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Prescription drug misuse: Epidemiology, prevention, identification, and management

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INTRODUCTION

Opioid analgesics, benzodiazepines, other sedatives and tranquilizers, and stimulants have important medical uses, but they also stimulate the reward center of the brain. In susceptible individuals, this can lead to misuse, substance use disorders, and other serious consequences. It has also led to the development and persistence of an illicit market for these medications, which creates additional public health risk due to mislabeled, contaminated, or counterfeit products.

Despite government regulation of these medications, prescription drug misuse and its consequences persist. Clinicians who prescribe these medications have an important role in preventing, identifying, and managing problems related to prescription drug misuse.

This topic reviews the epidemiology, prevention, identification, and management of prescription drug misuse. The epidemiology, pathogenesis, clinical manifestations, course, assessment, diagnosis, and treatment of opioid use disorder, benzodiazepine use disorder, and stimulant use disorder are discussed separately.

- (See "Opioid use disorder: Epidemiology, clinical features, health consequences, screening, and assessment".)
- (See "Opioid use disorder: Pharmacologic management".)
- (See "Benzodiazepine use disorder".)

- (See "Methamphetamine use disorder: Epidemiology, clinical features, and diagnosis".)
- (See "Cocaine use disorder: Epidemiology, clinical features, and diagnosis".)
- (See "Stimulant use disorder: Psychosocial management".)
- (See "Stimulant use disorder: Treatment overview".)

TERMINOLOGY

Controlled substances — Due to their potential for misuse, addiction, and illicit diversion, opioid analgesics, stimulants, and benzodiazepines and other sedatives/hypnotics are regulated, restricting whether and how they can be prescribed. In the United States, these drugs are referred to as "controlled substances" and subject to federal regulations (table 1).

Prescription drug misuse — Any use of a prescription medication that is outside of the manner and intent for which it was prescribed. This includes overuse, use to get high, diversion (sharing or selling to others), nonprescribed use or nonclinician sources of the medication, having nondisclosed prescribers, and concurrent use of alcohol, illicit substances, or nonprescribed controlled medications. While commonly present in cases of substance use disorder, misuse is not sufficient for diagnosis of a substance use disorder.

Nonmedical use — Initially defined by the National Survey on Drug Use and Health (NSDUH), as use of a medication that was not prescribed to the individual, or use "only for the feeling or experience it caused" [1]. The NSDUH has eliminated the term in favor of "misuse," which the survey defines as use in any way not directed by a clinician, including use without a prescription of one's own; use in greater amounts, more often, or longer than told to take a drug; or use in any other way not directed by a clinician.

Prescription drug use disorder — Misuse of a prescription drug meeting the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria as a substance use disorder, which can be specified as mild, moderate, or severe [2]. Substance use disorder replaced the terms substance abuse and substance dependence from the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). Prescription drug use disorders can also be characterized by the type of prescription drug used. (See "Benzodiazepine use disorder" and "Opioid use disorder: Epidemiology, clinical features, health consequences, screening, and assessment".)

EPIDEMIOLOGY

Misuse of prescription drugs has generally increased concurrently with greater prescribing of medication for therapeutic use, with some declines in misuse as prescribing rates have fallen. This is particularly true of opioid analgesics prescribed for patients with chronic pain, stimulants prescribed for individuals with attention deficit hyperactivity disorder (ADHD), and benzodiazepines prescribed for anxiety/insomnia; prescribing for each increased markedly between 2000 and 2010 [3-5]. After decades of increasing prescription opioid use, data since the mid-2010s indicated a decline in opioid prescribing [6] and in nonmedical opioid use by adolescents [7]. With decreasing opioid prescribing, more commercially insured adults in the United States were prescribed depressants such as benzodiazepines and "z drugs" than were prescribed opioids from 2014 to 2019 [8].Prescription opioid use disorder has been reported to affect 1.8 percent of individuals 12 and over, more than twice as many as were affected by prescription tranquilizer or sedative use disorder (0.8 percent), and more than three times as many affected by prescription stimulant use disorder (0.5 percent) [9].

Opioid analgesics

Misuse — Estimates of the prevalence of opioid misuse among patients who are prescribed opioid analgesics vary widely, from 12 to 78 percent [10-17], reflecting differences in the sample populations and definitions of opioid misuse among studies.

As an example, the National Survey on Drug Use and Health (NSDUH) in the United States estimated that among approximately 76 million United States adults prescribed opioid drugs in the prior year, 12 percent reported prescription opioid misuse [17]. Compared with individuals who used prescribed opioids and did not report misuse, those reporting misuse of prescription opioids reported higher rates of other substance use, including cannabis, heroin, and benzodiazepine use, and were more likely to be depressed.

As opioid prescribing has decreased over the last several years, so have rates of misuse, particularly in certain age groups. A study analyzing NSDUH survey years 2015 to 2019 found significant declines in past-year opioid misuse in adolescents, young adults, and adults 26 to 34 years and a nonsignificant decline among adults 35 to 64 years, with a nonsignificant increase in those 65 and older [18].

Motives for prescription opioid misuse tend to differ by age group. Among 5800 individuals with prescription opioid misuse who participated in the 2015 to 2016 NSDUH, a greater proportion of adults 50 years or older misused opioids solely for the purpose of pain relief compared with young adults age 18 to 25 (65 versus 35 percent) [19]. Other motives for prescription opioid misuse included for relaxation, experimentation, and sleep. Prescription opioid misuse for

motives other than pain relief was associated with greater odds of benzodiazepine misuse, substance use disorder, and suicidal ideation in the prior year.

A National Institute on Drug Abuse-funded survey of over 45,000 public and private high school students found a marked decline in past-year misuse of prescription opioids among high school seniors over the previous six years: from 8.7 to 4.2 percent [20].

Another study reported an association between nonmedical prescription opioid misuse and subsequent initiation of heroin use in adolescents [21].

Use disorder — In a systematic review, the incidence of opioid use disorder among patients prescribed opioids for chronic pain was estimated to be 8 to 12 percent [22]. Cross-sectional studies from 2008 to 2015 reported the prevalence of opioid use disorder among patients prescribed long-term opioids for chronic pain to range from 3 to 26 percent [10,23,24]:

- 26 percent of patients within a large United States health system who were prescribed long-term opioids met criteria for DSM-IV opioid dependence in the past year [23]
- 19.7 percent of primary care patients prescribed long-term opioids met criteria specifically for prescription drug misuse or dependence in the past year [24]
- 3 percent of primary care patients prescribed long-term opioids met criteria for current opioid dependence using a more conservative 30-day measure [10]

The prevalence of opioid use disorder involving prescription opioids among the United States general population rose markedly from the mid-1990s to the mid-2010s and has since decreased. The proportion of United States individuals seeking substance use disorder treatment who reported prescription opioids as the primary substance used increased from 1.0 to 9.3 percent between 1995 and 2013 [25]; 88 percent of these individuals were White [25,26]. From 1995 to 2010, individuals in rural counties were more likely than those in urban counties to report prescription opioids as the primary substance (10.6 versus 4.0 percent) [27]. In 2019, 6.8 percent of United States individuals seeking substance use disorder treatment reported prescription opioids as the primary substance [28], compared with 23.4 percent for heroin.

Morbidity and mortality — Concurrent with increased use of opioid analgesics for pain management from the 1990s to the mid-2010s, associated morbidity and mortality rose markedly. In a national survey, from among 63,600 deaths in the United States in a single year, approximately 42,000 (66 percent) involved opioids [29]. However, while opioid prescribing has decreased, opioid-related overdose deaths have continued to rise, with approximately 68,000 in 2020 [30]. Of overdose deaths involving opioids, approximately 30 percent additionally involved

benzodiazepines [31], which compound the sedating and respiratory-depression effects of opioids and increase overdose risk. The majority of decedents from drug overdose were males between 1999 and 2014; however, overdose deaths involving opioid analgesics increased 516 percent among females and 300 percent among males [32]. The pathway from prescription opioid use disorder to heroin has been increasingly recognized [33], and the Centers for Disease Control and Prevention identified three waves of the overdose epidemic: prescription opioids, heroin, and most recently, ultra-potent illegally manufactured fentanyl [29]. The epidemiology of opioid overdose and prevention of lethal opioid overdose is discussed in greater detail separately. (See "Prevention of lethal opioid overdose in the community".)

Risk factors — Patient factors that have been associated with increased risk for opioid analgesic misuse when prescribed the medication for chronic pain include:

- Substance use disorder, including tobacco or alcohol use disorder, is consistently identified as a risk factor [11-13,24,34,35]
- Family history of a substance use disorder [24,36]
- Mental health disorder, including depression, posttraumatic stress disorder, and anxiety disorders [10,23,24,34,36-38]
- History of legal problems or incarceration [16,17,24]
- Age less than 40 to 45 years old, in most studies [10,11,16,34,39]

Studies are most robust for misuse, but the risk factors noted above are also generally considered to be risk factors for developing opioid use disorder and for overdose. (See "Opioid use disorder: Epidemiology, clinical features, health consequences, screening, and assessment", section on 'Risk factors'.)

Stimulants

Misuse — Stimulant prescribing for ADHD has increased since the 1990s [3,8]. Focusing on pharmaceutical stimulants only, data from the NSDUH has found that the general population past-year prevalence of prescription stimulant use (eg, methylphenidate or amphetamine products) was 6.4 percent and prevalence of misuse was 2.1 percent in the United States [40,41]. Prevalence of prescription stimulant misuse was highest among 18- to 25-year-olds. Several studies have focused exclusively on younger populations; the reported prevalence of past-year pharmaceutical stimulant misuse was 5 to 9 percent [42], and past-year methylphenidate use was 2 to 5 percent [43] among high school students. For college students, studies reported past-year pharmaceutical stimulant misuse prevalence rates of 5 to 6 percent,

and lifetime prevalence rates of 5 to 43 percent [40]. Another study analyzing NSDUH survey years 2015 to 2019 found significant annual declines in prescription stimulant misuse in young adults but slightly increasing annual rates among adults 35 to 49 years. In all other age groups, annualized changes in past-year stimulant misuse were nonsignificant [18].

Use disorder — According to the NSDUH, among individuals 12 or older who sought substance use treatment in the past year, 3.4 percent were for stimulant use disorder [41]. Another study reported that approximately 0.5 percent of United States individuals 12 or older had a past-year prescription stimulant use disorder [9]. However, robust estimates of the prevalence of pharmaceutical stimulant use disorders are lacking.

Morbidity and mortality — In 2019, over 16,000 individuals in the United States died of overdose death involving psychostimulants (methamphetamine, amphetamine, and methylphenidate). This corresponds to a more than six-fold increase in the age-adjusted rate of overdose from 2012 to 2019 [44]. The number of emergency department visits involving psychostimulants increased similarly from 2.2 per 10,000 residents to 12.9 per 10,000 residents, from 2008 to 2018 [45].

Stimulants may:

- Increase blood pressure
- Increase heart rate
- Increase body temperature
- Decrease sleep
- Decrease appetite
- Cause agitation
- Cause anxiety
- Cause paranoia

These symptoms are all more likely to occur when higher-than-prescribed doses are taken.

The overdose toxidrome may include [46]:

- Mydriasis
- Tremor
- Agitation
- Hyperreflexia
- Combative behavior
- Confusion
- Hallucinations

- Delirium
- Anxiety
- Paranoia
- Seizures
- Movement disorders

Risk factors — Studies of risk factors for pharmaceutical stimulant misuse have been predominantly among youths and young adults ages 12 to 25, especially college students. Reported risk factors for stimulant misuse include [40,47]:

- White race
- Involvement in a fraternity or sorority
- Grade point average below 3.5
- At least one episode of binge drinking in the past two weeks
- Past-month cannabis use
- Presence of conduct disorder

Sedatives-hypnotics

Misuse — Surveys of a nationally representative sample of United States residents age 12 and older found a fairly stable prevalence of past-month nonmedical use of sedatives (0.1 to 0.2 percent of respondents) and tranquilizers (0.7 to 0.9 percent of respondents) from 2002 to 2014 [48]. In another survey, the prevalence of past-year tranquilizer misuse among United States residents age 12 and older was 2.3 percent [49]. Benzodiazepine misuse accounted for the vast majority (89 percent) of tranquilizer misuse, and alprazolam products were the most commonly misused benzodiazepines. A study analyzing NSDUH survey years 2015 to 2019 found significant annual declines in benzodiazepine misuse in young adults but slightly increasing annual rates among adults 35 to 49 years. In all other age groups, changes in past-year benzodiazepine misuse were nonsignificant [18].

Use disorder — According to a national drug survey, estimated past-year prescription sedative or tranquilizer use disorder in the United States affected 682,000 individuals, or 0.2 percent of people age 12 or older. While this has been fairly stable since 2015 [50], combined opioid use disorder and benzodiazepine use disorder increased dramatically in the past twenty years; an analysis of substance use disorder treatment admissions showed a 569.7 percent increase in treatment admissions with both benzodiazepine and prescription opioid use from 2000 to 2010 [51]. Specific substance use disorders are described separately. (See "Benzodiazepine use disorder" and "Opioid use disorder: Epidemiology, clinical features, health consequences, screening, and assessment".)

Morbidity and mortality — Sedatives and tranquilizers have potent, dose-dependent central nervous system depressant effects. In the United States, overdose death involving benzodiazepines increased more than fourfold from 2002 to 2015 [32]. Co-ingestion of sedatives and tranquilizers with alcohol or opioids is an increasingly recognized and prevalent cause of overdose death [5,52-54]. From 2002 to 2015, there was a fivefold increase in overdose deaths involving both benzodiazepines and opioids [32]. In a multistate study of benzodiazepine-involved overdose deaths, 92.7 percent also involved an opioid, and the majority involved fentanyl [55]. Importantly, products sold illicitly as benzodiazepine medications such as diazepam or lorazepam have been found to contain synthetic opioids such as fentanyl, increasing their overdose risk.

Risk factors — A study of three years of United States survey data identified risk factors for past year nonmedical use of sedatives or tranquilizers [56]:

- White race
- Female sex
- Uninsured
- Unemployed
- Panic symptoms
- Other psychiatric symptoms
- Alcohol use disorder
- Cigarette use
- Illicit drug use
- History of IV drug use

PREVENTION

Principal strategies for clinicians to prevent prescription drug misuse and its consequences are optimizing alternative treatments, including avoiding prescribing controlled substances in situations where alternative treatments are likely to be safe and effective; conducting ongoing assessment of risk for each patient; establishing a treatment plan that includes clear communication with the patient; and limiting dose to the lowest effective dose.

Optimize alternative treatments — The first principle in prevention is to avoid prescribing controlled substances when safer alternatives are available and are likely to be effective. Clinical indications for prescribing controlled substances, such as pain, anxiety, and attention deficit hyperactivity disorder, each have evidenced-based treatment modalities that can replace or complement use of controlled substances. These include nonpharmacologic treatment with

self-management strategies, behavioral treatments, physical therapy, as well as noncontrolled pharmacotherapy. (See 'Controlled substances' above and "Approach to the management of chronic non-cancer pain in adults" and "Attention deficit hyperactivity disorder in adults: Treatment overview" and "Generalized anxiety disorder in adults: Management".)

Patient risk assessment — Consensus-based guidelines recommend that clinicians initiate or chose to continue controlled substances only in patients for whom the likely benefits will outweigh the risks [57,58]. Contraindications to treatment with controlled substances include [57]:

- Current untreated substance use disorder
- Poorly controlled psychiatric illness
- Inconsistent follow-up

There are scant data on predicting likelihood of benefit and harm in controlled substance prescribing. Tools have been developed to help predict risk of developing misuse [59-61], but none have been shown to impact outcomes, and few have been validated in primary care, where most controlled substances are prescribed.

To assess risk for prescription drug misuse, it is generally necessary to collect both patient-reported data and collateral data from other providers and objective sources. Patient-reported data include a thorough substance use history, mental health history, family and social history, as well as physical examination to assess for signs of substance use (eg, track marks and stigmata of chronic liver disease). It is also helpful to review medical records, speak with previous or current providers, check the state prescription monitoring program, and conduct drug testing. (See 'Urine drug testing' below.)

The risk assessment should help to inform decisions about whether to prescribe controlled substances, and, if the clinician chooses to prescribe them, will help to inform the intensity of monitoring and determine which adjuvant treatments (eg, behavioral health) are indicated.

Establishing a treatment plan — We discuss the potential risks, benefits, and treatment alternatives with a patient before starting a controlled substance [58]. We also discuss the strategies that will be used to monitor for and respond to risks of potential misuse that arise in the course of treatment, including defining conditions in which a safe discontinuation of controlled substances and/or transition to substance use disorder treatment would be indicated. Clear communication is critical; patients need to know what is and is not considered safe use of controlled substances. We recommend this be done in a nonjudgmental, nonstigmatizing way that promotes patients' understanding and comfort in asking questions.

Written documents such as informed consents, agreements on terms of treatment, or treatment plans can be useful to document this information/agreement between patients and prescribers. Though evidence for a treatment agreement's effectiveness in reducing misuse of controlled substances is not robust [62], most experts promote its role in documenting shared decision-making, treatment goal-setting, informed consent, and defining the monitoring plan [57].

Limiting exposure — Limiting exposure to controlled substances can help prevent prescription drug misuse. This includes choosing alternate treatments when possible and when controlled substances are prescribed, limiting the dose, duration, or number of prescriptions. The most rigorous data to support these strategies are for opioid prescribing. Greater daily opioid doses and greater numbers of prescriptions per month are associated with a higher risk of overdose death [63-65]. Based on these findings, the Centers for Disease Control and Prevention [58] recommended in its Guideline for Prescribing Opioids for Chronic Pain that clinicians avoid increasing the dose of prescribed opioids for chronic pain beyond 90 morphine milligram equivalents per day. Of note, the updated guideline removed mention of specific dose thresholds but still strongly recommends limiting to the lowest effective dose [58].

It is important to frequently perform detailed medication reconciliation to understand how patients actually take controlled substances, rather than relying exclusively on close-ended questions like, “Do you take your medication as prescribed?” Prescribing quantities of controlled substances that exceed what the patient consumes can contribute to hoarding of medication and increase the risk of diversion and misuse.

As above, each patient’s daily dose should be limited to the lowest effective dose for the individual patient. When a patient’s symptoms are controlled, it is prudent in many cases to offer and attempt dose reductions as tolerated to minimize exposure and risk. Given evidence of harms of rapid tapering or discontinuation including opioid withdrawal and suicidality, it is important to make tapering decisions in a collaborative and tolerable way [66-73]. The 2022 guideline from the Centers for Disease Control and Prevention includes guidance on patient-centered prescription opioid tapering [74].

IDENTIFICATION AND MANAGEMENT

Clinicians have a clinical responsibility to monitor patients to whom they prescribe controlled substances on an ongoing basis for misuse of these medications [57,58,75]. Practitioners should adhere to policies of their state boards in the United States, and medical regulatory authorities in other countries, which may include specific actions not discussed here. Experts

recommend a "universal precautions" [76] approach incorporating a standard prescribing and monitoring framework for all patients prescribed the medications that includes:

- Establishing a clear clinician-patient relationship, as with any patient.
- Documenting in the patient's medical record [57,77]:
  - A medical history, including substance use and mental health
  - Physical examination
  - Medical decision-making, including assessment of benefit and harm
  - Plan of care
- Regular follow-up with standardized monitoring for benefit and harm. (See 'Regular follow-up' below.)
- Drug testing. (See 'Urine drug testing' below.)
- Use of prescription monitoring programs where available. (See 'Prescription monitoring programs' below.)
- Discussing all planned monitoring strategies in a treatment agreement. (See 'Establishing a treatment plan' above.)

Regular follow-up — Frequent in-person follow-up with patients on controlled substances is preferred; however, if not feasible (eg, due to distance or frailty), video-based visits may be acceptable. During follow-up visits, we monitor for and document benefits and harms of treatment, including concerning behaviors that may indicate misuse or a use disorder. Guidelines vary, but visits should generally occur at least every three months and more frequently in higher risk circumstances, such as during periods of dose adjustment [58].

For follow-up assessment of risks and benefits in patients who are prescribed opioids for chronic pain, the "Five A's" provides a useful framework:

- Analgesia
- Activities of daily living (ie, assessment of functional status)
- Addiction
- Adverse effects
- Adherence to the treatment plan

Physical examination is essential and can provide evidence of intoxication, oversedation, withdrawal, or findings indicative of drug injection or intranasal use. Involving a patient's family

member or friend can be useful for obtaining collateral history about a patient's functioning and use of the medications.

Urine drug testing — Urine drug testing provides objective data to confirm that patients have taken the prescribed medication and to help identify use of nonprescribed substances that could interfere with the safety or effectiveness of treatment [57]. Random drug testing, as opposed to scheduled testing, may be more likely to detect undisclosed drug use. While evidence that routine urine drug testing decreases controlled substance misuse is lacking [62], urine drug testing is effective at identifying illicit and nonprescribed drug use [78-81]; it has been shown to be better than clinician assessment alone [10,79,82]. As an example, among patients whose clinicians believed were not at risk for medication misuse, 60 percent had urine drug tests showing the presence of an illicit drug or the absence of a prescribed medication [83].

Urine is the most commonly tested bodily fluid for drugs in clinical care because the window of detection is longer than for blood and because oral fluid testing is susceptible to false negatives, particularly in smokers. Clinicians must be aware of the limitations (eg, false-positive and false-negative results) of the drug test assays that they use. Misinterpretation of results is common and could negatively affect patient care [84-86]. (See "Testing for drugs of abuse (DOAs)" and "Urine drug testing for patients with chronic pain".)

Prescription monitoring programs — Prescription monitoring programs (PMP) provide an online database listing all prescriptions of controlled substances dispensed for each patient by pharmacies in the covered region. All states in the United States have operational PMPs; other countries have similar programs. Where possible, and in accordance with state policies, prescribers should query the PMP before prescribing controlled substances to a patient, to check for undisclosed prescriptions for controlled substances. Receiving undisclosed controlled substances from other prescribers is a type of prescription drug misuse, could indicate substance use disorder or diversion, and elevates the risk for drug-drug interactions and overdose. Reviewing PMP data also helps the clinician determine when prescriptions were filled, to more accurately assess expected end date and avoid unintentional early refills.

Clinicians making use of PMP data should be aware that PMP databases may not include all medical sources. As an example, PMP data in the United States usually does not include information on methadone dispensed for the treatment of opioid use disorder from opioid treatment programs. Access to dispensing data from neighboring states is variable and increasing. Occasionally, reporting errors from pharmacies occur, and calling a pharmacy directly may be necessary to confirm an unexpected finding in the PMP.

Clinician education — An epidemic of lethal opioid overdoses in the United States has prompted numerous initiatives to educate clinicians about appropriate opioid use and influencing their prescribing practices [74,87,88]. As an example, practice guidelines have been disseminated by a variety of organizations targeting various clinician populations and clinical settings, in some cases with follow-up measurement of their impact.

As an example, dissemination of a practice guideline aimed at reducing inappropriate opioid prescribing by emergency clinicians in Ohio was associated with a 12 percent reduction (95% CI 17.7 to -6.3) in prescriptions per month statewide [89]. The guideline encouraged emergency clinicians, when considering an opioid prescription, to review the patient's recent prescription history in the state's prescription drug monitoring database; limit the quantity provided; refer the patient for further evaluation, treatment, and monitoring; and provide education about opioid risks and limited benefits. (See 'Prescription monitoring programs' above.)

Addressing misuse — Before starting treatment with a controlled substance, providers should have a well thought-out plan for how to respond to evidence of prescription drug misuse. An approach that is communicated with patients as part of a treatment agreement and, whenever possible, standardized across a practice, improves time efficiency and fairness. Prescription drug misuse occurs along a spectrum of risk, from lower risk behaviors (eg, a single episode of a patient taking an extra dose because of severe pain) to higher risk behaviors (eg, regular nonprescribed use). The first clinician response to misuse behaviors should always be discuss it with the patient in a nonjudgmental way and to assess for substance use disorder and overdose risk. Decisions about changes to the treatment plan depend on risk. As an example, a response to a single minor deviation from the patient's treatment agreement may be to counsel the patient and intensify monitoring; a response to severe or persistent misuse may be to safely taper or discontinue controlled substances and initiate treatment for substance use disorder if present.

In most cases of prescription drug misuse, it is appropriate to slowly taper rather than abruptly discontinuing the medication to avoid precipitating a severe withdrawal syndrome [90,91] and other negative consequences.

If a patient is suspected of having a substance use disorder, tapering is insufficient and offering or referring for addiction treatment is essential. Many effective treatment options are available [58].

Treatment of substance use disorder is discussed in detail elsewhere:

- (See "Opioid use disorder: Treatment overview" and "Opioid use disorder: Pharmacologic management" and "Opioid use disorder: Psychosocial management".)

- (See "Benzodiazepine use disorder", section on 'Treatment'.)
- (See "Stimulant use disorder: Treatment overview" and "Stimulant use disorder: Psychosocial management".)
- (See "Cocaine use disorder: Epidemiology, clinical features, and diagnosis".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Cannabis use disorder and withdrawal" and "Society guideline links: Opioid use disorder and withdrawal" and "Society guideline links: Stimulant use disorder and withdrawal" and "Society guideline links: Benzodiazepine use disorder and withdrawal".)

SUMMARY AND RECOMMENDATIONS

- **Terminology** – Prescription drug misuse is defined as use of a prescription medication that is outside of the manner and intent for which it was prescribed; this includes overuse, use to get high, diversion (sharing or selling to others), having multiple prescribers or nonprescribed sources of the medication, and concurrent use of alcohol, illicit substances, or nonprescribed controlled medications. Misuse is a necessary but not sufficient criterion for a substance use disorder. (See 'Prescription drug misuse' above.)

  Due to their potential for misuse, addiction, and illicit diversion and sale, opioid analgesics, stimulants, and benzodiazepines and other sedatives/hypnotics are regulated, restricting whether and how they can be prescribed. In the United States, these drugs are referred to as "controlled substances" and subject to Federal regulations (table 1). (See 'Controlled substances' above.)

- **Epidemiology** – Misuse of prescription drugs has generally followed trends concurrent with prescribing of medication for therapeutic use. This was particularly true of opioid analgesics prescribed for patients with chronic pain, stimulants prescribed for individuals with attention deficit hyperactivity disorder, and benzodiazepines prescribed for patients with anxiety; misuse increased with greater prescribing for each between 2000 and 2015. (See 'Epidemiology' above.)

- **Opioid-related deaths** – Use of opioid analgesics for pain management increased markedly from the 1990s to the mid-2010s, concurrent with marked increases in associated morbidity and mortality from use and/or misuse of these drugs. While rates of

overdose deaths involving prescription opioids have plateaued over the past decade, opioid-related deaths overall have continued to grow, driven by illicit opioids. Higher daily doses of prescribed opioids are associated with a greater risk of overdose for the patient they were prescribed to. (See 'Morbidity and mortality' above.)

- **Prevention** – Principal strategies for clinicians to prevent prescription drug misuse and its consequences are optimization of alternative treatments, patient risk assessment, use of a treatment agreement, and limiting dose and early refills. Patient risk assessment should include a history, physical examination, and consideration of the presence of contraindications to prescribing controlled substances (see 'Prevention' above):
  - Current untreated substance use disorder
  - Poorly controlled psychiatric illness
  - Erratic follow-up
- **Identification and monitoring** – Monitoring patients who are prescribed a controlled substance should include regular follow-up, drug testing, and use of prescription monitoring programs or other information sources about patients who receive these medications from multiple prescribers. Monitoring should include documentation of benefits and harms of treatment, including assessment of functional status to assure that function is stable or improving on the current regimen, and evaluation for concerning behaviors that may indicate misuse or a substance use disorder. (See 'Identification and management' above.)
- **Addressing misuse** – Prescription drug misuse occurs along a spectrum of risk, from lower risk behaviors (eg, a single episode of a patient taking more than prescribed) to more severe behaviors (eg, undisclosed prescription sources). The clinician's response should be commensurate with the severity and the pattern of the behaviors. Patients suspected of having a substance use disorder should be assessed by an addiction specialist. (See 'Addressing misuse' above.)

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