.\(^\text{10}\)

The following sections describe each of the stages in more detail. But first, it is necessary to explain four behaviors that are central to the addiction cycle: impulsivity, positive reinforcement, negative reinforcement, and compulsivity.

For many people, initial substance use involves an element of impulsivity, or acting without foresight or regard for the consequences. For example, an adolescent may impulsively take a first drink, smoke a cigarette, begin experimenting with marijuana, or succumb to peer pressure to try a party drug. If the experience is pleasurable, this feeling positively reinforces the substance use, making the person more likely to take the substance again.

Another person may take a substance to relieve negative feelings such as stress, anxiety, or depression. In this case, the temporary relief the substance brings from the negative feelings negatively reinforces
substance use, increasing the likelihood that the person will use again. Importantly, positive and negative reinforcement need not be driven solely by the effects of the drugs. Many other environmental and social stimuli can reinforce a behavior. For example, the approval of peers positively reinforces substance use for some people. Likewise, if drinking or using drugs with others provides relief from social isolation, substance use behavior could be negatively reinforced.

The positively reinforcing effects of substances tend to diminish with repeated use. This is called tolerance and may lead to use of the substance in greater amounts and/or more frequently in an attempt to experience the initial level of reinforcement. Eventually, in the absence of the substance, a person may experience negative emotions such as stress, anxiety, or depression, or feel physically ill. This is called withdrawal, which often leads the person to use the substance again to relieve the withdrawal symptoms.

As use becomes an ingrained behavior, impulsivity shifts to compulsivity, and the primary drivers of repeated substance use shift from positive reinforcement (feeling pleasure) to negative reinforcement (feeling relief), as the person seeks to stop the negative feelings and physical illness that accompany withdrawal. Eventually, the person begins taking the substance not to get “high,” but rather to escape the “low” feelings to which, ironically, chronic drug use has contributed. Compulsive substance seeking is a key characteristic of addiction, as is the loss of control over use. Compulsivity helps to explain why many people with addiction experience relapses after attempting to abstain from or reduce use.

The following sections provide more detail about each of the three stages—binge/intoxication, withdrawal/negative affect, and preoccupation/anticipation—and the neurobiological processes underlying them.

### Binge/Intoxication Stage: Basal Ganglia

The binge/intoxication stage of the addiction cycle is the stage at which an individual consumes the substance of choice. This stage heavily involves the basal ganglia (Figure 2.4) and its two key brain sub-regions, the nucleus accumbens and the dorsal striatum. In this stage, substances affect the brain in several ways.
Addictive Substances “Hijack” Brain Reward Systems

All addictive substances produce feelings of pleasure. These “rewarding effects” positively reinforce their use and increase the likelihood of repeated use. The rewarding effects of substances involve activity in the nucleus accumbens, including activation of the brain’s dopamine and opioid signaling system. Many studies have shown that neurons that release dopamine are activated, either directly or indirectly, by all addictive substances, but particularly by stimulants such as cocaine, amphetamines, and nicotine (Figure 2.4). In addition, the brain’s opioid system, which includes naturally occurring opioid molecules (i.e., endorphins, enkephalins, and dynorphins) and three types of opioid receptors (i.e., mu, delta, and kappa), plays a key role in mediating the rewarding effects of other addictive substances, including opioids and alcohol. Activation of the opioid system by these substances stimulates the nucleus accumbens directly or indirectly through the dopamine system. Brain imaging studies in humans show activation of dopamine and opioid neurotransmitters during alcohol and other substance use (including nicotine). Other studies show that antagonists, or inhibitors, of dopamine and opioid receptors can block drug and alcohol seeking in both animals and humans.

**KEY TERMS**

**Antagonist.** A chemical substance that binds to and blocks the activation of certain receptors on cells, preventing a biological response. Naloxone is an example of an opioid receptor antagonist.
Cannabinoids such as delta-9-tetrahydrocannabinol (THC), the primary psychoactive component of marijuana, target the brain’s internal or endogenous cannabinoid system. This system also contributes to reward by affecting the function of dopamine neurons and the release of dopamine in the nucleus accumbens.

**Figure 2.5: Actions of Addictive Substances on the Brain**

Notes: Figure 2.5 is a simplified schematic of converging acute rewarding actions of addictive substances on the nucleus accumbens (NAc). Dopamine neurons that originate in the ventral tegmental area (VTA) project to the NAc. Opioid peptides act both in the VTA and NAc. Despite diverse initial actions, addictive substances produce some common effects on the VTA and NAc. Stimulants directly increase dopamine (DA) transmission in the NAc. Opioids, alcohol, and inhalants (e.g., the solvent toluene) do the same indirectly. Alcohol also activates the release of opioid peptides. Heroin and prescribed opioid pain relievers directly activate opioid peptide receptors. Nicotine activates dopamine neurons in the VTA. Cannabinoids may act in the VTA to activate dopamine neurons but also act on NAc neurons themselves.

Source: Modified with permission from Nestler, (2005).

**Stimuli Associated with Addictive Substances Can Trigger Substance Use**

Activation of the brain’s reward system by alcohol and drugs not only generates the pleasurable feelings associated with those substances, it also ultimately triggers changes in the way a person responds to stimuli associated with the use of those substances. A person learns to associate the stimuli present while using a substance—including people, places, drug paraphernalia, and even internal states, such as mood—with the substance’s rewarding effects. Over time, these stimuli can activate the dopamine system on their own and trigger powerful urges to take the substance. These “wanting” urges are called incentive salience and they can persist even after the rewarding effects of the substance have diminished. As a result, exposure to people, places, or things previously associated with substance use can serve as “triggers” or cues that promote substance seeking and taking, even in people who are in recovery.
Figure 2.6 shows the major neurotransmitter systems involved in the binge/intoxication stage of addiction. In this stage, the neurons in the basal ganglia contribute to the rewarding effects of addictive substances and to incentive salience through the release of dopamine and the brain’s natural opioids.

Figure 2.6: Major Neurotransmitter Systems Implicated in the Neuroadaptations Associated with the Binge/Intoxication Stage of Addiction

Notes: Blue represents the basal ganglia involved in the Binge/Intoxication stage. Red represents the extended amygdala involved in the Negative Affect/Withdrawal stage. Green represents the prefrontal cortex involved in the Preoccupation/Anticipation stage.

Abbreviations: PFC - prefrontal cortex, DS - dorsal striatum, NAc - nucleus accumbens, BNST - bed nucleus of the stria terminalis, CeA - central nucleus of the amygdala, VTA - ventral tegmental area.

Source: Modified with permission from Koob & Volkow, (2010).

Early studies in animals demonstrated how incentive salience works. For example, after researchers repeatedly gave an animal a stimulant drug (e.g., cocaine) along with a previously neutral stimulus, such as a light or a sound, they found that the neutral stimulus by itself caused the animal to engage in drug-seeking behavior, and it also resulted in dopamine release that had previously occurred only in response to the drug. Even more compelling results were seen when scientists recorded the electrical activity of dopamine-transmitting neurons in animals that had been exposed multiple times to a neutral (non-
drug) stimulus followed by a drug. At first, the neurons responded only when they were exposed to the drug. However, over time, the neurons stopped firing in response to the drug and instead fired when they were exposed to the neutral stimulus associated with it. This means that the animals associated the stimulus with the substance and, in anticipation of getting the substance, their brains began releasing dopamine, resulting in a strong motivation to seek the drug. Imaging studies in humans have shown similar results. For example, dopamine is released in the brains of people addicted to cocaine when they are exposed to cues they have come to associate with cocaine. This effect occurs even though cocaine itself causes less dopamine to be released in these individuals compared to those who are not addicted to cocaine (an effect also seen with other substances).

Together, these studies indicate that stimuli associated with addictive drugs can, by themselves, produce drug-like effects on the brain and trigger drug use. These findings help to explain why individuals with substance use disorders who are trying to maintain abstinence are at increased risk of relapse if they continue to have contact with the people they previously used drugs with or the places where they used drugs.

**Substances Stimulate Areas of the Brain Involved in Habit Formation**

A second sub-region of the basal ganglia, the dorsal striatum, is involved in another critical component of the binge/intoxication stage: habit formation. The release of dopamine (along with activation of brain opioid systems) and release of glutamate (an excitatory neurotransmitter) can eventually trigger changes in the dorsal striatum. These changes strengthen substance-seeking and substance-taking habits as addiction progresses, ultimately contributing to compulsive use.

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**In Summary: The Binge/Intoxication Stage and the Basal Ganglia**

The “reward circuitry” of the basal ganglia (i.e., the nucleus accumbens), along with dopamine and naturally occurring opioids, play a key role in the rewarding effects of alcohol and other substances and the ability of stimuli, or cues, associated with that substance use to trigger craving, substance seeking, and use.

As alcohol or substance use progresses, repeated activation of the “habit circuitry” of the basal ganglia (i.e., the dorsal striatum) contributes to the compulsive substance seeking and taking that are associated with addiction.

The involvement of these reward and habit neurocircuits helps explain the intense desire for the substance (craving) and the compulsive substance seeking that occurs when actively or previously addicted individuals are exposed to alcohol and/or drug cues in their surroundings.

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**Withdrawal/Negative Affect Stage: Extended Amygdala**

The withdrawal/negative affect stage of addiction follows the binge/intoxication stage, and, in turn, sets up future rounds of binge/intoxication. During this stage, a person who has been using alcohol or drugs experiences withdrawal symptoms, which include negative emotions and, sometimes, symptoms of physical illness, when they stop taking the substance. Symptoms of withdrawal may occur with all
addictive substances, including marijuana, though they vary in intensity and duration depending on both the type of substance and the severity of use. The negative feelings associated with withdrawal are thought to come from two sources: diminished activation in the reward circuitry of the basal ganglia and activation of the brain’s stress systems in the extended amygdala (Figure 2.7).

Figure 2.7: The Withdrawal/Negative Affect Stage and the Extended Amygdala

![Diagram of brain showing the extended amygdala and basal ganglia]

When used over the long-term, all substances of abuse cause dysfunction in the brain’s dopamine reward system. For example, brain imaging studies in humans with addiction have consistently shown long-lasting decreases in a particular type of dopamine receptor, the D2 receptor, compared with non-addicted individuals (Figure 2.8). Decreases in the activity of the dopamine system have been observed during withdrawal from stimulants, opioids, nicotine, and alcohol. Other studies also show that when an addicted person is given a stimulant, it causes a smaller release of dopamine than when the same dose is given to a person who is not addicted.

These findings suggest that people addicted to substances experience an overall reduction in the sensitivity of the brain’s reward system (especially the brain circuits involving dopamine), both to addictive substances and also to natural reinforcers, such as food and sex. This is because natural reinforcers also depend upon the same reward system and circuits. This impairment explains why those who develop a substance use disorder often do not derive the same level of satisfaction or pleasure from once-pleasurable activities. This general loss of reward sensitivity may also account for the compulsive escalation of substance use as addicted individuals attempt to regain the pleasurable feelings the reward system once provided.
Figure 2.8: Time-Related Decrease in Dopamine Released in the Brain of a Cocaine User

Notes: These fMRI images compare the brain of an individual with a history of cocaine use disorder (middle and right) to the brain of an individual without a history of cocaine use (left). The person who has had a cocaine use disorder has lower levels of the D2 dopamine receptor (depicted in red) in the striatum one month (middle) and four months (right) after stopping cocaine use compared to the non-user. The level of dopamine receptors in the brain of the cocaine user are higher at the 4-month mark (right), but have not returned to the levels observed in the non-user (left).

Source: Modified with permission from Volkow et al., (1993).\(^{29}\)

At the same time, a second process occurs during the withdrawal stage: activation of stress neurotransmitters in the extended amygdala. These stress neurotransmitters include corticotropin-releasing factor (CRF), norepinephrine, and dynorphin (Figure 2.9).\(^ {30}\)

Studies suggest that these neurotransmitters play a key role in the negative feelings associated with withdrawal and in stress-triggered substance use. In animal and human studies, when researchers use special chemicals called antagonists to block activation of the stress neurotransmitter systems, it has the effect of reducing substance intake in response to withdrawal and stress. For example, blocking the activation of stress receptors in the brain reduced alcohol consumption in both alcohol-dependent rats and humans with an alcohol use disorder.\(^ {31}\) Thus, it may be that an additional motivation for drug and alcohol seeking among individuals with substance use disorders is to suppress overactive brain stress systems that produce negative emotions or feelings. Recent research also suggests that neuroadaptations in the endogenous cannabinoid system within the extended amygdala contribute to increased stress reactivity and negative emotional states in addiction.\(^ {32}\)

The desire to remove the negative feelings that accompany withdrawal can be a strong motivator of continued substance use. As noted previously, this motivation is strengthened through negative reinforcement, because taking the substance relieves the negative feelings associated with withdrawal, at least temporarily. Of course, this process is a vicious cycle: Taking drugs or alcohol to lessen the symptoms of withdrawal that occur during a period of abstinence actually causes those symptoms to be even worse the next time a person stops taking the substance, making it even harder to maintain abstinence.
**Figure 2.9: Major Neurotransmitter Systems Implicated in the Neuroadaptations Associated with the Withdrawal/Negative Affect Stage of Addiction**

**Notes:** Not shown is the neurotransmitter norepinephrine which is also activated in the extended amygdala during withdrawal.

**Abbreviations:** PFC - prefrontal cortex, DS - dorsal striatum, NAc - nucleus accumbens, BNST - bed nucleus of the stria terminalis, CeA - central nucleus of the amygdala, VTA - ventral tegmental area.

**Source:** Modified with permission from Koob & Volkow, (2010).\(^{14}\)

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**In Summary: The Withdrawal/Negative Affect Stage and the Extended Amygdala**

This stage of addiction involves a decrease in the function of the brain reward systems and an activation of stress neurotransmitters, such as CRF and dynorphin, in the extended amygdala. Together, these phenomena provide a powerful neurochemical basis for the negative emotional state associated with withdrawal. The drive to alleviate these negative feelings negatively reinforces alcohol or drug use and drives compulsive substance taking.

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**Preoccupation/Anticipation Stage: Prefrontal Cortex**

The preoccupation/anticipation stage of the addiction cycle is the stage in which a person may begin to seek substances again after a period of abstinence. In people with severe substance use disorders, that period of abstinence may be quite short (hours). In this stage, an addicted person becomes preoccupied with using substances again. This is commonly called “craving.” Craving has been difficult to measure in human studies and often does not directly link with relapse.
This stage of addiction involves the brain’s prefrontal cortex (Figure 2.10) the region that controls executive function: the ability to organize thoughts and activities, prioritize tasks, manage time, make decisions, and regulate one’s own actions, emotions, and impulses. Executive function is essential for a person to make appropriate choices about whether or not to use a substance and to override often strong urges to use, especially when the person experiences triggers, such as stimuli associated with that substance (e.g., being at a party where alcohol is served or where people are smoking) or stressful experiences.

Figure 2.10: The Preoccupation/Anticipation Stage and the Prefrontal Cortex

To help explain how the prefrontal cortex is involved in addiction, some scientists divide the functions of this brain region into a “Go system” and an opposing “Stop system.” The Go system helps people make decisions, particularly those that require significant attention and those involved with planning. People also engage the Go system when they begin behaviors that help them achieve goals. Indeed, research shows that when substance-seeking behavior is triggered by substance-associated environmental cues (incentive salience), activity in the Go circuits of the prefrontal cortex increases dramatically. This increased activity stimulates the nucleus accumbens to release glutamate, the main excitatory neurotransmitter in the brain. This release, in turn, promotes incentive salience, which creates a powerful urge to use the substance in the presence of drug-associated cues.

The Go system also engages habit-response systems in the dorsal striatum, and it contributes to the impulsivity associated with substance seeking. Habitual responding can occur automatically and subconsciously, meaning a person may not even be aware that they are engaging in such behaviors. The
neurons in the Go circuits of the prefrontal cortex stimulate the habit systems of the dorsal striatum through connections that use glutamate (Figure 2.11).

**Figure 2.11: Major Neurotransmitter Systems Implicated in the Neuroadaptations Associated with the Preoccupation/Anticipation Stage of Addiction**

Abbreviations: PFC - prefrontal cortex, DS - dorsal striatum, NAc - nucleus accumbens, BNST - bed nucleus of the stria terminalis, CeA - central nucleus of the amygdala, VTA - ventral tegmental area.

Source: Modified with permission from Koob & Volkow, (2010). 14

The Stop system inhibits the activity of the Go system. Especially relevant to its role in addiction, this system controls the dorsal striatum and the nucleus accumbens, the areas of the basal ganglia that are involved in the binge/intoxication stage of addiction. Specifically, the Stop system controls habit responses driven by the dorsal striatum, and scientists think that it plays a role in reducing the ability of substance-associated stimuli to trigger relapse—in other words, it inhibits incentive salience. 34

The Stop system also controls the brain’s stress and emotional systems, and plays an important role in relapse triggered by stressful life events or circumstances. Stress-induced relapse is driven by activation of neurotransmitters such as CRF, dynorphin, and norepinephrine in the extended amygdala. As described above, these neurotransmitters are activated during prolonged abstinence during the withdrawal/negative affect stage of addiction. More recent work in animals also implicates disruptions in the brain’s cannabinoid system, which also regulates the stress systems in the extended amygdala, in relapse. Studies show that lower activity in the Stop component of the prefrontal cortex is associated with increased activity of stress circuitry involving the extended amygdala, and this increased activity drives substance-taking behavior and relapse. 37
Brain imaging studies in people with addiction show disruptions in the function of both the Go and Stop circuits.\textsuperscript{35-37} For example, people with alcohol, cocaine, or opioid use disorders show impairments in executive function, including disruption of decision-making and behavioral inhibition. These executive function deficits parallel changes in the prefrontal cortex and suggest decreased activity in the Stop system and greater reactivity of the Go system in response to substance-related stimuli.

Indeed, a smaller volume of the prefrontal cortex in abstinent, previously addicted individuals predicts a shorter time to relapse.\textsuperscript{38} Studies also show that diminished prefrontal cortex control over the extended amygdala is particularly prominent in humans with post-traumatic stress disorder (PTSD), a condition that is frequently accompanied by drug and alcohol use disorders.\textsuperscript{39} These findings bolster support for the role of the prefrontal cortex-extended amygdala circuit in stress-induced relapse, and suggest that strengthening prefrontal cortex circuits could aid substance use disorder treatment.

In Summary: The Preoccupation/Anticipation Stage and the Prefrontal Cortex

This stage of the addiction cycle is characterized by a disruption of executive function caused by a compromised prefrontal cortex. The activity of the neurotransmitter glutamate is increased, which drives substance use habits associated with craving, and disrupts how dopamine influences the frontal cortex.\textsuperscript{2} The over-activation of the Go system in the prefrontal cortex promotes habit-like substance seeking, and the under-activation of the Stop system of the prefrontal cortex promotes impulsive and compulsive substance seeking.

To recap, addiction involves a three-stage cycle—binge/intoxication, withdrawal/negative affect, and preoccupation/anticipation—that worsens over time and involves dramatic changes in the brain reward, stress, and executive function systems. Progression through this cycle involves three major regions of the brain: the basal ganglia, the extended amygdala, and the prefrontal cortex, as well as multiple neurotransmitter systems (Figure 2.12). The power of addictive substances to produce positive feelings and relieve negative feelings fuels the development of compulsive use of substances. The combination of increased incentive salience (binge/intoxication stage), decreased reward sensitivity and increased stress sensitivity (withdrawal/negative affect stage), and compromised executive function (preoccupation/anticipation stage) provides an often overwhelming drive for substance seeking that can be unrelenting.

Different Classes of Substances Affect the Brain and Behavior in Different Ways

Although the three stages of addiction generally apply to all addictive substances, different substances affect the brain and behavior in different ways during each stage of the addiction cycle. Differences in the pharmacokinetics of various substances determine the duration of their effects on the body and partly account for the differences in their patterns of use. For example, nicotine has a short half-life, which means smokers need to smoke often to maintain the effect. In contrast, THC, the primary psychoactive compound in marijuana, has a much longer half-life. As a result, marijuana smokers do not typically smoke
as frequently as tobacco smokers. Typical patterns of use are described below for the major classes of addictive substances. However, people often use these substances in combination. Additional research is needed to understand how using more than one substance affects the brain and the development and progression of addiction, as well as how use of one substance affects the use of others.

Figure 2.12: The Primary Brain Regions and Neurotransmitter Systems Involved in Each of the Three Stages of the Addiction Cycle

**Opioids**

Opioids attach to opioid receptors in the brain, which leads to a release of dopamine in the nucleus accumbens, causing euphoria (the high), drowsiness, and slowed breathing, as well as reduced pain signaling (which is why they are frequently prescribed as pain relievers). Opioid addiction typically involves a pattern of: (1) intense intoxication, (2) the development of tolerance, (3) escalation in use, and (4) withdrawal signs that include profound negative emotions and physical symptoms, such as

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**KEY TERMS**

**Pharmacokinetics.** What the body does to a drug after it has been taken, including how rapidly the drug is absorbed, broken down, and processed by the body.
bodily discomfort, pain, sweating, and intestinal distress and, in the most severe cases, seizures. As use progresses, the opioid must be taken to avoid the severe negative effects that occur during withdrawal. With repeated exposure to opioids, stimuli associated with the pleasant effects of the substances (e.g., places, persons, moods, and paraphernalia) and with the negative mental and physical effects of withdrawal can trigger intense craving or preoccupation with use.

**Alcohol**

When alcohol is consumed it interacts with several neurotransmitter systems in the brain, including the inhibitory neurotransmitter GABA, glutamate, and others that produce euphoria as well as the sedating, motor impairing, and anxiety-reducing effects of alcohol intoxication. Alcohol addiction often involves a similar pattern as opioid addiction, often characterized by periods of binge or heavy drinking followed by withdrawal. As with opioids, addiction to alcohol is characterized by intense craving that is often driven by negative emotional states, positive emotional states, and stimuli that have been associated with drinking, as well as a severe emotional and physical withdrawal syndrome. Many people with severe alcohol use disorder engage in patterns of binge drinking followed by withdrawal for extended periods of time. Extreme patterns of use may evolve into an opioid-like use pattern in which alcohol must be available at all times to avoid the negative consequences of withdrawal.

**Stimulants**

Stimulants increase the amount of dopamine in the reward circuit (causing the euphoric high) either by directly stimulating the release of dopamine or by temporarily inhibiting the removal of dopamine from synapses, the gaps between neurons. These drugs also boost dopamine levels in brain regions responsible for attention and focus on tasks (which is why stimulants like methylphenidate [Ritalin®] or dextroamphetamine [Adderall®] are often prescribed for people with attention deficit hyperactivity disorder). Stimulants also cause the release of norepinephrine, a neurotransmitter that affects autonomic functions like heart rate, causing a user to feel energized.

Addiction to stimulants, such as cocaine and amphetamines (including methamphetamine), typically follows a pattern that emphasizes the binge/intoxication stage. A person will take the stimulant repeatedly during a concentrated period of time lasting for hours or days (these episodes are called binges). The binge is often followed by a crash, characterized by negative emotions, fatigue, and inactivity. Intense craving then follows, which is driven by environmental cues associated with the availability of the substance, as well as by a person’s internal state, such as their emotions or mood.

**Marijuana (Cannabis)**

Like other drugs, marijuana (also called cannabis) leads to increased dopamine in the basal ganglia, producing the pleasurable high. It also interacts with a wide variety of other systems and circuits in the brain that contain receptors for the body’s natural cannabinoid neurotransmitters. Effects can be different from user to user, but often include distortions in motor coordination and time perception. Cannabis addiction follows a pattern similar to opioids. This pattern involves a significant binge/
intoxication stage characterized by episodes of using the substance to the point of intoxication. Over time, individuals begin to use the substance throughout the day and show chronic intoxication during waking hours. Withdrawal is characterized by negative emotions, irritability, and sleep disturbances. Although the craving associated with cannabis has been less studied than for other substances, it is most likely linked to both environmental and internal states, similar to those of other addictive substances.

**Synthetic Drugs**

Different classes of chemically synthesized (hence the term synthetic) drugs have been developed, each used in different ways and having different effects in the brain. Synthetic cathinones, more commonly known as “bath salts,” target the release of dopamine in a similar manner as the stimulant drugs described above. To a lesser extent, they also activate the serotonin neurotransmitter system, which can affect perception. Synthetic cannabinoids, sometimes referred to as “K2”, “Spice”, or “herbal incense,” somewhat mimic the effects of marijuana but are often much more powerful. Drugs such as MDMA (ecstasy) and lysergic acid diethylamide (LSD) also act on the serotonin neurotransmitter system to produce changes in perception. Fentanyl is a synthetic opioid medication that is used for severe pain management and is considerably more potent than heroin. Prescription fentanyl, as well as illicitly manufactured fentanyl and related synthetic opioids, are often mixed with heroin but are also increasingly used alone or sold on the street as counterfeit pills made to look like prescription opioids or sedatives.

**Factors that Increase Risk for Substance Use, Misuse, and Addiction**

Not all people use substances, and even among those who use them, not all are equally likely to become addicted. Many factors influence the development of substance use disorders, including developmental, environmental, social, and genetic factors, as well as co-occurring mental disorders. Other factors protect people from developing a substance use disorder or addiction. The relative influence of these risk and protective factors varies across individuals and the lifespan. The following sections discuss some of these factors.

**Early Life Experiences**

The experiences a person has early in childhood and in adolescence can set the stage for future substance use and, sometimes, escalation to a substance use disorder or addiction. Early life stressors can include physical, emotional, and sexual abuse; neglect; household instability (such as parental substance use and conflict, mental illness, or incarceration of household members); and poverty. Research suggests that the stress caused by these risk factors may act on the same stress circuits in the brain as addictive substances, which may explain why they increase addiction risk.

Adolescence is a critical period in the vulnerability to substance use and use disorders, because a hallmark of this developmental period is risk taking and experimentation, which for some young people includes trying alcohol, marijuana, or other drugs. In addition, the brain undergoes significant changes during this life stage, making it particularly vulnerable to substance exposure. Importantly,
the frontal cortex—a region in the front part of the brain that includes the prefrontal cortex—does not fully develop until the early to mid-20s, and research shows that heavy drinking and drug use during adolescence affects development of this critical area of the brain.49

About three quarters (74 percent) of 18- to 30-year-olds admitted to treatment programs began using substances at the age of 17 or younger.50 Individuals who start using substances during adolescence often experience more chronic and intensive use, and they are at greater risk of developing a substance use disorder compared with those who begin use at an older age. In other words, the earlier the exposure, the greater the risk.51

Not all adolescents who experiment with alcohol, cigarettes, or other substances go on to develop a substance use disorder, but research suggests that those who do progress to more harmful use may have pre-existing differences in their brains. For example, a brain imaging study of adolescents revealed that the volume of the frontal cortex was smaller in youth who transitioned from no or minimal drinking to heavy drinking over the course of adolescence than it was in youth who did not drink during adolescence.49 Additional research can shed light on how these differences contribute to the progression from use to a disorder, as well as how changes caused by substance use affect brain function and behavior and whether they can be reversed.

Genetic and Molecular Factors

Genetic factors are thought to account for 40 to 70 percent of individual differences in risk for addiction.52,53 Although multiple genes are likely involved in the development of addiction, only a few specific gene variants have been identified that either predispose to or protect against addiction. Some of these variants have been associated with the metabolism of alcohol and nicotine, while others involve receptors and other proteins associated with key neurotransmitters and molecules involved in all parts of the addiction cycle.54 Genes involved in strengthening the connections between neurons and in forming drug memories have also been associated with addiction risk.55,56 Like other chronic health conditions, substance use disorders are influenced by the complex interplay between a person’s genes and environment. Additional research on the mechanisms underlying gene by environment interactions is expected to provide insight into how substance use disorders develop and how they can be prevented and treated.

Use of Multiple Substances and Co-occurring Mental Health Conditions

Many individuals with a substance use disorder also have a mental disorder,57,58 and some have multiple substance use disorders. For example, according to the 2015 National Survey on Drug Use and Health (NSDUH), of the 20.8 million people aged 12 or older who had a substance use disorder during the past year, about 2.7 million (13 percent) had both an alcohol use and an illicit drug use disorder, and 41.2 percent also had a mental illness.59 Particularly striking is the 3- to 4-fold higher rate of tobacco smoking among patients with schizophrenia and the high prevalence of co-existing alcohol use disorder in those meeting criteria for PTSD. It is estimated that 30-60 percent of patients seeking treatment for
alcohol use disorder meet criteria for PTSD, and approximately one third of individuals who have experienced PTSD have also experienced alcohol dependence at some point in their lives.

The reasons why substance use disorders and mental disorders often occur together are not clear, and establishing the relationships between these conditions is difficult. Still, three possible explanations deserve attention. One reason for the overlap may be that having a mental disorder increases vulnerability to substance use disorders because certain substances may, at least temporarily, be able to reduce mental disorder symptoms and thus are particularly negatively reinforcing in these individuals. Second, substance use disorders may increase vulnerability for mental disorders, meaning that the use of certain substances might trigger a mental disorder that otherwise would have not occurred. For example, research suggests that alcohol use increases risk for PTSD by altering the brain's ability to recover from traumatic experiences. Similarly, the use of marijuana, particularly marijuana with a high THC content, might contribute to schizophrenia in those who have specific genetic vulnerabilities.

Third, it is also possible that both substance use disorders and mental disorders are caused by shared, overlapping factors, such as particular genes, neurobiological deficits, and exposure to traumatic or stressful life experiences. As these possibilities are not mutually exclusive, the relationship between substance use disorders and mental disorders may result from a combination of these processes.

Regardless of which one might influence the development of the other, mental and substance use disorders have overlapping symptoms, making diagnosis and treatment planning particularly difficult. For example, people who use methamphetamine for a long time may experience paranoia, hallucinations, and delusions that may be mistaken for symptoms of schizophrenia. And, the psychological symptoms that accompany withdrawal, such as depression and anxiety, may be mistaken as simply part of withdrawal instead of an underlying mood disorder that requires independent treatment in its own right. Given the prevalence of co-occurring substance use and mental disorders, it is critical to continue to advance research on the genetic, neurobiological, and environmental factors that contribute to co-occurring disorders and to develop interventions to prevent and treat them.

Biological Factors Contributing to Population-based Differences in Substance Misuse and Substance Use Disorders

Differences Based on Sex

Some groups of people are also more vulnerable to substance misuse and substance use disorders. For example, men tend to drink more than women and they are at higher risk for alcohol use disorder, although the gender differences in alcohol use are declining. Men are also more likely to have other substance use disorders. However, clinical reports suggest that women who use cocaine, opioids, or alcohol progress from initial use to a disorder at a faster rate than do men (called “telescoping”). Compared with men, women also exhibit greater symptoms of withdrawal from some drugs, such as nicotine. They also report worse negative affects during withdrawal and have higher levels of the stress hormone cortisol.
Sex differences in reaction to addictive substances are not particular to humans. Female rats, in general, learn to self-administer drugs and alcohol more rapidly, escalate their drug taking more quickly, show greater symptoms of withdrawal, and are more likely to resume drug seeking in response to drugs, drug-related cues, or stressors. The one exception is that female rats show less withdrawal symptoms related to alcohol use. Researchers are investigating the neurobiological bases for these differences.

Differences Based on Race and Ethnicity

Research on the neurobiological factors contributing to differential rates of substance use and substance use disorders in particular racial and ethnic groups is much more limited. A study using functional magnetic resonance imaging (fMRI) found that African American smokers showed greater activation of the prefrontal cortex upon exposure to smoking-related cues than did White smokers, an effect that may partly contribute to the lower smoking-cessation success rates observed among African Americans.

Alcohol research with racial and ethnic groups has shown that approximately 36 percent of East Asians carry a gene variant that alters the rate at which members of that racial group metabolize alcohol, causing a buildup of acetaldehyde, a toxic byproduct of alcohol metabolism that produces symptoms such as flushing, nausea, and rapid heartbeat. Although these effects may protect some individuals of East Asian descent from alcohol use disorder, those who drink despite the effects are at increased risk for esophageal and head and neck cancers. Another study found that even low levels of alcohol consumption by Japanese Americans may result in adverse effects on the brain, a finding that may be related to the differences in alcohol metabolism described above. Additional research will help to clarify the interactions between race, ethnicity, and the neuroadaptations that underlie substance misuse and addiction. This work may inform the development of more precise preventive and treatment interventions.

Recommendations for Research

Decades of research demonstrate that chronic substance misuse leads to profound disruptions of brain circuits involved in the experience of pleasure or reward, habit formation, stress, and decision-making. This work has paved the way for the development of a variety of therapies that effectively help people reduce or abstain from alcohol and drug misuse and regain control over their lives. In spite of this progress, our understanding of how substance use affects the brain and behavior is far from complete. Four research areas are specifically emphasized in the text below.

Effects of Substance Use on Brain Circuits and Functions

Continued research is necessary to more thoroughly explain how substance use affects the brain at the molecular, cellular, and circuit levels. Such research has the potential to identify common neurobiological mechanisms underlying substance use disorders, as well as other related mental disorders. This research is expected to reveal new neurobiological targets, leading to new medications and non-pharmacological treatments—such as transcranial magnetic stimulation or vaccines—for the treatment of substance use disorders. A better understanding of the neurobiological mechanisms underlying substance use disorders could also help to inform behavioral interventions. Therefore, basic research that further elucidates the neurobiological framework of substance use disorders and
co-occurring mental disorders, as well as research leading to the development of new medications and other therapeutics to treat the underlying neurobiological mechanisms of substance use disorders should be accelerated.

As with other diseases, individuals vary in the development and progression of substance use disorders. Not only are some people more likely to use and misuse substances than are others and to progress from initial use to addiction differently, individuals also differ in their vulnerability to relapse and in how they respond to treatments. For example, some people with substance use disorders are particularly vulnerable to stress-induced relapse, but others may be more likely to resume substance use after being exposed to drug-related cues. Developing a thorough understanding of how neurobiological differences account for variation among individuals and groups will guide the development of more effective, personalized prevention and treatment interventions. Additionally, determining how neurobiological factors contribute to differences in substance misuse and addiction between women and men and among racial and ethnic groups is critical.

Continued advances in neuroscience research will further enhance our understanding of substance use disorders and accelerate the development of new interventions. Data gathered through the National Institutes of Health’s Adolescent Brain Cognitive Development study, the largest long-term study of cognitive and brain development in children across the United States, is expected to yield unprecedented information about how substance use affects adolescent brain development. The Human Connectome Project and the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative are poised to spur an explosion of knowledge about the structure and function of brain circuits and how the brain affects behavior. Technologies that can alter the activity of dysfunctional circuits are being explored as possible treatments. Moreover, continued advances in genomics, along with President Obama’s Precision Medicine Initiative, a national effort to better understand how individual variability in genes, environment, and lifestyle contribute to disease, are expected to bring us closer to developing individually-tailored preventive and treatment interventions for substance-related conditions.

**Neurobiological Effects of Recovery**

Little is known about the factors that facilitate or inhibit long-term recovery from substance use disorders or how the brain changes over the course of recovery. Developing a better understanding of the recovery process, and the neurobiological mechanisms that enable people to maintain changes in their substance use behavior and promote resilience to relapse, will inform the development of additional effective treatment and recovery support interventions. Therefore, an investigation of the neurobiological processes that underlie recovery and contribute to improvements in social, educational, and professional functioning is necessary.
Adolescence, Brain Change, and Vulnerability to Substance Use Disorders

Although young people are particularly vulnerable to the adverse effects of substance use, not all adolescents who experiment with alcohol or drugs go on to develop a substance use disorder. Prospective, longitudinal studies are needed to investigate whether pre-existing neurobiological factors contribute to adolescent substance use and the development of substance use disorders, how adolescent substance use affects brain structure and function, and whether the changes in brain structure and function that accompany chronic substance use can recover over time. Studies that follow groups of adolescents over time to learn about the developing human brain should be conducted. These studies should investigate how pre-existing neurobiological factors contribute to substance use, misuse, and addiction, and how adolescent substance use affects brain function and behavior.

Neurobiological Effects of Polysubstance Use and Emerging Drug Products

Patterns of alcohol and drug use change over time. New drugs or drug combinations, delivery systems, and routes of administration emerge, and with them new questions for public health. For example, concern is growing that increasing use of marijuana extracts with extremely high amounts of THC could lead to higher rates of addiction among marijuana users. Concerns also are emerging about how new products about which little is known, such as synthetic cannabinoids and synthetic cathinones, affect the brain. Additional research is needed to better understand how such products - as well as emerging addictive substances - affect brain function and behavior, and contribute to addiction.
Chapter 3. Prevention Programs and Policies

Chapter 3 Preview

As discussed in earlier chapters, the misuse of alcohol and drugs and substance use disorders has a huge impact on public health in the United States. In 2014, over 43,000 people died from a drug overdose, more than in any previous year on record and alcohol misuse accounts for about 88,000 deaths in the United States each year (including 1 in 10 total deaths among working-age adults). The yearly economic impact of alcohol misuse and alcohol use disorders is estimated at $249 billion ($2.05 per drink) in 2010 and the impact of illicit drug use and drug use disorders is estimated at $193 billion—figures that include both direct and indirect costs related to crime, health, and lost productivity. Over half of these alcohol-related deaths and three-quarters of the alcohol-related economic costs were due to binge drinking. In addition, alcohol is involved in about 20 percent of the overdose deaths related to prescription opioid pain relievers.

Substance misuse is also associated with a wide range of health and social problems, including heart disease, stroke, high blood pressure, various cancers (e.g., breast cancer), mental disorders, neonatal abstinence syndrome (NAS), driving under the influence (DUI) and other transportation-related injuries, sexual assault and rape, unintended pregnancy, sexually transmitted infections, intentional and unintentional injuries, and property crimes.

Given the impact of substance misuse on public health and the increased risk for long-term medical consequences, including substance use disorders, it is critical to prevent substance misuse from starting and to identify those who have already begun to misuse substances and intervene early. Evidence-based prevention interventions, carried out before the need for treatment, are critical because they can delay early use and stop the progression from use to problematic use or to a substance use disorder (including its severest form, addiction), all of which are associated with costly individual, social, and public health consequences. This chapter will demonstrate that prevention can markedly reduce the burden of disease and related costs. The good news is that there is strong scientific evidence supporting the effectiveness of prevention programs and policies.
This chapter uses the term evidence-based interventions (EBIs) to refer to programs and policies supported by research. The chapter discusses the predictors of substance use initiation early in life and substance misuse throughout the lifespan, called risk factors, as well as factors that can mitigate those risks, called protective factors. The chapter also includes a system of categorizing prevention strategies defined by the Institute of Medicine (IOM). This discussion is followed by a review of rigorous research on substance use initiation and misuse prevention programs that have demonstrated evidence of effectiveness. The chapter continues with a review of the rigorous research on the effectiveness and population impact of prevention policies, most of which are associated with alcohol misuse, as there is limited scientific literature on policy interventions for other drugs. Detailed reviews of these programs and policies are in Appendix B - Evidence-Based Prevention Programs and Policies. The chapter then describes how communities can build the capacity to implement effective programs and policies community wide to prevent substance use and related harms, and concludes with research recommendations.

KEY FINDINGS*

- Well-supported scientific evidence exists for robust predictors (risk and protective factors) of substance use and misuse from birth through adulthood. These predictors show much consistency across gender, race and ethnicity, and income.

- Well-supported scientific evidence demonstrates that a variety of prevention programs and alcohol policies that address these predictors prevent substance initiation, harmful use, and substance use-related problems, and many have been found to be cost-effective. These programs and policies are effective at different stages of the lifespan, from infancy to adulthood, suggesting that it is never too early and never too late to prevent substance misuse and related problems.

- Communities and populations have different levels of risk, protection, and substance use. Well-supported scientific evidence shows that communities are an important organizing force for bringing effective EBIs to scale. To build effective, sustainable prevention across age groups and populations, communities should build cross-sector community coalitions which assess and prioritize local levels of risk and protective factors and substance misuse problems and select and implement evidence-based interventions matched to local priorities.

- Well-supported scientific evidence shows that federal, state, and community-level policies designed to reduce alcohol availability and increase the costs of alcohol have immediate, positive benefits in reducing drinking and binge drinking, as well as the resulting harms from alcohol misuse, such as motor vehicle crashes and fatalities.

- There is well-supported scientific evidence that laws targeting alcohol-impaired driving, such as administrative license revocation and lower per se legal blood alcohol limits for adults and persons under the legal drinking age, have helped cut alcohol-related traffic deaths per 100,000 in half since the early 1980s.

- As yet, insufficient evidence exists of the effects of state policies to reduce inappropriate prescribing of opioid pain medications.

*The Centers for Disease Control and Prevention (CDC) summarizes strength of evidence as: “Well-supported”: when evidence is derived from multiple controlled trials or large-scale population studies; “Supported”: when evidence is derived from rigorous but fewer or smaller trials; and “Promising”: when evidence is derived from a practical or clinical sense and is widely practiced.
Why We Should Care About Prevention

Beginning in the twentieth century, the major illnesses leading to death shifted from infectious diseases, such as tuberculosis and infections in newborns, to noncommunicable diseases, such as heart disease, diabetes, and cancer. This shift was a result of effective public health interventions, such as improved sanitation and immunizations that reduced the rate of infectious diseases, as well as increased rates of unhealthy behaviors and lifestyles, including smoking, poor nutrition, physical inactivity, and substance misuse. In fact, behavioral health problems such as substance use, violence, risky driving, mental health problems, and risky sexual activity are now the leading causes of death for those aged 15 to 24.19

To effectively prevent substance misuse, it is important to understand the nature of the problem, including age of onset. Although people generally start using and misusing substances during adolescence, misuse can begin at any age and can continue to be a problem across the lifespan. As seen in Figure 3.1, likelihood of substance use escalates dramatically across adolescence, peaks in a person’s twenties, and declines thereafter. For example, the highest prevalence of past month binge drinking and marijuana use occurs at ages 21 and 20, respectively. Other drugs follow similar trajectories, although their use typically begins at a later age.20 Early substance misuse, including alcohol misuse, is associated with a greater likelihood of developing a substance use disorder later in life.21,22 Of those who begin using a substance, the percentage of those who develop a substance use disorder, and the rate at which they develop it, varies by substance.

Figure 3.1: Past-Month Alcohol Use, Binge Alcohol Use, and Marijuana Use, by Age: Percentages, 2015 National Survey on Drug and Health (NSDUH)

Note: Binge alcohol use is defined as drinking five or more drinks (for males) or four or more drinks (for females) on the same occasion (i.e., at the same time or within a couple of hours of each other) on at least 1 day in the past 30 days.

Source: Center for Behavioral Health Statistics and Quality, (2016).20
It is important to note that the vast majority of people in the United States who misuse substances do not have substance use disorders. Nonetheless, substance misuse can put individual users and others around them at risk of harm, whether or not they have a disorder. Also, early initiation, substance misuse, and substance use disorders are associated with a variety of negative consequences, including deteriorating relationships, poor school performance, loss of employment, diminished mental health, and increases in sickness and death (e.g., motor vehicle crashes, poisoning, violence, or accidents). It is therefore critical to prevent the full spectrum of substance misuse problems in addition to treating those with substance use disorders.

Preventing or reducing early substance use initiation, substance misuse, and the harms related to misuse requires the implementation of effective programs and policies that address substance misuse across the lifespan. The prevention science reviewed in this chapter demonstrates that effective prevention programs and policies exist, and if implemented well, they can markedly reduce substance misuse and related threats to the health of the population. However, evidence-based programs and policies are underutilized. For example, studies have found that many schools and communities are using prevention programs and strategies that have little or no evidence of effectiveness. In fact, underuse of effective prevention programs and policies was the impetus for the creation of Communities That Care (CTC), a prevention service delivery system that promotes healthy youth development, improves youth outcomes, and reduces substance use and other problem behavior.

At the policy level, research shows that higher alcohol prices reduce alcohol misuse and related harms (e.g., alcohol-related motor vehicle crashes) and taxes are one component of price. As of January 1, 2015, 42 states had a beer excise tax of less than $0.50 per gallon, while only four states had an excise tax more than $1.00 per gallon (Table 3.4).

### Risk and Protective Factors

Longitudinal research has identified predictors of substance use and other behavioral health problems that are targets for preventive interventions. Risk and protective factors influence the likelihood that a person will use a substance and whether they will develop a substance use disorder.

Risk and protective factors become influential at different times during development, and they often relate to physiological changes that occur over the course of development or to factors in a person’s environment—for example, biological transitions such as puberty or social transitions such as attending a new school, parental divorce or military deployment, or graduation. These factors can be influenced by programs and policies at multiple levels, including the federal, state, community, family, school, and individual levels. Targeted programs implemented at the family, school, and individual levels can complement the broader population-level policy interventions, and assist in reducing specific risk factors (Table 3.1) and promoting protective factors (Table 3.2). Although there are exceptions, most
risk and protective factors associated with substance use also predict other problems affecting youth, including delinquency, psychiatric conditions, violence, and school dropout. Therefore, programs and policies addressing those common or overlapping predictors of problems have the potential to simultaneously prevent substance misuse as well as other undesired outcomes.42-44

Some risk and protective factors appear to have consistent effects across cultural and gender groups, although low-income and disadvantaged populations are generally exposed to more risk factors, including risk factors within the environment, and to fewer protective factors than are other groups in the population. However, research has shown that binge drinking is more common among individuals in higher income households as compared to lower income households.45 This has implications for the types of prevention programs and policies that might be most successful with disadvantaged populations. Despite the similarities in many identified risk factors across groups, it is important to examine whether there are subpopulation differences in the exposure of groups to risk factors.

Table 3.1: Risk Factors for Adolescent and Young Adult Substance Use

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Definition</th>
<th>Adolescent Substance Use</th>
<th>Young Adult Substance Use</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Individual/Peer</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early initiation of substance use46,47</td>
<td>Engaging in alcohol or drug use at a young age.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Early and persistent problem behavior48,49</td>
<td>Emotional distress, aggressiveness, and “difficult” temperaments in adolescents.</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Rebelliousness48,50</td>
<td>High tolerance for deviance and rebellious activities.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Favorable attitudes toward substance use51,52</td>
<td>Positive feelings towards alcohol or drug use, low perception of risk.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Peer substance use53-55</td>
<td>Friends and peers who engage in alcohol or drug use.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Genetic predictors56</td>
<td>Genetic susceptibility to alcohol or drug use.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Family</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family management problems (monitoring, rewards, etc.)57-60</td>
<td>Poor management practices, including parents’ failure to set clear expectations for children’s behavior, failure to supervise and monitor children, and excessively severe, harsh, or inconsistent punishment.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Family conflict61-63</td>
<td>Conflict between parents or between parents and children, including abuse or neglect.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Favorable parental attitudes64,65</td>
<td>Parental attitudes that are favorable to drug use and parental approval of drinking and drug use.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Family history of substance misuse66,67</td>
<td>Persistent, progressive, and generalized substance use, misuse, and use disorders by family members.</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
## Risk Factors

<table>
<thead>
<tr>
<th>School</th>
<th>Definition</th>
<th>Adolescent Substance Use</th>
<th>Young Adult Substance Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Academic failure beginning in late elementary school</td>
<td>Poor grades in school.</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Lack of commitment to school</td>
<td>When a young person no longer considers the role of the student as meaningful and rewarding, or lacks investment or commitment to school.</td>
<td>✔️</td>
<td>✔️</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Community</th>
<th>Definition</th>
<th>Adolescent Substance Use</th>
<th>Young Adult Substance Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low cost of alcohol</td>
<td>Low alcohol sales tax, happy hour specials, and other price discounting.</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>High availability of substances</td>
<td>High number of alcohol outlets in a defined geographical area or per a sector of the population.</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Community laws and norms favorable to substance use</td>
<td>Community reinforcement of norms suggesting alcohol and drug use is acceptable for youth, including low tax rates on alcohol or tobacco or community beer tasting events.</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Media portrayal of alcohol use</td>
<td>Exposure to actors using alcohol in movies or television.</td>
<td></td>
<td>✔️</td>
</tr>
<tr>
<td>Low neighborhood attachment</td>
<td>Low level of bonding to the neighborhood.</td>
<td></td>
<td>✔️</td>
</tr>
<tr>
<td>Community disorganization</td>
<td>Living in neighborhoods with high population density, lack of natural surveillance of public places, physical deterioration, and high rates of adult crime.</td>
<td></td>
<td>✔️</td>
</tr>
<tr>
<td>Low socioeconomic status</td>
<td>A parent’s low socioeconomic status, as measured through a combination of education, income, and occupation.</td>
<td></td>
<td>✔️</td>
</tr>
<tr>
<td>Transitions and mobility</td>
<td>Communities with high rates of mobility within or between communities.</td>
<td></td>
<td>✔️</td>
</tr>
</tbody>
</table>

### Table 3.2: Protective Factors for Adolescent and Young Adult Substance Use

<table>
<thead>
<tr>
<th>Protective Factors</th>
<th>Definition</th>
<th>Adolescent Substance Use</th>
<th>Young Adult Substance Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social, emotional, behavioral, cognitive, and moral competence</td>
<td>Interpersonal skills that help youth integrate feelings, thinking, and actions to achieve specific social and interpersonal goals.</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Self-efficacy</td>
<td>An individual’s belief that they can modify, control, or abstain from substance use.</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Spirituality</td>
<td>Belief in a higher being, or involvement in spiritual practices or religious activities.</td>
<td>✔️</td>
<td>✔️</td>
</tr>
</tbody>
</table>
### Protective Factors

<table>
<thead>
<tr>
<th>Protective Factors</th>
<th>Definition</th>
<th>Adolescent Substance Use</th>
<th>Young Adult Substance Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resiliency&lt;sup&gt;58&lt;/sup&gt;</td>
<td>An individual’s capacity for adapting to change and stressful events in healthy and flexible ways.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Family, School, and Community</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opportunities for positive social involvement&lt;sup&gt;93,94&lt;/sup&gt;</td>
<td>Developmentally appropriate opportunities to be meaningfully involved with the family, school, or community.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Recognition for positive behavior&lt;sup&gt;51&lt;/sup&gt;</td>
<td>Parents, teachers, peers and community members providing recognition for effort and accomplishments to motivate individuals to engage in positive behaviors in the future.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Bonding&lt;sup&gt;95,97&lt;/sup&gt;</td>
<td>Attachment and commitment to, and positive communication with, family, schools, and communities.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Marriage or committed relationship&lt;sup&gt;98&lt;/sup&gt;</td>
<td>Married or living with a partner in a committed relationship who does not misuse alcohol or drugs.</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Healthy beliefs and standards for behavior&lt;sup&gt;51,99&lt;/sup&gt;</td>
<td>Family, school, and community norms that communicate clear and consistent expectations about not misusing alcohol and drugs.</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Note: These tables present some of the key risk and protective factors related to adolescent and young adult substance initiation and misuse.

## Types of Prevention Interventions

The IOM has described three categories of prevention interventions: universal, selective, and indicated.<sup>18</sup> Universal interventions are aimed at all members of a given population (for instance, all children of a certain age); selective interventions are aimed at a subgroup determined to be at high-risk for substance use (for instance, justice-involved youth); indicated interventions are targeted to individuals who are already using substances but have not developed a substance use disorder. Communities must choose from these three types of preventive interventions, but research has not yet been able to suggest an optimal mix. Communities may think it is best to direct services only to those with the highest risk and lowest protection or to those already misusing substances.<sup>100</sup> However, a relatively high percentage of substance misuse-related problems come from people at lower risk, because they are a much larger group within the total population than are people at high-risk. This follows what is known as the Prevention Paradox: “a large number of people at a small risk may give rise to more cases of disease than the small number who are at a high risk.”<sup>71</sup> By this logic, providing prevention interventions to everyone (i.e., universal interventions) rather than only to those at highest risk is likely to have greater benefits.<sup>3</sup>

One advantage of a properly implemented universal prevention intervention is that it is likely to reach most or all of the population (for example, school-based interventions are likely to reach all students). Targeted (selective and indicated) approaches are likely to miss a large percentage of their targets, but
they provide more intensive services to those who are reached. Because the best mix of interventions has not yet been determined, it is prudent for communities to provide a mix of universal, selective, and indicated preventive interventions.

**Universal Prevention Interventions**

Universal interventions attempt to reduce specific health problems across all people in a particular population by reducing a variety of risk factors and promoting a broad range of protective factors. Examples of universal interventions include policies—such as the setting of a minimum legal drinking age (MLDA) or reducing the availability of substances in a community—and school-based programs that promote social and emotional competencies to reduce stress, express emotion appropriately, and resist negative social influences. Because they focus on the entire population, universal interventions tend to have the greatest overall impact on substance misuse and related harms relative to interventions focused on individuals alone.¹⁸

**Selective Interventions**

Selective interventions are delivered to particular communities, families, or children who, due to their exposure to risk factors, are at increased risk of substance misuse problems. Target audiences for selective interventions may include families living in poverty, the children of depressed or substance-using parents, or children who have difficulties with social skills. Selective interventions typically deliver specialized prevention services to individuals with the goal of reducing identified risk factors, increasing protective factors, or both. Selective programs focus effort and resources on interventions that are intentionally designed for a specific high-risk group.¹⁰¹ Selective programs have an advantage in that they focus effort and resources on those who are at higher risk for developing behavioral health problems. In so doing, they allow planners to create interventions that are more specifically designed for that audience. However, they are typically not population-based and therefore, compared to population-level interventions, they have more limited reach.

**Indicated Interventions**

Indicated prevention interventions are directed to those who are already involved in a risky behavior, such as substance misuse, or are beginning to have problems, but who have not yet developed a substance use disorder. Such programs are often intensive and expensive but may still be cost-effective, given the high likelihood of an ensuing expensive disorder or other costly negative consequences in the future.¹⁰²

**Evidence-based Prevention Programs**

This section identifies universal, selective, and indicated prevention programs that have been shown to successfully reduce the number of people who start using alcohol or drugs or who progress to harmful use. Inclusion of the programs here was based on an extensive review of published research studies. Of the 600 programs considered, 42 met criteria to be included in this Report. Studies on programs that
included people who already had a substance use or related disorder were excluded. The review used standard literature search procedures which are summarized in detail in Appendix A - Review Process for Prevention Programs.

The vast majority of prevention studies have been conducted on children, adolescents, and young adults, but prevention trials of older populations meeting the criteria were also included. Programs that met the criteria are categorized as follows: Programs for children younger than age 10 (or their families); programs for adolescents aged 10 to 18; programs for individuals ages 18 years and older; and programs coordinated by community coalitions. Due to the number of programs that have proven effective, the following sections highlight just a few of the effective programs from the more comprehensive tables in Appendix B - Evidence-Based Prevention Programs and Policies, which describe the outcomes of all the effective prevention programs. Representative programs highlighted here were chosen for each age group, domain, and level of intervention, and with attention to coverage of specific populations and culturally based population subgroups. It is important to note that screening and brief intervention (SBI) and electronic SBI for reducing alcohol misuse have been recognized as effective strategies for identifying and reducing substance misuse among adults, but these are discussed in detail in Chapter 4 - Early Intervention, Treatment, and Management of Substance Use Disorders as effective early intervention strategies.103-106

Interventions for Youth Aged 0 to 10

Few substance use prevention programs for children under the age of 10 have been evaluated for their effect on substance misuse and related problems. Such studies are rare because they require expensive long-term follow-up tracking and assessment to demonstrate an impact on substance initiation or misuse years or decades into the future. Consistent with general strategies to increase protective factors and decrease risk factors, universal prevention interventions for infants, preschoolers, and elementary school students have primarily focused on building healthy parent-child relationships, decreasing aggressive behavior, and building children’s social, emotional, and cognitive competence for the transition to school. Both universal and selective programs have shown reductions in child aggression and improvements in social competence and relations with peers and adults (generally predictive of favorable longer-term outcomes), but only a few have studied longer-term effects on substance use.107,108 Select programs showing positive effects are described below.

Nurse-Family Partnership

Only one program that focused on children younger than age 5—the Nurse-Family Partnership—has shown significant reductions in the use of alcohol in the teen years compared with those who did not receive the intervention.109,110 This selective prevention program uses trained nurses to provide an intensive home visitation intervention for at-risk, first-time mothers during pregnancy. This intervention provides ongoing education and support to improve pregnancy outcomes and infant health and development while strengthening parenting skills.
The Good Behavior Game and Classroom-Centered Intervention

One universal elementary school-based prevention program has shown long-term preventive effects on substance use among a high-risk subgroup, males with high levels of aggression. The Good Behavior Game is a classroom behavior management program that rewards children for acting appropriately during instructional times through a team-based award system. Implemented by Grade 1 and 2 teachers, this program significantly lowered rates of alcohol, other substance use, and substance use disorders when the children reached the ages of 19 to 21.\textsuperscript{111} The Classroom-Centered Intervention, which combined the Good Behavior Game with additional models of teacher instruction, also reduced rates of cocaine and heroin use in middle and high school, but it had no preventive effects on alcohol or marijuana initiation.\textsuperscript{112,113}

Raising Healthy Children

A number of multicomponent, universal, elementary school programs involving both schools and parents are effective in preventing substance misuse.\textsuperscript{114,115} One example is the Raising Healthy Children program (also known as Seattle Social Development Project) which targets Grades 1 through 6 and combines social and emotional learning, classroom instruction and management training for teachers, and training for parents conducted by school-home coordinators, who work with the children in school and the parents at home, focusing on in-home problem solving and similar workshops. Studies of this program showed reductions in heavy drinking at age 18 (6 years after the intervention)\textsuperscript{114,115} and in rates of alcohol and marijuana use.\textsuperscript{115}

The Fast Track Program

Two multicomponent selective and universal prevention programs were effective. An example is the Fast Track Program, an intensive 10-year intervention that was implemented in four United States locations for children with high rates of aggression in Grade 1. The program includes universal and selective components to improve social competence at school, early reading tutoring, and home visits as well as parenting support groups through Grade 10. Follow-up at age 25 showed that individuals who received the intervention as adolescents decreased alcohol and other substance misuse, with the exception of marijuana use.\textsuperscript{116}

Interventions for Adolescents Aged 10 to 18

A variety of universal interventions focused on youth aged 10 to 18 have been shown to affect either the initiation or escalation of substance use.\textsuperscript{117-124} In general, school-based programs share a focus on building social, emotional, cognitive, and substance refusal skills and provide children accurate information on rates and amounts of peer substance use.\textsuperscript{119,120,124}

School-based Programs

One well-researched and widely used program is LifeSkills Training, a school-based program delivered over 3 years.\textsuperscript{117} Research has shown that this training delayed early use of alcohol, tobacco, and other substances and reduced rates of use of all substances up to 5 years after the intervention ended. A multicultural model, keepin’it REAL, uses student-developed videos and narratives and has shown...
positive effects on substance use among Mexican American youth in the Southwestern United States. Another example is Project Toward No Drug Abuse, which focuses on youth who are at high risk for drug use and violence. It is designed for youth who are attending alternative high schools but can be delivered in traditional high schools as well. The twelve 40-minute interactive sessions have shown positive effects on alcohol and drug misuse.

Family-based Programs

A number of family-focused, universal prevention interventions show substantial preventive effects on substance use. For example, Strengthening Families Program: For Parents and Youth 10–14 (SFP) is a widely used seven-session universal, family-focused program that enhances parenting skills—specifically nurturing, setting limits, and communicating—as well as adolescent substance refusal skills. Across multiple studies conducted in rural United States communities, SFP showed reductions in tobacco, alcohol, and drug use up to 9 years after the intervention (i.e., to age 21) compared with youth who were not assigned to the SFP. SFP also shows reductions in prescription drug misuse up to 13 years after the intervention (i.e., to age 25), both on its own and when paired with effective skills-focused school-based prevention. Strong African American Families, a cultural adaptation of SFP, shows reductions in early initiation and rate of alcohol use for Black or African American rural youth.

Three selective programs focus on interventions with families. An example is Familias Unidas, a family-based intervention for Hispanic or Latino youth. It includes both multi-parent groups (eight weekly 2-hour sessions) and four to ten 1-hour individual family visits and has been shown to lower substance use or delay the start of substance use among adolescents.

A number of selective and indicated interventions successfully prevent substance misuse when delivered to youth aged 10 to 18. Most of these interventions target students who show early aggressive behavior, delinquency, or early substance use, as these are risk factors for later substance misuse, and some offer both a youth component in the classroom setting and a parent component. An example is Coping Power, a 16-month program for children in Grades 5 and 6 who were identified with early aggression. The program, which is designed to build problem-solving and self-regulation skills, has both a parent and a child component and reduces early substance use.

Internet-based Programs

A number of computer- and Internet-based interventions also show positive effects on preventing substance use. An example is I Hear What You’re Saying, which involves nine 45-minute sessions to improve communication, establish family rules, and manage conflict. Specifically focused on mothers and daughters, follow-up results showed lower rates of substance use in an ethnically diverse sample. Additionally, Project Chill, a brief intervention (30 to 45 minutes) delivered in primary care settings through either a computer or a therapist, reduced the number of youth who started using marijuana.
Programs for Young Adults

Young adulthood is a key developmental period, when individuals are exposed to new social contexts with greater freedom and less social control than they experienced during their high school years. Social roles are changing at the same time that social safety net supports are weakening. In addition, many young adults are undergoing transitions, such as leaving home, leaving the compulsory educational system, beginning college, entering the workforce, and forming families. As a result of all these forces, young adulthood is typically associated with increases in substance use, misuse, and misuse-related consequences.

Numerous studies have examined the effectiveness of brief alcohol interventions for adolescents and young adults. One review examined 185 such experimental studies among adolescents aged 11 to 18 and adults aged 19 to 30. Overall, brief alcohol interventions were associated with significant reductions in alcohol consumption and alcohol-related problems in both adults and adolescents, and in some studies, effects persisted up to one year. The United States Preventive Services Task Force has recommended screening and brief intervention for reducing alcohol misuse among adults, as discussed in Chapter 4 - Early Intervention, Treatment, and Management Of Substance Use Disorders, and the American Academy of Pediatrics recommends that screening and brief interventions for alcohol misuse or use disorders be implemented for adolescent patients as well.

Programs for College Students

Many interventions have been developed to reduce alcohol and marijuana misuse among college students. Several literature reviews of alcohol screening and brief interventions in this population have reported that these interventions reduce college student drinking and several other interventions for college students have shown longer term reductions in substance misuse. One analysis reviewed 41 studies with 62 individual or group interventions and found that recipients of interventions experienced reduced alcohol use and fewer alcohol related problems up to four years post intervention. Effective intervention components were personalized feedback, protective strategies to moderate drinking, setting alcohol-related goals, and challenging alcohol expectancies. Interventions with four or more components were most effective. Two example interventions for college students are described below.

*Brief Alcohol Screening and Intervention for College Students (BASICS)* is an example of a brief motivational intervention for which results have been positive. BASICS is designed to help students reduce alcohol misuse and the negative consequences of their drinking. It consists of two 1-hour interviews, with a brief online assessment after the first session. The first interview gathers information about alcohol consumption patterns and personal beliefs about alcohol, while providing instructions for self-monitoring drinking between sessions. The second interview uses data from the online assessment to develop personalized, normative feedback that reviews negative consequences and risk factors, clarifies perceived risks and benefits of drinking, and provides options for reducing alcohol use and its consequences. Follow-up studies of students who used BASICS have shown reductions in drinking quantity in the general college population, among fraternity members, with heavy drinkers who volunteered to use BASICS, and among those who were mandated to engage in the program from college disciplinary bodies.
A second intervention, the *Parent Handbook*, focuses on teaching parents how and when to intervene during the critical time between high school graduation and college entry to disrupt the escalation of heavy drinking during the first year of college. The *Parent Handbook* is distributed during the summer before college, and parents receive a booster call to encourage them to read the materials. Research has found that the timing for the *Parent Handbook* is critical. If parents received it during the summer before college, it reduced the odds of students becoming heavy drinkers, but this intervention was not effective if used after the transition to college. One study showed the combination of BASICS, and the *Parent Handbook* significantly reduced alcohol consumption among incoming college students who showed heavy rates of high school drinking.

Many other interventions have been developed for this population that have not shown effects beyond 3 or 6 months after the intervention, and most positive effects are not maintained by 12-month follow-up. For example, even though brief motivational interviewing (BMI) interventions have appeared promising, a recent analysis of 17 randomized trials demonstrated little effectiveness among college-aged individuals.

### A Resource: The National Institute on Alcohol Abuse and Alcoholism’s (NIAAA’s) CollegeAIM: Alcohol Intervention Matrix

In an effort to inform colleges and universities of the rapidly growing evidence base of programs and policies that can reduce harmful and underage drinking and related harms by college students, NIAAA has published *CollegeAIM-the College Alcohol Intervention Matrix*. 

*CollegeAIM* reviews nearly 60 interventions, including both individual-level strategies and environmental-level policy strategies. The strategies are ranked by effectiveness (higher, moderate, lower, not effective, and too few studies to evaluate). Implementation costs (lower, mid-range, and higher) and implementation barriers (higher, moderate, and lower) are also ranked, as is public health reach (broad or focused).

### Programs in Adult Workplaces

Two programs met this *Report’s* criteria for workplace or clinic-based prevention programs; others have not shown significant preventive effects longer than 6 months. The successful programs, *Team Awareness* and *Team Resilience*, were delivered in three 2-hour sessions to restaurant workers and led to decreases in heavy drinking and work-related problems. These programs reached approximately 30,000 workers in diverse settings, including military, tribal, and government settings, and with ex-offenders, young restaurant workers, and more.

### Programs for Older Adults

Only two studies showed preventive effects on alcohol use in older adults. One is *Project Share*, which showed reductions in heavy drinking among those aged 60 and older. *Project Share* provided personalized feedback to at-risk older drinkers, which included a personalized patient report, discussion with a physician, and three phone calls from a health educator. A second study, the *Computerized Alcohol-Related Problems Survey* (CARPS) assessed personalized reports of drinking risks and
benefits accompanied with education for physicians and patients aged 65 and older. The study found a significant decrease in alcohol misuse, including reductions in the quantity and frequency that older individuals reported drinking.\(^{175}\)

## Economics of Prevention

The Washington State Institute for Public Policy developed a standardized model using scientifically rigorous standards to estimate the costs and benefits associated with various prevention programs. Benefit-per-dollar cost ratios for EBIs ranged from small returns per dollar invested to more than $64 for every dollar invested. These estimates are illustrated below in Table 3.3.

### Table 3.3: Cost-Benefit of EBIs Reviewed by the Washington State Institute for Public Policy, 2016

<table>
<thead>
<tr>
<th>Program</th>
<th>Benefit per Dollar Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nurse-Family Partnership</td>
<td>$1.61</td>
</tr>
<tr>
<td>Raising Healthy Children/SSDP</td>
<td>$4.27</td>
</tr>
<tr>
<td>Good Behavior Game</td>
<td>$64.18</td>
</tr>
<tr>
<td>LifeSkills Training</td>
<td>$17.25</td>
</tr>
<tr>
<td>keepin' it REAL</td>
<td>$11.79</td>
</tr>
<tr>
<td>Strengthening Families Program 10-14</td>
<td>$5.00</td>
</tr>
<tr>
<td>Guiding Good Choices</td>
<td>$2.69</td>
</tr>
<tr>
<td>Positive Family Support/ Family Check Up</td>
<td>$0.62</td>
</tr>
<tr>
<td>Project Towards No Drug Abuse</td>
<td>$6.54</td>
</tr>
<tr>
<td>BASICS</td>
<td>$17.61</td>
</tr>
</tbody>
</table>

*Cost estimates are per participant, based on 2015 United States dollars.

Note: This is a general indication of the potential health and social value of EBIs. It is not possible to estimate specific cost-benefit for every EBI due to challenges in calculating accurate intervention effect sizes, the failure to document costs, the variation of methods used, and few mandates or incentives to complete this research. Reaching a consensus on standards for cost-benefit analyses and making them a routine part of prevention program evaluation could help policymakers choose EBIs that both prevent substance misuse and ensure that investments return benefits over the life course.

Source: Washington State Institute for Public Policy, (2016).\(^{176}\)

## Evidence-based Community Coalition-based Prevention Models

Community-based prevention programs can be effective in helping to address major challenges raised by substance misuse and its consequences. Such programs are often coordinated by local community coalitions composed of representatives from multiple community sectors or organizations (e.g., government, law enforcement, health, education) within a community, as well as private citizens.
These coalitions work to change community-level risk and protective factors and achieve community-wide reductions in substance use by planning and implementing one or more prevention strategies in multiple sectors simultaneously, with the goal of reaching as many members of the community as possible with accurate, consistent messages. For example, interventions may be implemented in family, educational, workplace, health care, law enforcement, and other settings, and they may involve policy interventions and publicly funded social and traditional media campaigns.28,74,177-179

A common feature of successful community programs is their reliance on local coalitions to select effective interventions and implement them with fidelity. An important requirement is that coalitions receive proactive training and technical assistance on prevention science and the use of EBIs and that they have clear goals and guidelines. Technical assistance can be provided by independent organizations such as Community Anti-Drug Coalitions of America (CADCA), academic institutions, the program developers, or others with expertise in the substance misuse prevention field. Three examples of effective community-based coalition models are provided below.

Communities That Care

Communities That Care (CTC) creates a broad-based community coalition to assess and prioritize risk and protective factors and substance use rates, using a school survey of all students in Grades 6, 8, 10, and 12. The coalition then chooses and implements EBIs that address their chosen priorities. CTC was tested in a 24-community trial, where 12 communities were randomly assigned to receive the CTC intervention.

Among a panel of students in Grade 5 who were enrolled in the study before the intervention, those in the CTC communities who were compared to the prevention as usual communities had lower rates of alcohol and tobacco initiation at Grades 10 and 12.26,180-182

PROmoting School-community-university Partnerships to Enhance Resilience

The PROmoting School-community-university Partnerships to Enhance Resilience (PROSPER) delivery system focuses on community-based collaboration and capacity building that links the land-grant university Cooperative Extension System with the public school system. Local teams select and implement family-focused EBIs in Grade 6 and a school-based EBI in Grade 7. PROSPER has shown reductions through Grade 12 in marijuana, methamphetamine, and inhalant use, and lifetime prescription opioid misuse and prescription drug misuse. Analysis showed greater intervention benefits for youth at higher versus lower risk for most substances.183,184

**KEY TERMS**

**Prescription drug misuse.** Use of a drug in any way a doctor did not direct an individual to use it.
Communities That Care - 24 Community Randomized Trials in Colorado, Illinois, Kansas, Maine, Oregon, Utah, and Washington

Agency or Organization:
University of Washington Center for Communities That Care

Purpose:
This evidence-based system provides communities with strategic consultation, training and research-based tools for prevention planning. The CTC system engages entire communities (e.g. youth, parents, elected officials, law enforcement, schools, businesses, etc.) and is tailored to the risks and needs of each defined community population.

Goals:
1. Promote positive development and healthy behaviors for all children and youth.
2. Prevent problem behaviors, including substance use, delinquency, teen pregnancy, school drop-out, and violence.

Outcomes:
- Following a panel of over 4,000 young people in 24 CTC communities from Grades 5 to 8, researchers found that compared to control communities not using the CTC model, youth in the CTC communities were:
  - 33 percent less likely to begin smoking;
  - 32 percent less likely to begin using alcohol;
  - 33 percent less likely to begin using smokeless tobacco; and
  - 25 percent less likely to initiate delinquent behavior (itself a risk factor for future substance use).

Communities Mobilizing for Change on Alcohol
Community coalition-driven environmental models attempt to reduce substance use by changing the macro-level physical, social, and economic risk and protective factors that influence these behaviors. Most research on environmental interventions has focused on alcohol misuse and related problems, including DUI, injuries, and alcohol use by minors.\(^{185-187}\) For example, Communities Mobilizing for Change on Alcohol (CMCA) implemented coalition-led policy changes aimed at reducing youth access to alcohol, including training for alcohol retailers to reduce sales to minors, increased enforcement of underage drinking laws, measures to reduce availability of alcohol at community events, and media campaigns emphasizing that underage drinking is not acceptable.\(^{188,189}\) In a randomized trial comparing seven communities in Minnesota and Wisconsin using CMCA with eight communities in states not implementing CMCA, significant reductions in alcohol-related problem behaviors were shown among young adults aged 18 to 20 from the beginning of the initiative to 2.5
years after coalition activities began. The proportion of young adults aged 19 to 20 who reported providing alcohol to other minors declined by 17 percent,\textsuperscript{188} and arrests for DUI decreased more for this age group in the intervention compared to the control sites.\textsuperscript{189}

**Evidence-based Prevention Policies**

This section primarily discusses the evidence of effectiveness for policies to reduce alcohol misuse, as well as the more limited body of scientific literature on the effectiveness of policies to prevent the misuse of prescription medications, including pain relievers, tranquilizers, stimulants, and sedatives.

**Policies to Reduce Alcohol Misuse and Related Problems**

Research has shown that policies focused on reducing alcohol misuse for the general population can effectively reduce alcohol consumption among adults as well as youth, and they can reduce alcohol-related problems including alcohol-impaired driving.\textsuperscript{190,191} In addition to discussing a number of effective population-level alcohol policies, this section will also describe policies designed specifically to reduce drinking and driving and underage drinking.

**Price and Tax Policies**

Evidence indicates that higher prices on alcoholic beverages are associated with reductions in alcohol consumption and alcohol-related problems, including alcohol-impaired driving. Several systematic reviews have linked higher alcohol taxes and prices with reduction in alcohol misuse, including both underage and binge drinking.\textsuperscript{20,21,72,192-197} One 2009 review examined 1,003 separate estimates from 112 studies.\textsuperscript{72} The authors concluded, “We know of no other prevention intervention to reduce drinking that has the numbers of studies and consistency of effects seen in the literature on alcohol taxes and prices.” Similarly, a 2010 review of 73 taxation studies found “consistent evidence that higher alcohol prices and alcohol taxes are associated with reductions in both alcohol misuse and related, subsequent harms.”\textsuperscript{73} For example, a study found that the price elasticity of binge drinking among individuals aged 18 to 21 was -0.95 for men and -3.54 for women, meaning that a 10.0 percent increase in the price of alcohol is expected to decrease binge drinking by 9.5 percent among men and 35.4 percent among women in that age group.\textsuperscript{198}

The effectiveness of increasing alcohol taxes as a strategy for reducing alcohol misuse and related problems has also been acknowledged outside the United States.\textsuperscript{28} For example, a 2009 World Health Organization (WHO) review stated that “when other factors are held constant, such as income and the price of other goods, a rise in alcohol prices leads to less alcohol consumption” and “[p]olicies that increase alcohol prices delay the time when young people start to drink, slow their progression towards drinking larger amounts, and reduce their heavy drinking and the volume of alcohol drunk on each occasion.”\textsuperscript{192} Additionally, studies have found that increasing alcohol taxes is not only cost effective but can result in a net cost savings (i.e., the savings outweigh the costs of the intervention).
Policies that Affect Access to and Availability of Alcohol

Policies Affecting Alcohol Outlet Density
Research suggests that an increase in the number of retail alcohol outlets in an area—called higher alcohol outlet density—is associated with an increase in alcohol-related problems in that area, such as violence, crime, and injuries.\(^{177,199,200}\) Four longitudinal studies of communities that reduced the number of alcohol outlets showed consistent and significant reductions in alcohol-related crimes, relative to comparison communities that had not reduced alcohol outlet density.\(^{199,201-203}\) Although no studies have explicitly analyzed the cost-benefit ratio of this intervention, research suggests that the costs of limiting the number of alcohol outlets is expected to be much smaller than the societal costs of alcohol misuse.\(^{177}\)

Commercial Host (Dram Shop) Liability Policies
Commercial host (dram shop) liability allows alcohol retailers—such as the owner or server(s) at a bar, restaurant, or other retail alcohol outlet—to be held legally liable for harms resulting from illegal beverage service to intoxicated or underage customers.\(^{204}\) In a systematic review, 11 studies assessed the association between dram shop laws and alcohol-related health outcomes.\(^{205}\) The review found a median reduction of 6.4 percent (range was 3.7 percent to 11.3 percent) in alcohol-related motor vehicle fatalities associated with these policies. Two studies on the effects of these laws did not find reductions in binge drinking.

Policies to Reduce Days and Hours of Alcohol Sales
A review of 11 studies of changing days of sale (both at on-premise alcohol outlets such as restaurants and bars, and off-premise outlets such as grocery, liquor, and convenience stores) indicated that increasing the number of days alcohol could be sold was associated with increases in alcohol misuse and alcohol-related harms, while reducing days alcohol is sold was associated with decreases in alcohol-related harms.\(^{206}\) Similarly, a review of 10 studies (none conducted in the United States) found that increasing hours of sale by two or more hours increased alcohol-related harms, while policies decreasing hours of sale by at least two hours reduced alcohol-related harms.\(^{207}\) One study found that lifting a ban on Sunday sales of alcohol led to an estimated 41.6 percent increase in alcohol-related fatalities on Sundays during the period from 1995 to 2000, equating to an additional cost of more than $6 million in medical care and lost productivity per year in one state.\(^{208}\) Banning sales of alcohol on Sundays has been recognized as a cost-effective strategy.

State Policies to Privatize Alcohol Sales
The privatization of alcohol sales involves changing from direct governmental control over the retail sales of one or more types of alcohol, and allowing private, commercial entities to obtain alcohol licenses, typically to sell liquor in convenience, grocery, or other off-premise locations. A systematic review of studies evaluating the impact of privatizing retail alcohol sales found that such policies increased per capita alcohol sales in privatized states by a median of 44.4 percent. Studies show that per capita alcohol sales is known to be a proxy for alcohol misuse.\(^{209,210}\)

Policies to Reduce Drinking and Driving
Since the early 1980s, alcohol-related traffic deaths in the United States have been cut by more than half (Figure 3.2). It has been estimated that reductions in driving after drinking prevented more than 300,000
deaths during this time period. In fact, declines in traffic deaths due to reductions in drinking and driving have exceeded declines from the combined effects of increased use of seat belts, airbags, and motorcycle and bicycle helmets. From 1982 to 2013, alcohol-related traffic deaths decreased by 67 percent, whereas non-alcohol-related traffic deaths decreased by only 14 percent.

Several policies and law enforcement approaches have been found to reduce rates of drinking and driving and related traffic crashes, injuries, and deaths within the general population, among both youth and adults. These DUI policies and enforcement approaches create deterrence by increasing the public’s awareness of the consequences of drinking and driving, including the possibility of arrest. Some of these strategies include:

- 0.08 percent criminal per se legal blood alcohol content (BAC) limits, meaning that no further evidence of intoxication beyond a BAC of 0.08 percent is needed for a DUI case; and
- Sobriety checkpoints.

Figure 3.2: Alcohol- Versus Non-alcohol-related Traffic Deaths, Rate per 100,000, All Ages, United States, 1982-2013
Other proven DUI prevention strategies fall under the rubric of indicated interventions as they target drivers who have been convicted of DUI to reduce recidivism:223

- Lower legal blood alcohol limits for people convicted of DUI;217,223
- Mandatory ignition interlock laws for all convicted offenders, including first offenders;223,225,226
- Mandatory assessment and treatment of persons convicted of DUI;223
- DUI courts;223
- Continuous 24/7 alcohol monitoring of persons with one or multiple DUI charges;223 and
- Vehicle impoundment or immobilization.223

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### The Implications of Drinking-Oriented and Driving-Oriented Policies to Reduce Harms

An examination of state-level data on 29 alcohol control policies in all 50 states from 2001-2009227 divided those policies into two mutually exclusive groups: (1) drinking-oriented policies, intended to regulate alcohol production, sales, and consumption, raise alcohol taxes, and prevent sales to minors; and (2) driving-oriented policies, which are intended to prevent an already intoxicated person from driving. State data on impaired driving from more than 12 million adults during the even years of 2002 through 2010 were evaluated, and four results were reported, two of which are presented here:

- **First**, the review found that drinking-oriented policies were slightly more effective in reducing impaired driving than driving-oriented policies, though both types of policy changes were independently associated with lower levels of impaired driving.

- **Second**, drinking-oriented policies appeared to exert their effects by reducing binge drinking, which in turn was associated with a lower likelihood of impaired driving. The authors concluded that most states may have a greater opportunity for adopting and aggressively implementing drinking-oriented policies to reduce overall harms, although there is a need to strengthen driving-oriented policies as well.

Overall, these findings support the importance of implementing a comprehensive range of alcohol policies to effectively reduce alcohol misuse and related harms, including strengthening both drinking-oriented policies and driving-oriented policies.

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### Policies to Reduce Underage Drinking

#### Raising the Minimum Legal Drinking Age

Before 1984, only 22 states had a MLDA of 21. To reduce DUls, Congress passed the National Minimum Drinking Age Act, which threatened to withhold a portion of states’ federal highway construction funds if states made the purchase or public possession of alcoholic beverages legal for those under the age of 21. By 1988, all states had adopted age 21 as the MLDA. In the 1982 Monitoring the Future annual national survey of middle and high school students, 71.2 percent of high school seniors reported that they drank in the past 30 days and 42 percent reported binge drinking in the past 2 weeks.228 In 2014, these same statistics were 37.4 percent and 19 percent respectively (Figure 3.3).213 These declines may be partially attributable to the MLDA214 along with other policy and behavior-change interventions occurring at the same time.
Many studies have shown the benefits of raising the MLDA. A Community Guide review found that raising the MLDA reduced crashes among drivers aged 18 to 20 by a median of 16 percent. A finding replicated in a prospective analysis of the National Highway Traffic Safety Administration’s (NHTSA’s) Fatality Analysis Reporting System (FARS) examining the ratio of drinking to non-drinking drivers aged 20 and younger. The analysis statistically adjusted for zero tolerance laws, graduated licensing restrictions (e.g., provisional licenses for new drivers that include restrictions on driving at night or with any measurable alcohol in their systems), use/lose laws, administrative license revocation, 0.08% BAC per se laws, per capita beer consumption, unemployment rate, vehicle miles traveled, frequency of sobriety check points, number of licensed drivers, and the ratio of drinking to non-drinking drivers in fatal crashes ages 26 and older. An additional analysis examined national alcohol-related fatal traffic crash data before and after states raised the MLDA to 21. Before those laws were instituted, 61 percent of drivers aged 16 to 20 had a positive BAC compared with 33 percent following institution of those laws. These analyses showed general declines in alcohol-related fatal crashes across age groups, but the declines were highest for drivers aged 16 to 20. Comparing the declines across ages is useful because these older drivers were not the main focus of the MLDA changes.

Figure 3.3: Trends in 2-Week Prevalence of 5 or More Drinks in a Row among 12th Graders, 1980-2015

Note: The first vertical bar indicates institution of the MLDA 21 policy change in 7 states in 1984. The second vertical bar indicates federal passage of the MLDA 21 policy in all states in 1988.

Source: Adapted from Hingson and White, (2014).
An extensive review concluded that raising the MLDA to 21 has been directly associated with less frequent drinking, less heavy drinking, and fewer alcohol-related traffic fatalities in the age groups targeted by the law.\textsuperscript{178} More specifically, NHTSA estimates that raising the MLDA to 21 may have prevented 30,323 traffic deaths since 1975.\textsuperscript{230}

**MLDA Compliance Checks**
As a complement to the MLDA laws, research has shown the importance of repeated compliance check surveys on alcohol sales to people younger than age 21. These compliance check surveys monitor the percentage of attempts to buy alcohol that result in a sale to a person appearing to be younger than age 21. Alcohol outlet owners are informed in writing whether or not they were observed selling alcohol to underage-appearing individuals, told about the penalties for selling to minors, which can include fines or license suspension, and informed that the surveys will be repeated. A review identified several studies that found these compliance check surveys reduce the percentage of underage alcohol buying attempts and sales of alcohol to youthful-looking decoys by more than 40 percent.\textsuperscript{187} This strategy is an effective way to reduce alcohol consumption by minors and can be implemented in conjunction with population level alcohol policies.

**Zero Tolerance Laws**
All 50 states have passed laws making it illegal for persons younger than age 21 to drive with any measurable BAC. These laws, called zero tolerance laws, were instituted because of the higher fatal crash risk among drivers younger than age 21\textsuperscript{215,231} and because of studies showing that lowering the drinking age below age 21 was related to increases in fatal crashes.\textsuperscript{232} Another study examined the first eight states to implement zero tolerance laws, comparing each with a nearby state that did not enact such a law.\textsuperscript{233} Examining an equal number of years before and after these laws changed, researchers found 20 percent fewer alcohol-related traffic crash deaths in the targeted age groups within the zero tolerance states compared to nearby states without these laws. Similarly, a more recent examination of *Monitoring the Future* survey data for high school seniors in 30 states before and after adoption of zero tolerance laws found that after the laws were enacted, a 19 percent decline in driving after drinking occurred as well as a 23 percent decline in driving after five or more drinks.\textsuperscript{234}

**Use/Lose Laws**
Use/lose laws allow states to suspend a person’s driver’s license for underage alcohol violations. An examination of the *Youth Risk Behavior Surveillance System* survey data by state (statistically adjusted to account for state differences in age, gender, race, ethnicity, and other factors) from 1999 to 2009 found past-month drinking declined after use/lose laws were instituted.\textsuperscript{235} The study also found that after these laws were instituted, survey respondents were half as likely to report driving after drinking compared with before the laws were instituted.

**Criminal Social Host Liability Laws**
Criminal state social host liability laws require law enforcement to prove intent to provide alcohol to underage guests. Specifically, “social host” refers to adults who knowingly or unknowingly host underage drinking parties on property that they own, lease, or otherwise control. With social host ordinances, law enforcement can hold adults accountable for underage drinking through fines and potentially criminal charges. More than 30 states have some form of social host liability laws. To see
the effect of these laws, researchers examined rates of alcohol consumption, binge drinking, and DUI between 1984 and 2004 from the annual *Behavioral Risk Factor Surveillance System*. They also looked at data from the FARS from 1975 to 2005 on alcohol-related versus non-alcohol-related fatal traffic deaths among those aged 18 to 20. After controlling for the state’s legal drinking age, several drinking laws, and socioeconomic factors, social host liability laws were independently associated with declines in binge drinking (3 percent), driving after drinking (1.7 percent), and alcohol-related traffic deaths (9 percent).236

**Civil Social Host Liability Laws**

In contrast to state-level criminal social host ordinances, city- or county-level civil liability ordinances allow for a lower burden of proof but still deter underage drinking parties. Through civil social host liability laws, adults can be held responsible for underage drinking parties held on their property, regardless of whether they directly provided alcohol to minors. To date, more than 150 cities or counties have social host liability ordinances in place. The research on this strategy is still emerging, but findings currently show that social host liability reduces alcohol-related motor vehicle crashes as well as other alcohol-related problems.28,237

**Proposals for Reductions in Alcohol Advertising**

Although evidence of a causal relationship is lacking, research has found an association between increased exposure to marketing and increased alcohol consumption among youth.27 For example, one study found that for every additional advertisement seen by youth per month, they drank one percent more, while for every additional dollar per capita spent on alcohol advertising in a youth’s media market, they drank three percent more.238 Typically, these studies have not controlled for other factors known to influence underage drinking, such as parental attitudes and drinking by peers. Further, studies have yet to determine whether reducing alcohol marketing leads to reductions in youth drinking. One study estimated that a 28 percent decrease in alcohol marketing in the United States could lead to a decrease in the monthly prevalence of adolescent drinking from 25 percent to between 21 and 24 percent.239 A separate study of alcohol advertising bans concluded that “there is a lack of robust evidence for or against recommending the implementation of alcohol advertising restrictions.”240

**Many Policy Interventions Are Not Consistently Implemented**

Despite the evidence discussed in this section, many policies are not consistently implemented in states or communities. For example, commercial host (dram shop) liability laws, which permit alcohol retail establishments to be held responsible for injuries or harms caused by service to intoxicated or underage patrons have not been implemented consistently, have been changed over time, or both. Consequently, as of January 1, 2015, only 20 states had dram shop liability laws with no major limitations; 25 states had these laws but with major limitations (e.g., restrictions on who this liability applied to and the evidence required to determine liability); and six states have no dram shop liability laws at all.241 These numbers have not changed since 2013 (Table 3.4).242

Policies related to the regulation of alcohol outlet density have changed over time. For example, as of 2013, only 18 states had exclusive local or joint state/local alcohol retail licensing authority, and eight states allowed no local control over alcohol retail licensing.
Additionally, one study analyzed FARS from 1982-2012. The authors compared the ratio of drinking drivers in fatal crashes to non-drinking drivers in fatal crashes among drivers aged 20 and younger and those 26 and older. Using advanced statistical analyses that adjusted for state DUI laws, safety belt laws, economic strength, driving exposure, and beer consumption, the authors identified nine laws designed to reduce underage drinking and driving whose implementation was prospectively, independently, and significantly associated with decreases in the ratio of drinking to non-drinking drivers under age 21 in fatal crashes, including laws prohibiting underage possession and purchase of alcohol; use alcohol lose your license (use/lose) laws; zero tolerance laws; laws requiring bartenders to be aged 21 or older; state responsible beverage/server programs; fake identification state support services for retailers; dram shop liability; and social host civil liability. Those nine laws were estimated to save approximately 1,135 lives annually, yet only five states have enacted all nine laws. The authors estimated that if all states adopted these laws an additional 210 lives could be saved every year.243

Table 3.4: Status of Selected Evidence-Based Strategies in States for Preventing Alcohol Misuse and Related Harms

<table>
<thead>
<tr>
<th>Alcohol Policy (Ratings categories)</th>
<th>Number of states by rating and year of CDC Prevention Status Report</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Green</td>
</tr>
<tr>
<td>State excise taxes on beer*</td>
<td>2013</td>
</tr>
<tr>
<td>(Green: ≥$1.00 per gallon; Yellow: $0.50-$0.99 per gallon; Red: &lt;$0.50 per gallon)</td>
<td>3</td>
</tr>
<tr>
<td>State excise taxes on distilled spirits*</td>
<td>2013</td>
</tr>
<tr>
<td>(Green: ≥$8.00 per gallon; Yellow: $4.00-$7.99 per gallon; Red: &lt;$4.00 per gallon)</td>
<td>3</td>
</tr>
<tr>
<td>State excise taxes on wine*</td>
<td>2013</td>
</tr>
<tr>
<td>(Green: ≥$2.00 per gallon; Yellow: $1.00-1.99 per gallon; Red: &lt;$1.00 per gallon)</td>
<td>2</td>
</tr>
<tr>
<td>(Green: Commercial host liability with no major limitations; Yellow: Commercial host liability with major limitations; Red: No commercial host liability)</td>
<td>21</td>
</tr>
<tr>
<td>Local authority to regulate alcohol outlet density</td>
<td>2013</td>
</tr>
<tr>
<td>(Green: Exclusive local or joint state/local alcohol retail licensing; Yellow: Exclusive state alcohol retail licensing but with local zoning authority or other mixed policies; Red: Exclusive state alcohol retail licensing)</td>
<td>18</td>
</tr>
</tbody>
</table>

Note: *The ratings reflect where each state’s tax fell within this range. N/A: Not Applicable.
Sources: Centers for Disease Control and Prevention, (2014)242 and (2016).241

These data suggest that effective alcohol control policies are not being widely implemented in the United States despite the well-documented, scientific evidence on the effectiveness of such policies for reducing alcohol misuse and related harms. To have maximum public health impact, it is critical to implement effective policy interventions that address alcohol misuse and related harms, and that recognize the widespread nature of the problem and the strong relationship between alcohol misuse, particularly binge drinking, and related harms among adults and youth in states.190,191,244
Policies to Reduce Other Substance Misuse and Related Problems

Preventing Prescription Drug Misuse

Policies to prevent prescription drug misuse and related harms have only begun to receive research attention. However, some studies have begun to examine the impact of prescription drug monitoring programs (PDMPs) on misuse of prescription medications. These state-initiated policies are designed to curb the rate of inappropriate prescribing of opioid pain relievers through various methods. Data from the U.S. Drug Enforcement Administration’s (DEA’s) Automation of Reports and Consolidated Orders System (ARCOS) showed little impact of these monitoring systems, perhaps because of the variability of the policies controlling different state systems. The ARCOS is an automated, comprehensive drug reporting system which monitors the movement of controlled substances from where they are manufactured through distribution at the retail level, such as hospitals, pharmacies, and practitioners.

Some studies associate state PDMPs with lower rates of prescription drug misuse and altered prescribing practices, although evidence is mixed and inconclusive. One reason for inconsistent findings may be low and variable prescriber utilization of PDMPs. Because mandates are relatively new, their efficacy in increasing PDMP utilization has not been formally studied. However, preliminary data suggest that in some states mandates have contributed to a rapid increase in provider enrollment and utilization of PDMPs and subsequent decreases in prescribing of controlled substances and the number of patients who visit multiple providers seeking the same or similar drugs. Data from Kentucky, Tennessee, New York and Ohio—early adopters of comprehensive PDMP use mandates—indicate substantial increases in queries, reductions in opioid prescribing, and declines in multiple provider episodes (doctor shopping) following implementation. In one of the most rigorous studies to date, Florida’s simultaneous institution of a prescription drug monitoring system and “pill mill” control policies was compared to Georgia, a state without either policy. This study demonstrated “modest reductions in total opioid volume, mean morphine milligram equivalent per transaction, and total number of opioid prescriptions dispensed, but no effect on duration of treatment. These reductions were generally limited to patients and prescribers with the highest baseline opioid use and prescribing.”

A 2016 study found that the implementation of a PDMP was associated with 1.12 fewer opioid-related overdose deaths per 100,000 people in the year immediately after the program was implemented, and if every state in the United States had a robust PDMP, there would be an estimated 600 fewer overdose deaths per year. However, another study analyzed eight types of laws that restricted the prescribing and dispensing of opioids (including PDMP laws but not including prescriber mandate laws) and found no relationship between the laws and opioid-related outcomes among disabled Medicare beneficiaries, who accounted for nearly 25 percent of opioid overdose deaths in 2008.
Collectively, these early results suggest the potential influence of PDMPs to reduce unsafe controlled substance prescribing and rates of misuse and diversion, but there is a need to conduct additional research on the effectiveness of specific strategies for implementation and use of PDMPs. Multiple efforts to address prescription drug misuse within states occurring in concert with mandatory PDMP legislation may limit the ability to draw causal conclusions about the effectiveness of mandatory use of PDMPs.

The CDC has developed the CDC Guideline for Prescribing Opioids for Chronic Pain, which provides research-based recommendations for the prescribing of opioids for pain in patients aged 18 and older in primary care settings. The guideline includes a discussion of when to start opioids for chronic pain, how to select the right opioid and dosage, and how to assess risks and address harms from opioid use. This guideline can help providers reduce opioid misuse and related harms among those with chronic pain.

### Adolescent Use of Marijuana

Marijuana use, in adolescents in particular, can cause negative neurological effects. Long-term, regular use starting in the young adult years may impair brain development and functioning. The main chemical in marijuana is delta-9-tetrahydrocannabinol (THC), which, when smoked, quickly passes from the lungs into the bloodstream, which then carries it to organs throughout the body, including the brain. THC disrupts the brain’s normal functioning and can lead to problems studying, learning new things, and recalling recent events. One study followed people from age 13 to 38 and found that those who began marijuana use in their teens and developed a persistent cannabis use disorder had up to an eight point drop in IQ, even if they stopped using in adulthood. Frequent marijuana use has also been linked to increased risk of psychosis in individuals with specific pre-existing genetic vulnerabilities. And marijuana use—particularly long-term, chronic use or use starting at a young age—can also lead to dependence and addiction.

These effects highlight the importance of prevention. To prevent marijuana use before it starts, or to intervene when use has already begun, parents and other caregivers as well as those with relationships with young people—such as teachers, coaches, and others—should be informed about marijuana’s effects in order to provide relevant and accurate information on the dangers and misconceptions of marijuana use. Comprehensive prevention programs focusing on risk and protective factors have shown success preventing marijuana use. Evidence-based strategies or best practices in community level prevention efforts can be used to assess, build capacity, plan, implement, and evaluate initiatives.

### Prevention Interventions for Specific Populations

An important consideration in any assessment of the overall effectiveness of EBIs is whether and to what extent they work with specific populations, such as Blacks or African Americans, Hispanics or Latino/as, Asians, American Indians or Alaska Natives, Native Hawaiians or Other Pacific Islanders, veterans, or lesbian, gay, bisexual, and transgender (LGBT) populations. The EBIs described in this chapter have been purposely selected because many have been implemented, tested, and found to be effective in diverse populations. It should be noted that while prevention policies have shown impacts for the entire population, and a number of prevention programs at each developmental period have shown positive outcomes with a mix of populations, most studies have not specifically examined their differential effects on racial and ethnic subpopulations. Studies finding significant prevention effects
across multiple population subgroups include LifeSkills Training, keepin’ it Real, Nurse Family Partnership, Raising Healthy Children, Good Behavior Game, Classroom-Centered Intervention, Fast Track, SODAs City, I Hear What You’re Saying, Project Chill, Positive Family Support, Coping Power, Project Towards No Drug Abuse, Communities That Care, Project Northland, and Project STAR.

The following programs were found to be equally effective in White and specific racial and ethnic minority populations: Fast Track, which is equally effective for White and Black or African American adolescents, LifeSkills Training, which is equally effective with White and Black or African American and Hispanic or Latino adolescents, and keepin’ it REAL, which is equally effective with White and Hispanic or Latino adolescents. In addition, some interventions developed for specific populations have been shown to be effective in those populations, i.e., Strong African American Families, Familas Unidas for Hispanics or Latinos, Bicultural Competence for American Indian or Alaska Natives, and PROSPER for rural communities.

Adaptation of EBIs in Diverse Communities

A goal of prevention and public health professionals is to broadly disseminate all tested-and-effective EBIs, thus making them readily available to communities and consumers. Achieving population-level exposure of an EBI to all population groups—or “going to scale”—raises critical issues of “fit” of the EBI’s contents and the needs and preferences of local community residents. Often, some form of local adaptation is necessary when a certain feature of the selected EBI fails to engage a specific group within a local community. However, not all EBIs may work with all community subgroups. The sometimes delicate balance that needs to be struck between fidelity to the program as originally designed and tested and the need for adapting it to the needs of specific subgroups is an important issue and requires sophisticated methodology to address. Currently, several cultural adaptations of an original EBI have been developed and tested.

Issues regarding the cultural adaptation of EBIs have been reviewed extensively within the past two decades. Early studies examined the utility of developing a culturally-focused version of the EBI LifeSkills Training to fit the needs of racially and ethnically diverse adolescents living in the New York City area. In general, the challenge involves the viability of implementing an EBI with total fidelity to its protocol, versus adapting it by making adjustments so the EBI is more relevant and responsive to the needs of local community residents. Producing an adapted version of an established EBI may not generalize well enough to create the same effects when implemented with a culturally different group from that used to validate the original intervention. Such limited generalizability might occur if the intervention is insufficiently sensitive, culturally or otherwise, to the unique stressors, resources, cultural traditions, family practices, and other prevailing sociocultural factors that govern the lives of residents from that community.
It is worth noting that the major racial and ethnic populations in the United States—Hispanics or Latinos, Blacks or African Americans, Asians, and American Indians or Alaska Natives—also exhibit significant within-population variations in important sociocultural characteristics. Beyond differential EBI efficacy that may appear by racial or ethnic status—Black or African American versus White, for example—differential efficacy may also be observed by one of several demographic or clinical variables that define any one racial or ethnic group. These variables include gender (male vs. female), age group (younger vs. older), grade level (Grade 8 vs. Grade 10), sexual and gender identity, neighborhood status (problem vs. non-problem), problem severity (moderate vs. high), level of education (middle school vs. high school or greater), level of acculturation (low acculturation, bicultural, high acculturation). It can also include sociocultural needs and preferences that can be incorporated into the culturally adapted prevention intervention.

Given the multiple sources of within-group variation, one dissenting view is that it is impractical to develop many different versions of an original EBI in efforts to respond to the needs of various groups. A contrasting view is that a few selective and directed adaptations may be sufficient to respond to the sociocultural needs of many of these groups “to ensure fit with diverse consumer populations.” Clusters of these groups may share common life experiences, such as their identity and identification as a person of color, experiences with discrimination and disempowerment, or the need for cultural validation.

All of these issues create a “Fidelity-Adaptation Dilemma:” How to make necessary local or cultural adaptations that are responsive to the needs of a growing diversity of cultural groups in the United States, while also not compromising the fundamental science-based components or “active ingredients” that drive the effectiveness of the original EBI. As originally formulated, the Fidelity-Adaptation Dilemma framed fidelity and adaptation as diametrically opposed approaches in the implementation of an EBI. After more than a decade of analysis and research, this conceptualization appears no longer productive, given that both fidelity and adaptation are now recognized as important for the effective implementation of an EBI, especially when delivered within diverse racial and ethnic communities. The dual aim for resolving the Fidelity-Adaptation Dilemma is to adhere with fidelity to the intervention’s theory, principles, goals, and mechanisms of effect for attaining the EBI’s intended outcomes, while also making well-reasoned “cultural adaptations” that remedy emerging problems with the EBI’s contents and/or activities. A partnership between intervention developers, persons delivering the intervention, and potential program participants who can represent the group’s concerns, is recommended for developing well-reasoned solutions to remedy specific features of the original EBI that are not working as intended. The ultimate aim is to craft needed adaptive adjustments that aptly remedy these emerging problems and that also enhance the efficacy of the intervention in attaining the intended outcomes with local community residents.

Several adaptations use a social participatory approach with a community advisory committee that is composed of local leaders who know the local community well. These individuals offer “insider” observations and recommendations that inform substantive deep-structure modifications that can make the original EBI more culturally responsive.

Although sufficient evidence has not yet accrued to inform a single best approach for addressing this Fidelity-Adaptation Dilemma, a review of the EBI adaptation literature shows a convergence of specifically prescribed steps for adapting an original EBI. Several models describe these steps in the
cultural adaptation and testing of an original EBI.\textsuperscript{266} Other approaches have introduced the concept of “adaptive interventions” that aim to tailor the intervention individually based on empirically-developed decision rules.\textsuperscript{278,279}

A future goal for effective cultural adaptation would be to identify robust principles and guidelines that can inform and guide the development of cultural adaptations. One emerging principle involves avoiding adaptations that produce detrimental changes, termed “misadaptations,” that erode the original EBI’s established efficacy for changing intended outcomes.\textsuperscript{263} A second emerging principle is to conduct adaptations that enhance consumer engagement based on curriculum activities that are culturally responsive to the needs and preferences of the local community of consumers. Additional research is needed to establish the robustness of these or other emerging principles and to generate clear and functional guidelines that can inform intervention design and implementation to promote both fidelity and adaptive fit. The aim of this adaptation is to maximize intervention effect when delivered to diverse groups of consumers.

EBI adaptation that is based on evidence-based outcomes data constitutes an empirically-based methodology to correct, refine, and enhance an original EBI. From this perspective, these adaptations or modifications transcend fidelity-adaptation issues, advance toward EBI refinement that is conducted systematically, increase efficacy as well as generalizability, and reach and benefit a greater number of those who are most in need of EBIs.

**Maximizing Prevention Program and Policy Effectiveness**

Although a variety of prevention policies and programs have been shown to reduce substance misuse and consequences of use, many are underutilized. Additionally, many programs are not currently being implemented with sufficient quality to effectively improve public health. For example, although it is difficult to collect data on this issue, research suggests that few family-serving agencies are using EBIs to address child behavioral and emotional problems,\textsuperscript{280,281} and surveys of school administrators indicate that only 8 to 10 percent report using EBIs to prevent substance misuse.\textsuperscript{282,283} Additionally, research has shown that untested or ineffective prevention programs are used more often than EBIs,\textsuperscript{282,283} and, when they are used, EBIs are often poorly implemented, do not serve large numbers of participants, and are not sustained.\textsuperscript{284,285} For example, family-based EBIs are often delivered with less intensity and/or to different types of participants than specified by program developers.\textsuperscript{286} School officials have reported low rates of implementation fidelity, including failure to deliver all required lessons, content, and activities; to use the required materials; to employ the recommended instructional strategies; to target the appropriate students with lessons; and/or to ensure that all teachers receive training.\textsuperscript{24,283,284,287,288} EBIs that are poorly implemented tend to have weak or no effects on participants.\textsuperscript{272,289-296} For example, in one study, the LifeSkills Training program delivered in middle and junior high schools has shown significant, long-term effects on Grade 12 students’ alcohol and marijuana use only among students whose teachers delivered at least 60 percent of the required material.\textsuperscript{292}
Research demonstrates that building prevention infrastructure; activating federal, state, local, and tribal stakeholders; ensuring collaboration; and helping communities select, implement, and sustain EBIs is possible and can be done effectively. For example, one large-scale study provided schools and various human service agencies with training and technical assistance to replicate nine EBIs rated as “Model” by the Blueprints for Healthy Youth Development. That study indicated that when provided with ongoing support, 74 percent of sites successfully implemented these systems. Evaluations of PROSPER and CTC, which provide community coalitions with prevention infrastructure to choose EBIs that addressed their needs and to implement the chosen EBIs with fidelity, have shown that communities using these delivery systems implement EBIs with high fidelity and sustain them over time. These and other studies indicate that prevention infrastructure can be generated by taking the actions discussed in the section on Improving the Dissemination and Implementation of Evidence-based Programs later in this chapter.

Additionally, strengthening state and local public health capacity will help to increase the surveillance and monitoring of risk and protective factors and substance misuse by adolescents and adults in the general population, including persons who drink to excess but are not dependent on alcohol. It is important to educate and raise awareness about the public health burden of substance misuse and effective program and policy interventions for preventing and reducing substance use across the population.

The History of Substance Use and Misuse Policy Formation and Implementation

The dissemination and implementation of evidence-based prevention programs have been studied extensively; less research has been conducted on evidence-based policy formation and implementation. This section describes three organizations or activities focusing on federal, state, and local policy to reduce substance misuse: Mothers Against Drunk Driving (MADD), CADCA, and the Congressional Sober Truth on Preventing Underage Drinking (STOP) Act.

In the early 1980s, President Ronald Reagan established a bipartisan presidential commission to reduce drunk driving. The commission’s first recommended action was to raise the MLDA to 21. In 1984 and with strong support from the newly founded MADD, Congress passed legislation to withhold federal highway construction funds from states that did not raise the MLDA to 21. MADD was also instrumental in supporting the passage of legislation in 1996 to withhold federal highway construction funds from states that did not have zero tolerance laws. They were a key player in 2000 legislation to withhold construction funds from states that did not lower the legal blood alcohol limit to 0.08 percent for adult drivers. Since the early 1980s, more than 2,000 other state laws have been passed to reduce driving after drinking, and MADD has been a major citizen activist force encouraging the passage of many of those laws.

MADD also has prepared and published periodic state and national “report cards” rating each state and the nation’s efforts to reduce alcohol-impaired driving. States have been rated on how many of the more than 30 laws scientifically demonstrated to reduce impaired driving had been passed and how many were passed since the previous report card. In one study, these state report cards were found to clearly predict the percent of respondents in each state who reported driving after drinking in the past month. Although the impact of the report cards in accelerating passage of the laws has never been empirically tested, media monitoring of news stories derived from the report cards indicated that at least one third of the United States population has been exposed to media coverage about the report cards.
One study compared characteristics of MADD chapters that had early success in raising the MLDA to 21 to chapters in states that did not raise the age. The analysis found that having chapters headed by people who lost immediate family members through drinking and driving crashes and those with higher percentages of such victim members were the most successful in early passage of MLDA laws. Of note, the size of chapters’ financial budget did not predict the passage of these laws.\(^{321}\)

Although MADD has helped to foster passage of more than 2,000 state-level laws, implementation of those laws is accomplished at the community level. This often requires the existence of trained coalitions focusing on substance use. One such collaboration, CADCA, has played a critical role in training local coalitions in implementing laws, particularly the MLDA law in all 50 states. CADCA’s membership includes more than 5,000 community coalitions nationwide that seek to reduce underage drinking and drug use. CADCA has partnered with MADD and federal organizations to develop a manual on how to reduce drinking and driving and underage drinking in communities.\(^{322}\) CADCA holds its annual leadership meeting in Washington, D.C. so that its members can also meet with congressional representatives to explore better ways to reduce alcohol and drug misuse and underage drinking.

In 2004, the IOM released *Reducing Underage Drinking: A Collective Responsibility*, a report on underage drinking in the United States.\(^{323}\) Partly in response to this report, Congress passed the STOP Act, which:

- Provided supplemental funding to community programs that were already addressing substance use so that they could also address underage drinking;
- Called on all states to test the BAC in anyone younger than age 21 who died from an injury or overdose;
- Encouraged every state to develop an interagency task force of officials from multiple state governmental departments and private citizens and organizations to develop strategic plans to reduce underage drinking (38 states have established task forces and strategic plans);
- Required the federal government to establish the Interagency Coordinating Committee for the Prevention of Underage Drinking (ICCPUD), comprising the following departments and agencies: Departments of Education, Health and Human Services, Transportation, and Defense; and the Federal Trade Commission. The Committee meets monthly to coordinate federal efforts to reduce underage drinking; and
- Required the federal government through ICCPUD and SAMHSA to provide annual reports to Congress on the magnitude of underage drinking and related problems and what the federal and state governments are doing to prevent and reduce underage drinking.
Improving the Dissemination and Implementation of Evidence-based Programs

The emerging field of dissemination and implementation research seeks to identify ways to increase the use and high-quality implementation of evidence-based programs and address challenges to implementation. This research indicates that the key to achieving significant gains in public health, including reductions in substance use initiation and substance misuse, is to build prevention infrastructure at the local level. This means increasing awareness of EBIs among community leaders, service providers, and local citizens. It also means providing tools to help communities select and use EBIs that will be feasible to implement and relevant for their populations. When agencies and staff are unaware of, do not support, or lack the ability to select and implement appropriate EBIs with quality, then dissemination, implementation, and sustainability will be hindered. In contrast, when local systems and agencies learn more about the effectiveness of prevention interventions, have a culture and climate that supports innovation and the use of EBIs, and have the budget and skills needed to plan for and monitor the implementation of EBIs, then effective dissemination and implementation will be fostered.

Coalition-based systems have been developed to assist communities in building these capacities, and when tested in randomized trials, these systems have been shown to improve community capacity for effective prevention; increase dissemination, implementation, and sustainability of EBIs; and produce community-wide reductions in youth substance use. An important feature of these systems is the provision of community coalitions with multiple training workshops and ongoing technical assistance. Just as organizations require technical assistance to ensure high-quality implementation of specific EBIs, coalitions need technical assistance to support and develop their prevention capacities. Each community model has different steps that outline their process; the following four steps are one example of how to build broader implementation of evidence-based prevention.

Step 1. Form Diverse, Representative, Cross-Sector Community Coalitions

Coalitions, or groups of stakeholders working together to achieve a common goal, are a useful mechanism for building and maintaining local prevention infrastructure and capacity. The first step in building a coalition is to decide on the “community” to be involved in prevention activities, including the geographic area in which services will be delivered, and to identify the organizations, agencies, groups, and individuals whose participation is necessary for success. The more the coalitions represent the community in terms of demographic diversity, organizations expected to deliver services, and groups or individuals expected to receive services, the more likely they are to ensure that EBIs will be supported. Similarly, such coalitions will be better equipped to implement multiple EBIs across diverse contexts and to a larger percentage of the population, all of which should make population-level improvements more likely. In addition, by sharing information and resources,
community coalitions can help minimize duplication of efforts and potentially offer more cost-effective services that are better implemented and more likely to be sustained.25,334-337

Step 2. Conduct a Needs Assessment and a Fit Assessment

Needs and fit assessments help coalitions select the right EBIs for their community. The right EBIs are those that address the highest-priority local risk and protective factors the coalition identifies (e.g., the risk factors that are most elevated and the protective factors that are most depressed in the community) and the groups or individuals most in need of services.330,338 Coalitions conduct needs assessments by gathering data on risk and protective factors, substance misuse, and related problems. For example, in the CTC system, needs assessments rely primarily on data reported by adolescents on school-based, anonymous surveys. These data are reviewed by coalition members and risk factors that are consistently elevated and protective factors that are consistently depressed are identified as targets that need to be addressed by EBIs.334 The priorities may vary by neighborhood in larger cities or by specific subpopulations (e.g., gender or racial and ethnic groups).334

To select the best-fitting EBIs, coalitions need to be familiar with the list of possible interventions that can address their needs, and must consider whether or not they can meet all the implementation requirements of the EBIs.294,312,339 Consulting a registry of EBIs, such as the National Registry of Evidence-based Programs and Practices (NREPP)340 and the Blueprints for Healthy Youth Development341 or NIAAA’s Alcohol Policy Information System342 for alcohol policies, can assist in creating the list of EBIs that meet community needs. These databases compile information about programs that have met rigorous evaluation criteria in a user-friendly format, which makes it easy for communities to learn about and compare intervention costs and requirements.343,344 The databases also describe the intervention methods and population(s) with which the interventions were tested to help coalitions determine whether the EBI is culturally relevant and compatible with the norms, values, and needs of the local community.

Step 3. Enhance Implementation Fidelity and Implementers’ Capacity

Some research suggests that EBIs can never be perfectly replicated in communities and that changes or adaptations to the EBI’s content, activities, materials, or methods of delivery will be necessary given the differences between well-controlled research trials and real-world settings.263,270,345-347 However, research has shown that when EBIs are implemented with fidelity, programs achieve expected results. While culturally relevant adaptations can be expected to increase the relevance of the material, better engage participants, and improve effectiveness, it is clear that poor or inappropriate adaptation can reduce effectiveness.268,295 For example, an evaluation showed that the effectiveness of the Nurse-Family Partnership program was significantly reduced when paraprofessionals rather than registered nurses delivered services in communities that lack registered nurses.348 These types of inappropriate adaptations emphasize the need for communities to learn as much as they can about EBIs during the fit assessment and select only those interventions that are considered feasible given resources.
Steps to Build Prevention Infrastructure for Effective Community-based Prevention

Conduct a local needs assessment:

- Collect data on levels of substance use;
- Collect data on risk and protective factors related to substance use; and
- Identify and prioritize elevated risk factors and depressed protective factors.

Conduct a resource assessment:

- Assess current prevention programming, including the risk and protective factors addressed by current services, numbers and types of populations served, effectiveness, and implementation quality; and
- Identify potential new services using EBI and policy registries.

Assess the fit of new EBIs with the local community:

- Determine whether or not each potential EBI addresses the identified substance misuse problems and priority risk and protective factors; and
- Assess the degree to which the new EBI is culturally relevant for the local population.

Assess local readiness and capacity to implement EBIs:

- Identify the organization(s) that will deliver each new EBI;
- Assess levels of support for each new EBI among all key personnel; and
- Identify the financial and human resources and all other requirements necessary to implement each EBI.

Select the intervention(s) that is the best fit for the community: The ones that are most likely to be fully supported meet prioritized needs, are culturally relevant, can be well implemented, and can be sustained over the long-term.

Ensure high quality implementation of each new EBI:

- Create a detailed implementation plan;
- Specify participant eligibility criteria, participation goals, and recruitment procedures;
- Create teams to oversee implementation;
- Hire all necessary staff and administrators;
- Ensure that all staff are trained and regularly supervised; and
- Seek regular technical assistance from intervention developers.

Evaluate the impact of the selected interventions: It is critical to systematically collect and analyze information about program activities, participant characteristics, and outcomes.

- Collect data on all aspects of implementation; and
- Regularly review implementation and outcomes data and improve procedures as needed.
In addition to appropriate cultural adaptations, staff competency is critical to successful delivery of EBIs, and coalition members can support local agencies to ensure that they hire staff who have the credentials and experience recommended by developers, and that they receive training in each EBI’s theory, content, and methods of delivery. Training is an important ingredient in ensuring greater levels of implementation fidelity, especially because the content, activities, and methods of delivery may be new to practitioners. In general, relatively few professionals responsible for implementing EBIs (including mental health counselors, teachers, psychologists, and social workers) receive training in substance misuse prevention, including knowledge of risk and protective factors that impact alcohol and drug use, the knowledge of EBIs that target these factors, or the importance of implementation fidelity when delivering interventions. These topics should be incorporated into undergraduate, graduate, and in-service professional training programs. In the meantime, staff should be supervised and receive coaching and corrective feedback to ensure they are implementing EBIs with quality.

Technical assistance from EBI developers can assist local agencies in staff supervision, and most EBIs offer support in how to monitor implementation activities, overcome challenges when they arise, and integrate EBIs into agency operations. Although experimental studies are lacking, observational studies have reported that technical assistance, implementation monitoring, and staff feedback help ensure the high-quality delivery and sustainability of EBIs.

**Step 4. Plan for Long-Term Sustainability**

A lack of funding is a significant barrier to the long-term sustainability of EBIs, and it is critical that, even before implementation, agencies and communities consider how each EBI will be integrated into existing systems and funded over time. Considering how a new EBI will address local needs can be useful in gaining support.

**Recommendations for Research**

Although much has been learned in prevention research over the past four decades, much remains to be understood. Future research should develop and evaluate new prevention interventions, both programs and policies, and continue to assess the effectiveness of existing interventions about which little is known. This research will help guide the field toward strategies with the greatest potential for reducing substance misuse and related problems.

Research also is needed to examine the effectiveness of screening and brief interventions for alcohol use in adolescents and for drug use in adolescents and adults; the combinations of evidence-based alcohol policies that most effectively reduce alcohol misuse and related harms; the public health impact of policies to reduce drug misuse; and the effectiveness of strategies to reduce marijuana misuse, driving after drug use, and simultaneous use of alcohol and drugs. In addition, the public health impact of marijuana decriminalization, legalization of medical marijuana, and legalization of recreational marijuana on marijuana, alcohol, and other drug use, as well as policies to reduce prescription drug misuse, should be monitored closely.
Research is needed to develop and test new prevention interventions, both policies and programs, to fill gaps in existing EBIs and to meet emerging public health needs across the lifecourse.

Given that racial and ethnic minority communities are often disproportionately affected by the adverse consequences of substance misuse, culturally-informed research should be conducted to examine ways to increase the cultural relevance, engagement, and effectiveness of prevention interventions for diverse communities. Additionally, studies of these interventions should be replicated and examined to determine the impact of prevention interventions for different cultural groups and contexts.

Consistent standards for evaluating interventions, conducting replication trials, and reporting the results should be developed. Examples of such standards have been developed by the Society for Prevention Research and the United Nations Office on Drugs and Crime.8 Studies evaluating the effectiveness of interventions for reducing substance misuse should collect data over extended periods of time to track the long-term effects of these interventions on persons of all ages. The impact of environmental interventions on substance misuse should also be followed for at least a year beyond the end of the period of intervention support. The field needs to develop a consensus on standardization of methods of cost-benefit analysis, and increase research on cost-effectiveness evaluations of prevention EBIs.

Evidence is also needed to develop improved strategies for intervention in primary health care settings to prevent the initiation and escalation of adolescent substance use. More research is also needed on linking screening with personalized interventions, improved strategies for effective referral to specialty treatment, and interventions for adolescents that use social media and capitalize on current technologies. Research should also consider the optimal conditions for bringing effective prevention interventions to scale, develop consensus on standardization of methods for cost-benefit analysis, and increase research on cost-effectiveness evaluations of prevention EBIs.

Surveillance of risky drinking, drug use, and related problems needs to be improved. All drivers in fatal crashes should have their blood alcohol content tested and be tested for drug use. All unintentional and intentional injury deaths, including overdoses, should be tested for both alcohol and drugs. Surveillance surveys need to add questions about simultaneous alcohol and drug use and questions about the maximum quantities consumed in a day and frequency of consumption at those levels. Efforts are needed to increase surveillance of the second-hand effects of alcohol and drug use, such as assaults, sexual assaults, motor vehicle crashes, homicides and suicides, and effects of substance use on academic and work performance. Efforts are needed to expand surveillance beyond national and state levels to the level of local communities.