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PART I History, Perspectives, Epidemiology, Diagnosis, and Classification

1 Emerging Health Perspectives

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CHAPTER OUTLINE

Introduction

This chapter addresses a few issues that are emerging as critical health issues with substance use perspectives. First, there is a brief review of the epidemiology of substance use; this is linked to the growing problem of prescription drug abuse. Second, the issue of screening and brief intervention for substance use disorders (SUDs) is addressed. Then the issue of new technologies as a vehicle for enhancing SUD services is reviewed. Finally, the issue of how to pay for SUD services is reviewed.

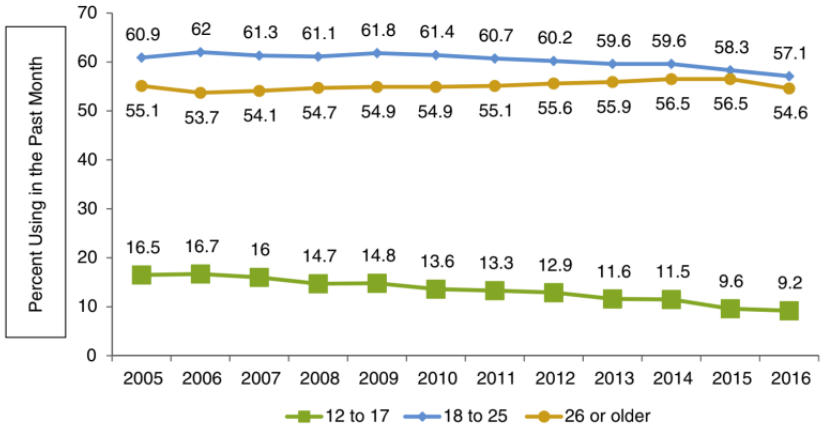
The epidemiology of substance use makes it quite clear that clinicians of any stripe will encounter patients or clients who use or misuse alcohol or psychoactive drugs. Therefore, the interrelationship between SUDs, brain function, and treatment outcome should be of interest to the clinician concerned with patient and client health.

Alcohol Use

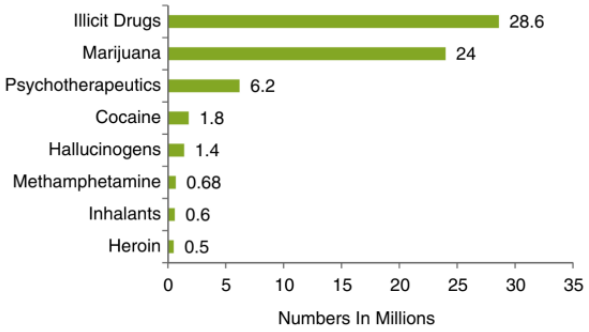
The National Survey on Drug Use and Health (NSDUH) annually interviews nearly 68,000 persons to establish national estimates of substance use.[9] More than half of Americans 12 years or older report being current drinkers of alcohol in the 2016 NSDUH; this means that almost 127 million people have had at least one drink in the past month. Other than underage drinking, current drinking is not inherently problematic. However, more than one-fifth (24.2%) of persons 12 years or older admit to binge drinking, which the NSDUH defines as five or more drinks on a single occasion for males and four or more drinks for females. Binge drinking is associated with a number of acute adverse events, including motor vehicle accidents, trauma, domestic violence, assaults, homicides, child abuse, suicide, fires, boating accidents, alcohol poisoning, and high-risk activities that threaten the health and well-being of the consumers. Another confounding population of alcohol consumers is the heavy drinking population. It is estimated by the NSDUH that 16.3 million people, or 6.0% of the population, 12 years of age or older admit to heavy drinking (binge drinking on at least 5 days in the past 30 days).

Naturally, alcohol consumption rates vary by—among other things—age, gender, and race/ethnicity. Among young adults 18–25 years of age, consumption rates are the highest in the current use, binge drinking, and heavy alcohol use categories. This age range is also associated with higher risk-taking and the consequences associated with risk-taking. Thus physicians and other clinicians who provide primary and/or emergency room care, or college health care practitioners, are more likely to see patients in this age group for a variety of alcohol-related injuries or conditions.

Among adolescents and young adults under the age of 21, alcohol consumption rises fairly rapidly from 1.4% for those who are 12 or 13 to 39% for those who are between the ages of 18 and 20. Fig. 1.1 shows the various levels of alcohol consumption for individuals 12 years or older by age grouping. It is apparent



• **Fig. 1.1** Current alcohol use among persons age 12 or older: 2005–2016. (Data from SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2002–2016.)



• **Fig. 1.2** Past-month use of specific illicit drugs among persons age 12 or older: 2016. (Data from SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2002–2016.)

from these prevalence rates that late adolescents and young adults are likely to engage in substantial alcohol consumption. Knowing whether alcohol use is related to a presenting physical or psychiatric complaint should be helpful to the clinician. Although many young adults 18- to 25-years-old will visit a clinician for very limited purposes, such as a job- or school-related physical, the prevalence of alcohol use problems in this age range clearly offers the clinician an opportunity to address the issue of alcohol-related medical, social, or behavioral problems. Clinicians should take advantage of such opportunities. In addition, Fig. 1.1 reveals that current alcohol use among youth 12- to 17-years-old has progressively declined from 2006 to 2016.

Illicit Drug Use

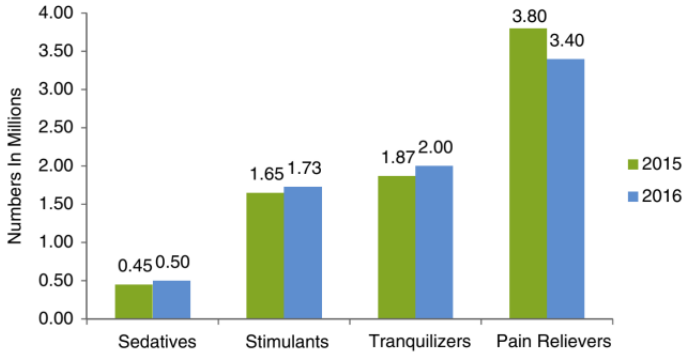
In 2016 there were an estimated 28.6 million Americans age 12 or older who admitted to using at least one illicit drug in the past month according to the NSDUH. This represented an estimated 10.6% of the population 12 years or older. For the purposes of the survey, illicit drugs included marijuana/hashish, cocaine (including crack), heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used nonmedically. Marijuana is the most commonly used illicit drug by Americans, with 24 million people admitting to past-month use. The second category of prevalent drug use is nontherapeutic or nonmedical use of prescription drugs (Fig. 1.2).

Specific categories of psychotherapeutics include a range of substances such as pain relievers, sedatives, tranquilizers, and stimulants. NSDUH data for persons age 12 or older reveal an elevation of nonmedical use of prescription pain relievers (Fig. 1.3).

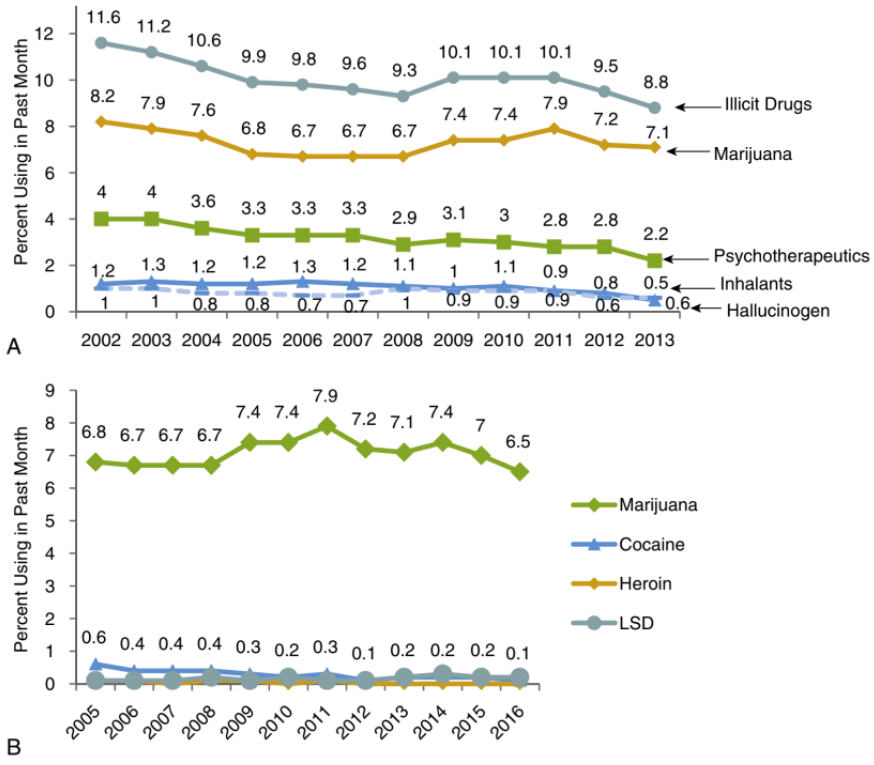
It has been recognized that use of prescription opioids is associated with higher rates of abuse and dependence than use of other substances, as well as increased mortality.[26] The misuse of benzodiazepines in combination with therapeutic opioids can create problems with respiration and cardiac functioning, predisposing to respiratory depression or cardiac dysrhythmia, leading to death.

Age Variations

However, as with alcohol use and misuse, there are age variations in illicit drug use. NSDUH data indicate that there has been a progressive decline, with some fluctuation, in the prevalence of drug use among adolescents age 12–17 years of age since 2011 (Fig. 1.4A–B). NSDUH data are supported by the Monitoring the Future Data, with both surveys revealing the same basic trends.[33]



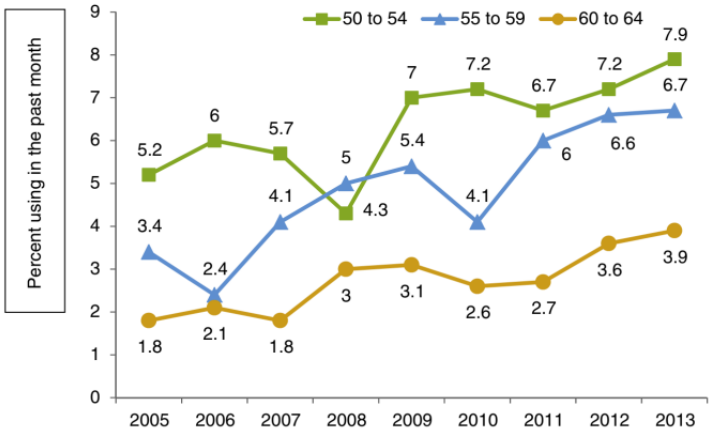
• **Fig. 1.3** Past-month nonmedical use of prescription drugs (psychotherapeutics) among persons age 12 or older: 2015–2016. (Data from SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2002–2016.)



• **Fig. 1.4** Past-month use of selected illicit drugs among persons 12 years or older: percent, 2002–2013. (A) Data from SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2002–2013. (B) Past-month use of selected illicit drugs among youths age 12–17: 2005–2016. (Data from SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2002–2016.)

It is important for primary care clinicians to recognize that the progress being made in reducing substance use of adolescents has not resulted in an elimination of the problem of drug use. Although substantial progress has been made, much effort needs to be exercised to keep up the pressure to continue to reduce the use of such substances among adolescents.

Another interesting observation seen in the 2016 NSDUH data involves adults 50–59 years of age. According to the survey data, this age group showed an irregular increasing trend between 2005 and 2013 regarding current illicit drug use. For adults ages 50–54, illicit drug use (past month) increased from 5.2% in 2005 to 7.9% in 2013. There was a greater increase in past-month use



• **Fig. 1.5** Past-month illicit drug use among adults age 50–64: 2005–2013. (Data from SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2002–2013.)

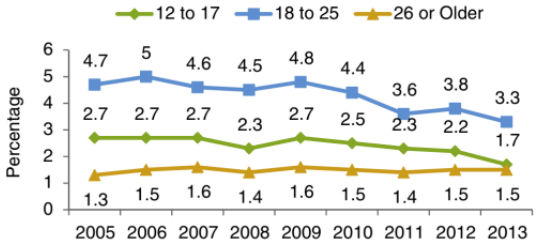
of illicit drugs for adults in the 55–59 age group—with an overall increase from 3.4% in 2005 to 6.7% in 2013 (Fig. 1.5). Although the NSDUH collection methodology changed for 2015 and 2016, making trend analysis comparison between those 2 years and the years up to 2013 impractical, prevalence rates for past-month illicit drug use for 2016 were 7.8% for adults 50–54, 9.3% for adults 55–59, and 5.4% for adults 60–64, further evidence of an important effect, quite possibly due to the "Baby Boomer" cohort moving across time.

For physicians—particularly those who specialize in the care of older patients—these trends indicate some of the challenges that may develop as the Baby Boomer population continues to age. According to the United States Census Bureau, one in five US residents will be 65 years or older in 2030. By 2050, it is projected that 84 million seniors will be 65 years or older, with 18 million of them 85 years or older.[65]

Nonmedical Use of Prescription Drugs

The nonmedical use of prescription drugs has become a major public health problem. Of particular concern is the rise in nonmedical use of prescription opioids and the rise in the use of illicit opioids such as heroin and illegally manufactured fentanyl or carfentanil. The fact that the nonmedical use of prescription drugs is the second most prevalent pattern of illicit substance use should be of great interest to SUD prevention and treatment specialists and to professionals in primary care, especially those who prescribe such medications. In addition, drug overdose deaths from exceed motor vehicle deaths and are projected to surpass 70,000 deaths by the end of 2019.[47]

As with alcohol misuse, there are age variations in the nonmedical use of prescription drugs. NSDUH data show a relatively stable rate in the nonmedical use of pain relievers in the past month, from 1.9% to 1.7% over 2005–2013. However, in young adults 18–25 years of age, there has been a gradual *decrease* in the nonmedical use of prescription drugs from 4.7% to 3.3% for the same period. Concomitantly, there has been a gradual increase for adults 26 or older from 1.3% to 1.5% during that period. In 2013 alone, an estimated 4.5 million individuals were currently misusing prescription pain relievers (Fig. 1.6). However, although the



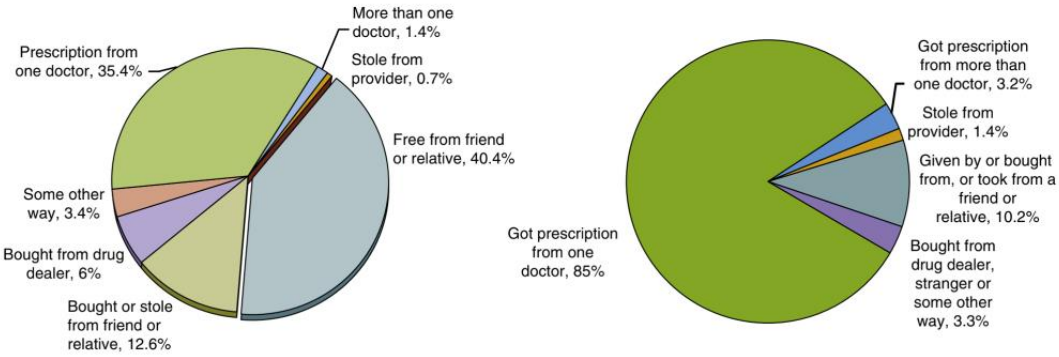
• **Fig. 1.6** Nonmedical use of prescription pain relievers in the past month, by age group: percentages, 2005–2013. (Data from SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2002–2013.)

methodology is not comparable between 2013 and 2016, in 2016 an estimated 3.35 million people were identified as misusing pain relievers, down from 3.8 million in 2015.

Additional data from the NSDUH highlight that 40% of persons who acquire prescription drugs for nonmedical use get them free from friends and family members. Another 12.6% have bought or stolen them from friends or relatives. Furthermore, when asked where the friends and family members got the prescription drugs, the majority of the respondents reported getting their drugs from a single physician (Fig. 1.7).

It is now well established that individuals are not just consuming prescription drugs "recreationally." Many are developing problems associated with their use. The NSDUH looked at individuals who meet criteria for abuse or dependence and found that number to be approximately 2.5 million age 12 or older. Within the prescription drug category, prescription pain relievers account for 1.75 million of the individuals who meet criteria for abuse or dependence, making prescription drugs the second most common category of drugs of misuse and the second most common category of abuse and dependence.

Thus it is clear that the misuse of prescription drugs is a public health problem of importance. In 2011 the Centers for Disease and Prevention (CDC) declared prescription drug abuse an epidemic. In addition during the same year, the Office of National Drug Control Policy (ONDCP) released a report entitled "Epidemic:



• **Fig. 1.7** Source where pain relievers were obtained for most recent nonmedical use among past-year users age 12 or older: 2016. Note: Totals may not sum to 100% because of rounding or because suppressed estimates are not shown. (Data from SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2016.)

Responding to America's Prescription Drug Abuse Crisis"; the ONDCP also promulgated a Prescription Drug Abuse Prevention Plan, which focused on (1) education, (2) monitoring, (3) proper medication disposal, and (4) enforcement. However, the problem of misuse of prescription drugs is complicated by the therapeutic need for the various agents, especially pain relievers, for clinical purposes. There does not seem to be any question about the need to treat pain adequately. In fact, NSDUH data reveals that in 2016, 62% of those who misused prescription pain relievers in the past year used those medications in their last episode of misuse to relieve physical pain.[9] It is not clear whether this physical pain was associated with withdrawal or with the undertreatment of nonwithdrawal-related physical pain.

Among the implications of these findings are that prescribers of prescription drugs must assume some role in the education of patients or clients about the appropriate use of prescription drugs, and that the appropriate disposition of unused prescription drugs by patients and clients needs to be emphasized. Because prescription drug misuse is intimately tied to the therapeutic use of critical medications, strategies that simply address drug dealing, Internet sales, misprescribing clinicians, and doctor shopping are inadequate. Forty-nine US states and the District of Columbia have prescription drug monitoring program (PDMP) laws as a way of tracking the behavior of both patients and prescribers.[40] Missouri's governor, by executive order, created a statewide PDMP, making Missouri the last state to adopt a PDMP.[29]

PDMPs continue to evolve with information technology. Some programs are hampered because they are not operating in real time but promise to become real time in the future. Another limitation of PDMPs is that they are often limited to specific states and do little to address patient or physician behavior across state jurisdictional lines. Furthermore, PDMPs may not be as effective in reducing doctor shopping or reducing diversion of controlled substances as intended.[37] Nevertheless, it appears that PDMPs are associated with reductions in opioid use among disabled and older Medicare beneficiaries.[39]

As suggested earlier, the category of prescription drugs that ranks highest in abuse is that of analgesics, particularly pain relievers in the Controlled Substances Act (CSA) Schedules II and III.[16] The treatment of pain in American society is the fundamental basis for the use of controlled substances, and access to appropriate pain medication is essential. Strategies designed to monitor the prescribing of pain relievers were historically not proffered as efforts to limit access to pain medication, but to discourage the misprescribing of pain medication. However, among prescribing practitioners the fear of legal consequences may have a "chilling" effect.

An older study by Goldenbaum et al. noted that only 725 physicians between 1998 and 2006 were criminally charged and/or administratively reviewed for offenses associated with the prescribing of opioid analgesics.[28] This represented only 0.1% of the estimated 691,873 patient-care physicians active in 2003. Furthermore, the study concluded that "Practicing physicians, including Pain Medicine specialists, have little objective cause for concern about being prosecuted by law enforcement or disciplined by state medical boards in connection with the prescribing of CS [controlled substances] pain medications."[28] However, times have changed.

Both state and federal prosecutors have brought charges against physicians and other prescribers for questionable pain management practices involving the use of opioid analgesics. In addition, attorneys general have filed claims against at least two pharmaceutical companies. Multiple state and local governments have sued Purdue Pharma, accusing it of deceptive marketing and of convincing physicians that oxycodone (OxyContin) had a low risk of addiction; as early as 2007 Purdue Pharma agreed to pay $634.5 million to resolve a US Department of Justice claim. In addition, in 2017, two companies, McKesson, a pharmaceutical drug distributor, and Mallinckrodt LLC, a pharmaceutical company, were required to pay the US government millions to settle claims that they violated provisions of the CSA and that they failed to design and implement effective systems to detect and report "suspicious orders" for controlled substances. McKesson agreed to pay $150 million and Mallinckrodt agreed to pay $35 million.[20,68]

Although Goldenbaum et al. concluded that physicians have little objective cause for concern, physicians are being held liable for misprescribing opioids and for the deaths of their patients who overdose on opioid analgesics.[28] An analysis of the National Practitioner Data Bank (NPDB), from 2011 to 2014, revealed that the United States Drug Enforcement Administration (DEA) has stepped up its actions against physicians; in 2011 there were 88 such cases, but in 2014, there were 371 cases.[74] Furthermore, in 2015, a California physician was convicted of murder for overprescribing opioid analgesics and sentenced to 30 years to life in

prison. Individual physicians in New York, Texas, and Oklahoma have also been charged with murder after overprescribing resulted in overdose deaths.[17]

It should be noted, however, that the average prescriber with a routine acute care population with requirements for low-dose, short-duration opioids should have little to fear from the administrative and legal processes monitoring physician-prescribing behavior. A study by Blue Cross/Blue Shield (BCBS) reviewed the rate of patients diagnosed with opioid use disorders and their opioid use by dosage and duration in 2015, and they found substantial increases in opioid use diagnoses for those with high dosage (more than 100 morphine-equivalent daily doses), whether short duration or long duration, compared to those with low dosage. Furthermore, the BCBS study found that with high dosage, it was the duration of the prescription that produced the highest rate of diagnosed opioid use disorder (OUD); high-dose opioid prescriptions beyond 7 days produced the highest rates of OUDs.[7]

The policy discussion about pain and the use of controlled substances for the management of pain in patients is an important one. With an estimated 50–60 million people within the United States with chronic pain, and a larger estimate of the prevalence of various acute pain syndromes, the availability of appropriate treatment strategies is of critical importance.

The legitimate role of controlled substances in the treatment of the spectrum of pain-related conditions is often discussed. Clinicians are admonished to use clinical guidelines, transparent practices with documentation, and conservative strategies when monitoring patient compliance and dysfunctional patient behavior. Clinicians are also told to anticipate that some percentage of their patients or clients may develop SUDs associated with their treatment regimens or may present to treatment with preexisting SUDs or vulnerabilities.

Prescription opioid dependence is also associated with other psychiatric conditions. Depression and posttraumatic stress disorders are two DSM-5 (*Diagnostic and Statistical Manual of Mental Disorders*, *Fifth Edition*) diagnoses found to be related to OUDs. Managing co-occurring disorders and chronic pain conditions requires specific treatment strategies that take into account the full spectrum of the patient's conditions.

In 2016, the CDC issued the "CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016."[19] These guidelines are recommendations for primary care clinicians who are prescribing opioids for chronic noncancer pain treatment; the guidelines are not for cancer treatment, palliative care, or end-of-life care. The guidelines focus on: "(1) when to initiate or continue opioids for chronic pain; (2) opioid selection, dosage, duration, follow-up, and discontinuation; and (3) assessing risk and addressing harms of opioid use."

In 2017, the Federation of State Medical Boards (FSMB) released an updated version of its "Guidelines for the Chronic Use of Opioid Analgesics."[24] The preamble of the FSMB Guidelines stated that the diagnosis and treatment of pain is integral to the practice of medicine. While noting that the FSMB Guidelines are not a specific standard of care for the safe and evidenced prescribing of opioids for the treatment of chronic, noncancer pain, the FSMB contends that the fact-specific totality of circumstances should govern the decision to use opioids over other pharmacological and nonpharmacological treatment of chronic noncancer pain.

In addition to the CDC and the FSMB, a number of states have promulgated their own guidelines for the use of opioid analgesics for the treatment of pain. Washington State,[71] Arizona,[2] Tennessee,[63] Ohio,[45] Indiana,[30] and Wisconsin[72] are just some examples.

To enhance pain research, the National Institutes of Health (NIH) Pain Consortium was established in 2006. This consortium promotes collaborative activities among researchers across the NIH institutes and centers that have programs and activities addressing pain.[42] The NIH Pain Consortium has the following goals:

- To develop a comprehensive and forward-thinking pain research agenda for the NIH—one that builds on what we have learned from our past efforts.
- To identify key opportunities in pain research, particularly those that provide for multidisciplinary and trans-NIH participation.
- To increase visibility for pain research—both within the NIH intramural and extramural communities, as well as outside the NIH. The latter audiences include our various pain advocacy and patient groups that have expressed their interests through scientific and legislative channels.
- To pursue the pain research agenda through public-private partnerships, wherever applicable. This underscores a key dynamic that has been reinforced and encouraged through the Roadmap process.

In addition to the NIH, the US Department of Health and Human Services (HHS) through the NIH established the Interagency Pain Research Coordinating Committee (IPRCC) to coordinate all pain research efforts within the HHS and across other federal agencies. The IPRCC was instrumental in 2016 in promulgating the National Pain Strategy, which outlined a coordinated plan for reducing the burden of chronic pain that affects millions of Americans. The Implementation of the National Pain Strategy includes such activities as (1) professional education and training, (2) public education and communication, (3) disparities, (4) prevention and care, (5) service delivery and payment, and (6) population research.[43]

Opioid Overdose Deaths

By the end of 2015, drug overdoses accounted for 52,404 deaths in the United States; this included 33,091 deaths (63.1%) that involved an opioid.[49] From 2014 to 2015, the death rate from synthetic opioids other than methadone, which includes fentanyl, increased by 72.2%, and heroin death rates increased by 20.6%.

The issue of the pain management and the appropriate use of opioids in a therapeutic context has been complicated by the advent of an increase in the use of illicitly manufactured fentanyl and carfentanil, in addition to heroin use. Fentanyl and its analog carfentanil were estimated to account for the single largest category of opioid overdose deaths in 2017, with an estimated 20,000 deaths, or 38% of all opioid deaths. The precursor to the wave of opioid overdoses and overdose deaths was thought to be the increase in prescribing of prescription opioids, which occurred even though there has been no change in the amount of pain experienced by people in the United States.[46]

The hue and cry about opioid overdoses resulted in actions by the US Congress discussed later in this chapter, and by the President of the United States. In 2017, President Trump appointed a Commission on Combating Drug Addiction and the Opioid Crisis. The Interim Report of that Commission called upon the President to declare a national emergency under either the Public Health Service Act or the Stafford Act.[46] In addition to calling for a National Emergency, the Interim Report called for, among other things to:

1. Rapidly increase treatment capacity. Grant waiver approvals for all 50 states to quickly eliminate barriers to treatment resulting from the federal Institutions for Mental Diseases (IMD) exclusion within the Medicaid program.

2. Mandate prescriber education initiatives with the assistance of medical and dental schools across the country to enhance prevention efforts. Mandate medical education training in opioid prescribing and risks of developing an SUD by amending the CSA to require all DEA registrants to take a course in proper treatment of pain. HHS should work with partners to ensure additional training opportunities, including continuing education courses for professionals.
3. Immediately establish and fund a federal incentive to enhance access to medication-assisted treatment (MAT). Require that all modes of MAT are offered at every licensed MAT facility and that those decisions are based on what is best for the patient. Partner with the NIH and the industry to facilitate testing and development of new MAT treatments.
4. Better align, through regulation, patient privacy laws specific to addiction with the Health Insurance Portability and Accountability Act (HIPAA) to ensure that information about SUDs be made available to medical professionals treating and prescribing medication to a patient.
5. Provide model legislation for states to allow naloxone dispensing via standing orders, as well as requiring the prescribing of naloxone with high-risk opioid prescriptions; we must equip all law enforcement in the United States with naloxone to save lives.
6. Prioritize funding and manpower to the Department of Homeland Security (DHS) Customs and Border Protection, the Department of Justice Federal Bureau of Investigation (FBI), and the DEA to quickly develop fentanyl detection sensors and disseminate them to federal, state, local, and tribal law enforcement agencies. Support federal legislation to staunch the flow of deadly synthetic opioids through the US Postal Service (USPS).
7. Provide federal funding and technical support to states to enhance interstate data sharing among state-based PDMPs to better track patient-specific prescription data and support regional law enforcement in cases of controlled substance diversion. Ensure federal health care systems, including veteran's hospitals, participate in state-based data sharing.
8. Enforce the Mental Health Parity and Addiction Equity Act (MHPAEA) with a standardized parity compliance tool to ensure that health plans cannot impose less favorable benefits for mental health and substance use diagnoses versus physical health diagnoses.

Notice how broad is the spectrum of efforts recommended to address the issue of opioid misuse and how focused are those efforts on engaging the medical establishment and changing its clinical behavior with regard to prescription opioids.

Naloxone and Opioid Overdose

As the President's Commission on Combating Drug Addiction and the Opioid Crisis observes, naloxone is a drug that can be used to reverse opioid overdose. The increase in opioid-related deaths has prompted the public health community to provide naloxone to at-risk individuals and their families. Community-based opioid-overdose prevention programs and first responders, such as police officers, have equipped themselves with naloxone in order to save the lives of individuals who have consumed opioids to the point of respiratory depression leading to coma. In 2014, the Substance Abuse and Mental Health Services Administration (SAMHSA) published an Opioid Overdose Prevention Toolkit that serves as a foundation for educating and training of (1) communities, (2) prescribers of opioid pain medications, (3) first responders, (4) patients who have been prescribed opioid medications, and (5) individuals and family members who have experienced an opioid overdose. Clinicians concerned about opioid overdose as a risk from prescribing opioids should access this overdose toolkit for themselves and their patients.[58]

Over the past decade, substantial research has been done to map out the dimensions of the prescription drug misuse problem. Clinical treatment strategies for patients with pain who require controlled substances will still need to be refined, whereas substance abuse prevention and treatment programs will need to develop targeted treatment protocols.

As previously mentioned, recent survey data indicate that approximately 40% of diverted pain relievers are obtained free from friends and family members. Another 12.6% of individuals either bought their pain relievers from a friend or a relative, or stole their pain relievers from a friend or relative. In short, almost 53% of individuals who admit to the nonmedical use of pain relievers got them from friends or family. This means that there is a substantial cultural component to prescription drug misuse. The attitudes and values of the community constitute a major component of the problem. This clearly means that public health and medical efforts need to be directed toward altering community attitudes as well as provider attitudes.

Clinicians, researchers, and others who are interested in the public health implications of prescription drug abuse should obviously focus more energy on addressing the social and behavioral features of the social network aspects of prescription drug transactions. An emphasis on appropriate prescribing, with minimal excess, and appropriate storage with limited access, should be incorporated into clinician-patient interactions. In addition, clinicians should advise patients or clients about the appropriate disposal of excess controlled substances; this enlists the patient further in accepting responsibility for the medication and enhances the awareness that controlled substances can be dangerous if misused. SUD specialists should also be aware of the increase in prevalence of prescription drug abuse, with a particular recognition that prescription opioids are a growing problem among individuals with abuse and dependence who might present for treatment.

Legislative, Regulatory, and Community Controls Over Opioid Prescribing

In the previous edition of this book, it was noted that clinicians in general should be aware that an ongoing problem of prescription drug misuse, particularly with narcotic analgesics, will produce calls for increased regulation and control of prescribing authority and patient access.

With one in four adults in the United States saying that they had a day-long bout of pain in the past month, and 1 in 10 saying that the pain lasted a year or more,[10] the issue of treatment of pain in this country is quite real. These numbers amount to 76 million people who have had a day-long bout of pain in the past month and 30.5 million who have had pain lasting a year or more. With 5.2 million people admitting to the nonmedical use of opioid pain relievers, the larger number of individuals potentially affected by legal or regular constraints of the prescription of controlled substances for therapeutic purpose would be those who have pain, not those who misuse or divert pain medications.

Common chronic pain complaints include headache, low back pain, cancer pain, arthritis pain, neurogenic pain (pain resulting from damage to the peripheral nerves or to the CNS itself), and psychogenic pain (pain not due to past disease or injury or any visible sign of damage inside or outside the nervous system). Whether all of these conditions require the use of specific opioid medications for any specific patient should be determined by research and clinical evidence. However, concerns have produced demands for change.

In 2012, the US Food and Drug Administration (FDA) published the extended-release (ER)/long-acting (LA) Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS). This was followed by the 2017 extension of REMS for immediate-release (IR) opioid analgesics.[70] The goal of this REMS is to reduce serious adverse outcomes resulting from inappropriate prescribing, misuse, and abuse of opioid analgesics while maintaining patient access to pain medications. Adverse outcomes of concern include addiction, unintentional overdose, and death. The REMS program requires health professional training in pain management, including the principles of acute and chronic pain management, nonpharmacologic treatments for pain, and pharmacologic treatments for pain (both nonopioid analgesic and opioid analgesic).

In 2014, the DEA rescheduled all hydrocodone combination products from Schedule III to Schedule II of the CSA; this action followed a public hearing that was required by Section 1139 of Public Law 112-144, the FDA Safety and Innovation Act (FDASIA) of 2012. In addition, the DEA put together its DEA 360 Strategy, which involves coordinated law enforcement operations targeting all levels of drug trafficking organizations and violent gangs that supply drugs to our neighborhoods; engaging drug manufacturers, wholesalers, practitioners, and pharmacists through diversion control to increase awareness of the opioid epidemic and encourage responsible prescribing practices, and use of opioid painkillers throughout the medical community; community outreach and partnership with local organizations following enforcement operations; and equipping and empowering communities to fight the opioid epidemic.[21]

Another strategy proposed by the DEA is to reduce the amount of controlled substance that may be manufactured in the United States. Schedule II opioid pain relievers such as oxycodone, hydrocodone, oxymorphone, hydromorphone, morphine, and fentanyl would be reduced by an average of 10% in 2019. Of interest, the DEA reports that the demand for these opioid medicines has dropped apparently as a result of state monitoring—using, among other things, PDMPs.[22,25]

Medication-Assisted Treatment Prescription Drug and Opioid Addiction Grant Program

In response to the growing opioid epidemic, in 2015, SAMHSA issued a grant program called the Medication-Assisted Treatment Prescription Drug and Opioid Addiction (MAT-PDOA) program. MAT-PDOA provides funding to states to:

- Enhance or expand their treatment service systems to increase access to MAT by building capacity.
- Provide MAT and recovery services that are accessible, effective, comprehensive, coordinated, and evidence-based.

Target populations include people with OUDs who are seeking or receiving MAT, with a particular focus on racial, ethnic, sexual, and gender-identity minority groups. Examples of some of these populations include pregnant and parenting women, people in the criminal justice system, veterans, and rural communities.[62]

The 2015 cohort of the MAT-PDOA grantees included only 11 states, which divided $12 million for this effort. The 2016 cohort of the MAT-PDOA grantees included another 11 states, with funding levels from $950,000 to $1 million.

Comprehensive Addiction and Recovery Act

In addition to the actions of the HHS to expand the number of patients that a physician can see, the Comprehensive Addiction and Recovery Act (CARA) of 2016, Public Law 114-198, made changes that were designed to respond to the opioid epidemic. CARA is a comprehensive authorization bill that ultimately got linked to a major appropriations bill, the 21st Century Cures Act discussed later.

CARA has nine titles that cover a wide range of issues: (1) Title I covers prevention and education; (2) Title II covers law enforcement and treatment; (3) Title III covers treatment and recovery; (4) Title IV covers a Government Accountability Office (GAO) Report on Recovery and Collateral Consequences; (5) Title V covers addiction and treatment services for women, families, and veterans; (6) Title VI covers state demonstration grants for comprehensive opioid abuse response; (7) Title VII covers miscellaneous provisions such as partial refills of Schedule II controlled substances and Good Samaritan assessments; (8) Title VIII deals with the protection of classified information in federal court challenges under the Foreign Narcotics Kingpin Designation Act; and (9) Title IX covers the Department of Veterans Affairs (VA) with four subtitles.[15]

Although the full act is too voluminous to cover here, there are several key provisions that are germane to the theme of this chapter. Section 101 of Title I authorized the creation of a Pain Management Best Practices Inter-Agency Task Force made up of a wide range of entities including representatives from the HHS, VA, the Department of Defense (DOD), the ONDCP, physicians, dentists, nonphysician prescribers, pharmacists, pain researchers, patient advocates, and patients; this task force has a 2-year term. A draft report describing preliminary recommendations of the Task Force will be finalized and submitted to Congress in 2019.

Section 107 of Title I, Improving Access to Overdose Treatment, authorized the Secretary of the HHS to award grants of up to $200,000 per year to federally qualified health centers (FQHCs), opioid treatment programs (OTPs), or any practitioner waivered to prescribe buprenorphine to establish a naloxone coprescription program, train health care providers on naloxone coprescribing, purchase naloxone, offset copayments for naloxone, or establish protocols to connect patients who have experienced an overdose with appropriate treatment.

Section 110 of Title I, Opioid Overdose Reversal Medication Access and Education program, authorized the HHS Secretary to make grants to states to implement strategies for pharmacists to dispense naloxone pursuant to a standing order and to develop naloxone training materials for the public.

Section 201 of Title II, Comprehensive Opioid Abuse Grant Program, authorized $103 million to the DOJ for a comprehensive opioid abuse grant program for alternatives to incarceration. Section 203 of Title II, Prescription Drug Take Back Expansion, authorized the expanding or making available disposal sites for unwanted prescription medications.

Section 301 of Title III, Evidence-based Prescription Opioid and Heroin Treatment and Interventions Demonstration,

authorizes the HHS Secretary to award grants to state substance abuse agencies, local governments, and nonprofit organizations in areas with high rates of or rapid increases in heroin or other opioid use to expand the availability of MAT. It authorizes $25 million for each fiscal year between 2017 and 2021.

Section 302 of Title III, Building Communities of Recovery, authorizes the HHS Secretary to award $1 million to be used for grants to recovery community organizations to enable them to develop, expand, and enhance recovery services. However, the federal share of the costs of a program funded by the grant may not exceed 50%.

Section 303 of Title III, Medication-Assisted Treatment for Recovery from Addiction, makes several changes to the law regarding office-based opioid addiction treatment with buprenorphine. Specifically, it:

- Expands prescribing privileges to nurse practitioners (NPs) and physician assistants (PAs) for 5 years (until October 1, 2021). NPs and PAs must complete 24 hours of training to be eligible for a waiver to prescribe and must be supervised by or work in collaboration with a qualifying physician if required by state law. The HHS Secretary has 18 months to issue updated regulations governing office-based opioid addiction treatment to include NPs and PAs.
- Gives the HHS Secretary the authority to exclude from the patient limit those patients to whom medications are directly administered.
- Allows states to lower the patient limit and allows states to require practitioners to comply with additional practice setting, education, or reporting requirements. States may not lower the patient limit below 30.
- Directs the HHS Secretary to review every 3 years the provision of opioid addiction treatment services in the United States and to submit a report to Congress, including an assessment of whether there is a need to change the patient limit.

Section 501 of Title V, Improving Treatment for Pregnant and Postpartum Women, reauthorizes a grant program for residential opioid addiction treatment of pregnant and postpartum women and their children and creates a pilot program for state substance abuse agencies to address identified gaps in the continuum of care, including nonresidential treatment services.

Section 601 of Title VI, State Demonstration Grants for Comprehensive Opioid Abuse Response, authorizes the HHS Secretary to award grants to states to establish a response plan to the opioid epidemic. The plan may include:

- Education efforts related to opioid use, treatment, and addiction recovery, including education of medical students, residents, physicians, and other controlled substances prescribers.
- Establishing, maintaining, or improving a PDMP.
- Expanding the availability of prescription opioid addiction treatment.
- Developing, implementing, and expanding efforts to prevent opioid overdose deaths.
- Advancing education and awareness of the public regarding the dangers of opioid misuse, safe medication disposal, and detection of early signs of opioid addiction.

Although CARA authorizes a number of new and innovative programs, it is not an appropriations bill. Thus it was not until the 21st Century Cures Act was passed and made into law in December of 2016 that resources were genuinely available to foster change. However, with respect to buprenorphine, the inclusion of appropriate NPs and PAs into the ranks of qualified prescribers promises to expand the number of clinicians available to prescribe the agent to those who need that medication. It should be noted that CARA only gave those NPs and PAs independent authority to prescribe buprenorphine in those jurisdictions where the right to practice independently existed and where the authority to prescribe Schedule II, III, or IV drugs was a part of that independent right.

21st Century Cures Act

The 21st Century Cures Act, Public Law 114-255, signed into law in December of 2016, is an important appropriations law that is divided into three divisions:

- Division A: 21st Century Cures
- Division B: Helping Families in Mental Health Crisis
- Division C: Increasing Choice, Access, and Quality in Health Care for Americans

Of the three divisions, several titles, and subtitles, while not discounting the importance of the other provisions, only several are of immediate interest to this chapter. Section 103 of Title I of Division A provides for an account for funding to the states. It provides for $1 billion over 2 years for grants to states to supplement opioid abuse prevention and treatment activities, such as improving PDMPs, implementing prevention activities, training for health care providers, and expanding access to opioid treatment programs. It provides for ensuring accountability without increasing burden on states by requiring grantees to report on activities funded by the grant in the substance abuse block grant report.[64]

Title VI of Division B of the 21st Century Cures Act, otherwise known as the Helping Families in Mental Health Crisis Act of 2016, focuses on the reorganization of the SAMHSA. Of note here is that it changes the top leadership of that agency from an administrator to an Assistant Secretary.

It requires the Assistant Secretary to, among other things:

- Work with relevant agencies of the HHS on integrating mental health promotion and SUD prevention with general health promotion and disease prevention, and integrating mental and SUD treatment services with physical health treatment services;
- Use by SAMHSA programs of evidence-based and promising best practices for prevention, treatment, and recovery support services for individuals with mental health and SUDs,
- Collaborate with the Secretary of Defense and the Secretary of Veterans Affairs to improve the provision of mental health and SUD services provided by the DOD and the VA to members of the Armed Forces, veterans, and the family members of such members and veterans, including through the provision of services using the telehealth capabilities of the DOD and VA;
- Advance, through existing programs, the use of performance metrics;
- Work with states and other stakeholders to develop and support activities to recruit and retain a workforce addressing mental health and SUDs.

CARA and the 21st Century Cures Act are important because they created the potential for an expanded substance abuse treatment system focusing on the opioid crisis. SAMHSA released funding for the first phase of the $1 billion appropriation under the 21st Century Cures in April of 2017. This initiative was called the State Targeted Response (STR) grant program. STR funding went to state authorities for subsequent programing involving community-based entities.

State-Targeted Response to the Opioid Crisis Grants (Short Title: Opioid STR)

SAMHSA, the Center for Substance Abuse Treatment (CSAT), and the Center for Substance Abuse Prevention (CSAP) accepted applications for fiscal year (FY) 2017 State Targeted Response to the Opioid Crisis Grants (Short Title: Opioid STR). The program aims to address the opioid crisis by increasing access to treatment, reducing unmet treatment need, and reducing opioid-related overdose deaths through the provision of prevention, treatment, and recovery activities for OUD (including prescription opioids as well as illicit drugs such as heroin). These grants were awarded to states and territories via formula based on unmet need for OUD treatment and drug-poisoning deaths.

Grantees are required to do the following: use epidemiological data to demonstrate the critical gaps in availability of treatment for OUDs in geographic, demographic, and service level terms; utilize evidence-based implementation strategies to identify which system design models will most rapidly address the gaps in their systems of care; deliver evidence-based treatment interventions including medication and psychosocial interventions; and report progress toward increasing availability of treatment for OUDs and reducing opioid-related overdose deaths based on measures developed in collaboration with the HHS.

The STR program supplements activities pertaining to opioids currently undertaken by the state agency or territory and supports a comprehensive response to the opioid epidemic using a strategic planning process to conduct needs and capacity assessments. The results of the assessments identify gaps and resources from which to build upon existing substance use prevention and treatment activities.

STR Grantees were required to describe how they would expand access to treatment and recovery. Grantees were also required to describe how they would advance substance misuse prevention in coordination with other federal efforts such as those funded by the CDC. Grantees must use funding to supplement and not supplant existing opioid prevention, treatment, and recovery activities in their state. Grantees were required to describe how they will improve retention in care, using a chronic care model. To the extent applicable, grantees should align STR prevention efforts with CDC's State's Opioid Program.[62]

Under the STR program, some states received as little as $2 million a year, whereas other states received substantially more. California, for example, received $44 million in extra funding, while Maine received $2 million. Abstracts from the funded STR grants can be found on the SAMHSA website.[62]

Most of the funds under the STR grant were for the use of medications. Thus narcotic treatment programs that use methadone and entities that use buprenorphine or naltrexone for the treatment of OUDs are playing a major role in addressing the opioid epidemic. Physicians and other prescribers will be mobilized to work under the auspices of the STR grant program.

Medication-Assisted Treatment

Methadone

The misuse of opioids can produce abuse and dependence that requires treatment. There are three treatment strategies: use of methadone, use of buprenorphine, and use of naltrexone. Methadone has been used for more than 40 years in the treatment of drug addiction. Its use for treatment of pain has increased in the last 5–10 years. Methadone can cause fatalities in individuals who have not developed any tolerance to opiates: children and adults who accidentally take methadone and those who experience fatal intoxications during the first weeks of treatment or as the result of adjusting a methadone dose. Several risk factors have been identified for methadone mortality: the concomitant use of benzodiazepines and other opioids, and/or alcohol; an elevated risk of some individuals for torsade de pointes; inadequate or erroneous induction dosing and monitoring by physicians, primarily when prescribing methadone for pain; and drug poisoning that occurs as a result of diversion of the drug and its nonmedical use.

It is important for the clinician to recognize that there are differences between prescribed methadone for pain and dispensed methadone for MAT. When methadone is used for pain treatment, no required risk management plan has been required. However, an FDA-required black box label cautions methadone prescribers about (1) addiction, abuse, and misuse; (2) life-threatening respiratory depression; (3) accidental ingestion; (4) life-threatening QT prolongation; (5) neonatal opioid withdrawal syndrome; (6) cytochrome P450 interaction; and (7) risks from concomitant use with benzodiazepines or other CNS depressants.[69] Prescribers who are unfamiliar with methadone should refer to the package insert and pay close attention to the black box warning.

When methadone is used for addiction treatment, the distribution is limited to certified, accredited, and registered programs. There are limits on the initial dose and restrictions on dispensing. The federal government, through SAMHSA, recognizes the following entities as accrediting bodies: Joint Commission on Accreditation of Health Care Organizations, Commission on Accreditation of Rehabilitation Facilities, Council on Accreditation, National Commission on Correctional Health Care, and the state authorities of Missouri and Washington. For detoxification and maintenance of opioid dependence, methadone should be administered in accordance with the treatment standards cited in 42 CFR Section 8, including limitations on unsupervised administration; these federal regulations govern the use of methadone for the treatment of opioid use disorders. In 2016, there are only about 1283 opioid treatment programs licensed by the federal government. Those programs treat approximately 345,443 individuals.

Another public health concern associated with the therapeutic use of opioids is the phenomenon of deaths associated with their use. The CDC reported that there has been a 9.1% decrease in methadone-related deaths between 2014 and 2015.[11]

Within the opioid treatment community, there is concern about the prolongation of the rate-corrected QT interval and its relationship with torsade de pointes, potentially leading to sudden death. As more methadone is being used for the treatment of pain, it has become clear that even in the treatment of opioid dependence some risk exists for patients. Special concern applies to patients who are being induced onto methadone.

SAMHSA's Center for Substance Abuse Treatment convened two expert panels over a 4-year period to examine etiologic factors related to methadone mortality. As a result of those reviews, it became clear that there were those in the medical community who believed that a routine preinduction electrocardiogram screening should occur for all patients to measure the QTc interval and a follow-up electrocardiogram should occur within 30 days and annually thereafter. Particular sensitivity should be exhibited for patients with histories of cardiac dysfunction.[34]

Although this advice is directed to opioid treatment programs, it applies to patients who are receiving methadone for the treatment of chronic pain. Such advice recognizes that there are clinical challenges in the use of opioid medications, such as methadone,