REPORT

Current and Emerging Options to Combat the Opioid Epidemic

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Responses to the Opioid Overdose Public Health Crisis

Responses to the opioid epidemic have included activities of law enforcement, government regulatory agencies, pharmaceutical companies, and healthcare providers. The Anti-Drug Abuse Act of 1988 created the Office of National Drug Control Policy (ONDCP) to combat drug abuse in the United States.[1] Over the next several decades, reauthorizations of the policy expanded the mandate of the agency to address the prescription opioid and heroin epidemic. Former President Barack Obama strengthened insurance coverage for mental health and substance use disorders (SUDs) under the Affordable Care Act.[2] In July 2016, he signed the Comprehensive Addiction and Recovery Act (CARA) of 2016 into law; it was the first major federal addiction legislation in 40 years.[3] The law addresses the opioid epidemic through a coordinated and balanced strategy of grant programs to expand prevention and education efforts while also promoting treatment and recovery.

The ONDCP provides administrative and financial support to the President's Commission on Combating Drug Addiction and the Opioid Crisis, established by an Executive Order in March 2017 by President Donald J. Trump.[1] In October 2017, President Trump declared the opioid crisis a national public health emergency under federal law, which created policy, but not funding, for "the United States to use all lawful means to combat the drug demand and opioid crisis currently afflicting our country. . . and exercise all appropriate emergency authorities."[4] Unlike the declaration of a national emergency, President Trump's directive does not on its own release any additional funds to deal with the opioid crisis, but it would allow for some grant money to be used to combat opioid abuse.[5]

As a response to the opioid crisis, the US Department of Health and Human Services (HHS) has developed strategies focusing on 5 major priorities[6]:

- Improving access to treatment and recovery services
- Strengthening understanding of the opioid epidemic through better public health surveillance
- Advancing better pain management practices
- Promoting the use of overdose-reversing drugs
- Providing support for innovative research on pain and addiction

ABSTRACT

Today's management of chronic pain presents a challenging clinical dilemma. Although clinicians wish to relieve a patient's suffering, they must do so without undertreating the pain or contributing to the drug abuse problem. Following a steady rise in opioid prescription rates from 2006 to 2012, increased national attention for the obioid abuse epidemic likely contributed to the decline in prescribing rates from 2012 to 2016. Although opioids have helped many patients, they are also associated with adverse events and a growing national crisis of misuse, abuse, and overdose.

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As a component of HHS, the National Institutes of Health is partnering with pharmaceutical companies and academic research centers to develop safe and effective strategies to manage chronic pain along with new medications and technologies to treat opioid use disorders (OUDs). Other research is being conducted to improve overdose prevention and reversal interventions to promote recovery.[6]

The FDA launched a comprehensive Opioids Action Plan in early 2016 to take concrete steps toward reducing the impact of opioid abuse on American families and communities.[7] These steps include[7]:

- Expanded use of advisory committees to provide advice from external experts before approving any new opioid that does not have abuse-deterrent properties or approving new pediatric opioid labeling
- Updated warnings and safety information for immediate-release opioid labeling to provide better information for doctors on safe prescribing
- Strengthened postmarketing requirements for pharmaceutical companies to provide data on the long-term impact of using extended-release/long-acting opioids
- Updated risk evaluation and mitigation strategy programs to increase the number of prescribers who receive training on pain management and safe opioid prescribing
- Expanded access to abuse-deterrent formulations (ADFs) of opioids to discourage abuse
- Increased support for better overdose treatment, better opioid prescribing guidelines developed by the Centers for Disease Control and Prevention (CDC), and more research to develop safer pain medicines
- Endorsed incorporation of the broader public health impact of opioid abuse in approval decisions[7]

As part of this plan, the FDA asked the National Academies of Sciences, Engineering, and Medicine to convene a committee to update the state of science on pain research, care, and education, as well as to identify actions that the FDA and others can take to respond to the opioid epidemic.[8] In addition to recommending that access to treatment for OUDs be increased, the committee recommended a constellation of policies, interventions, and tools related to access to opioids and clinical decision making to reduce harms while also meeting the needs of patients requiring pain management.

Practice Guidelines for Chronic Pain Management

In general, practice guidelines from the American Pain Society, the American Academy of Pain Medicine, the American Society of Interventional Pain Physicians, and the Office of Veterans Health Administration and Department of Defense Health Affairs (VA/DoD) recommend that opioids be prescribed only after the patient has received a thorough evaluation, including a pain history, assessment of the impact of pain, a directed physical examination, a review of previous treatments, a drug history, and an assessment of coexisting diseases or conditions.[9-11] When appropriate, the patient should undergo baseline urine drug monitoring (UDM).

In March 2016, the CDC released a new set of opioid prescribing recommendations to guide primary care clinicians who write most prescriptions for opioid analgesics.[12] These recommendations include using nonopioids for most cases of chronic pain, checking with the state's prescription drug monitoring program (PDMP) before prescribing opioids, using the lowest effective dose when prescribing opioids, maintaining a dose ceiling, and ensuring that patients who are treated with opioids are closely monitored.[12] Guidelines also suggest starting opioid therapy with an immediate-release opioid due to increased risk for opioid overdose associated with long-acting opioids in opioid-naïve patients.[11,12]

The CDC Guideline for Prescribing Opioids for Chronic Pain has received criticism related to the recommendations and the manner in which they were released to the public. Schatman and Ziegler note that the guideline, by failing to recognize the complexity of the issues involved in both reducing the harm from prescription drugs while ensuring appropriate access, impedes the ability of the public and policymakers to understand the complexity of the problem and to create solutions that are balanced and effective.[13] According to these authors, drugs such as heroin and illicit fentanyl, and not prescription opioids and overprescribing, are the drivers of unintentional overdose deaths in the United States. Failure to make this distinction has far-reaching consequences for policy, pain treatment, substance abuse prevention, and reduction of intentional overdose.[13]

Despite its criticisms, the guideline includes recommendations that are intended to improve communication between providers and patients about the risks associated with long-term opioid therapy and overdose. Prescribers and pharmacists are encouraged to work collaboratively to optimize pain management and prevent opioid misuse.[14] As members of the healthcare team, pharmacists must verify a prescriber's Drug Enforcement Agency registration, check with the state's PDMP, and contact the prescriber if questions arise (**Table 1**).[14,15] In addition, pharmacists should advise patients on the proper use and storage of opioids and review common adverse events (AEs). To reduce harm, pharmacists should discuss the possibility of tolerance and abuse with patients and caretakers when filling opioid prescriptions and communicate any concerns about misuse or abuse to providers, including recommendations for addiction treatment if indicated.[14,15]

Mitigating Risks of Opioid Misuse and Abuse

Risk assessment for all patients prior to opioid prescribing is recommended and includes the use of screening tools, treatment agreements, and regular UDM. Several factors have been identified that increase an individual's risk of opioid overdose or addiction (**Table 2**).[11,16] Additional factors have been shown to increase the

likelihood of abuse as well as the likelihood of using a riskier route of abuse. These include past or current substance abuse, long duration of prior abuse, young age, untreated psychiatric disorder, male sex, and living in a rural setting or social or family environment that encourages misuse. Clinicians should consider these factors when prescribing an opioid analgesic in an individual patient.[17,18]

Unfortunately, risk assessment strategies have not reduced overall rates of opioid misuse or overdose. Newer strategies for reducing opioid-related risks include more selective prescription and avoidance of co-prescription with sedative hypnotics. Ongoing monitoring using analgesia, AEs, activities of daily living, and aberrant behavior—collectively referred to as the "4As"—provide information about how the patient is responding to opioid therapy and whether treatment needs to be modified.[19] Nevertheless, although the number of outpatient opioid prescriptions dropped 13% nationally between 2012 and 2015, the national overdose death rate surged 38% during those years, leading some to postulate that the opioid crisis is a manifestation of unfulfilled and complex physical and mental health needs.[20]

TABLE 1. Role of the Pharmacist in Dispensing Prescription Opioids[14,15]

Proper use	• Discuss taking medications exactly as prescribed
Adverse events	• Review common adverse events and encourage patients to report them to prescriber • Recommend over-the-counter treatment for opioid-induced constipation
Prescription fills	• Check prescription drug monitoring programs
Stockpiling	• Encourage patients to safely discard unused or expired medications
Storage	• Explain proper and safe storage of prescriptions
Harm reduction	• Educate patients on risk factors for opioid overdose and appropriate response to opioid overdose • Identify and address dangerous drug–drug interactions (eg, opioids and benzodiazepines) • Distribute naloxone and provide guidance for use • Recommend addiction treatment • Suggest nonopioid and nonpharmacologic alternatives

TABLE 2. Select Risk Factors for Opioid Overdose or Addiction[11,16]

Risk factor for addiction	• Adolescence
Risk factors for overdose	• Extended-release or long-acting formulation (methadone, fentanyl patch) • Severe respiratory instability or sleep apnea • Acute psychiatric instability or intermediate to high suicide risk • History of drug overdose • Age younger than 30 years or older than 65 years • Coadministration of benzodiazepines • Renal or hepatic impairment
Risk factors for addiction and overdose	• Duration longer than 3 months and dose higher than 100 morphine mg equivalents • Substance use disorder • Depression, anxiety disorder, and personality disorders

Informed Consent

Several guidelines discuss informed consent. The CDC Guideline and VA/DoD Guideline suggest that providers discuss the risks, benefits, and alternatives of chronic opioid therapy at the outset and throughout treatment.[11,12] This reinforces the use of opioids when the benefits outweigh the risks. Also, it is recommended to discuss patient and provider responsibilities.[12] This discussion is also a good time to establish realistic treatment goals.[21] The VA/DoD Guideline intentionally moves away from the use of opioid treatment agreements or pain contracts as these were seen as detrimental to the therapeutic relationship and an intimidation tactic.[11] Unfortunately, evidence for the use of opioid treatment agreements to reduce opioid misuse has been weak.[11]

Abuse-Deterrent Formulations

Managing chronic pain is a conundrum for many clinicians, particularly those in primary care. The abuse potential of opioids can make it challenging to offer them to patients who are at elevated risk for opioid misuse and abuse, yet clinicians increasingly have need to treat severe pain in such patients. Existing ADFs of opioid analgesics are intended to provide pain relief to patients while deterring misuse and abuse. According to FDA Commissioner Scott Gottlieb, MD, until new nonopioid forms of pain management are available, it is critical to promote the development of opioids that are harder to manipulate and abuse and to encourage their use over opioids that offer no form of abuse deterrence.[22]

In a recent report, the National Academies of Sciences, Engineering, and Medicine recommend caution and ongoing studies on the optimal role of ADFs in reducing misuse of prescription opioids.[8] According to this report, ADFs have the potential for benefit, but reliance on them may undermine a successful public health response to the opioid epidemic.[8] Although the direct and indirect cost savings of ADFs may be substantial, these benefits have been accompanied

by an increase in abuse of other opioids, particularly heroin.[17] Data collected with the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS) System Web Monitoring Program, an online surveillance system that collects and organizes posts about prescription drugs from social media websites, blogs, and forums, indicated that users will gravitate to non-ADFs in general, and specifically to immediate-release, non-ADFs as long as these options remain on the market.[23] Nevertheless, the introduction of an immediate-release ADF that resists physical methods of abuse—such as crushing, grinding, or extraction—in commonly used solvents, is hoped to offer clinicians a new approach for treating patients in pain while simultaneously fighting against the potential for abuse.[24]

Opioid analgesics can be abused simply by being taken at or above the recommended dosage, and ADFs do not protect against swallowing several intact capsules or tablets to achieve a feeling of euphoria.[25] However, many who abuse opioids tamper with the drug product to ingest more of the active drug. For this reason, extended release/long-acting formulations are often the preferred formulation over short-acting formulations, as these contain greater amounts of the active agent.[26] Tampering could include crushing or grinding the drug for ingestion, smoking, or rectal administration. The drug could also be dissolved in a solvent such as water or ethanol for injection. Oral ingestion is the most common route of abuse, followed by inhalation and injection.[17] Those who abuse may also take the opioid with alcohol or another drug such as a benzodiazepine. Differences in the routes of abuse vary between drug formulations, duration of abuse, age, sex, and geographic location.

Pharmacologic approaches to deter opioid abuse have included incorporating characteristics designed to make it more difficult to tamper with the oral tablets to obtain rapid absorption of the opioid.[25] These include adding an opioid antagonist such as naloxone, adding an agent that induces unpleasant symptoms with excessive intake, and incorporating physicochemical barriers intended to confer resistance to tablet tampering.

To help transition to a market in which most opioids have abuse-deterrent properties, the FDA recently issued its Guidance for Industry: Abuse-Deterrent Opioids—Evaluation and Labeling on the development of generic versions of approved ADF opioids.[27] The guidance includes recommendations about the type of studies companies should conduct to demonstrate that the generic drug is no less abuse deterrent than its brand-name counterpart. In addition, the FDA is investigating ways to help generic ADF manufacturers bring their drugs to market as quickly and efficiently as possible, such as improved testing methodologies for evaluating abuse deterrence and advancing new review policies.[22]

Currently, 9 extended-release/long-acting opioids and 1 immediate-release opioid are FDA approved with labeling describing abuse-deterrent properties that are consistent with the FDA's guidance.[25,28] For more information on these agents, see **Table 3.**[29-38]

The uptake of ADFs has been slow among physicians because of lack of awareness of their availability, uncertainty about when to prescribe them, and limited postmarketing evidence demonstrating effectiveness.[39] Price can also be a significant barrier as new formulations are available only as brand-name products and therefore are more expensive than non-ADFs and their generic counterparts.[22] The higher costs of ADF therapy may necessitate prior authorization requirements that require clinicians' time and could impact productivity and patient care.[40]

In addition, an economic modeling analysis of costs related to prescribing ADF opioids indicate that they have the potential to substantially reduce the incidence of abuse in patients who have been prescribed opioids for chronic pain relative to non-ADF opioids, but at significantly higher costs to the healthcare system. Unless ADF opioids are discounted by 41% from current prices, healthcare cost neutrality could not be achieved, even if the effectiveness of ADF opioids in preventing abuse were 100%.[40]

Prescription Drug Monitoring Programs

PDMPs are state-run, electronic databases used to track the prescribing and dispensing of controlled prescription drugs to patients. This information is monitored for suspected drug abuse or diversion. It can provide the prescriber or pharmacist with information on a patient's controlled-substance prescription history, identify patients using more than 1 pharmacy or more than 1 prescriber, or identify those with inappropriate prescriptions. As of September 2017, 49 states had active PDMPs, as well as the District of Columbia and St. Louis county in Missouri, which is the only state without an active PDMP.[41]

Research has shown that the outcomes of using PDMPs have been mixed because of under-usage of the database and limited effectiveness in reducing overdose deaths and the consumption of controlled substances.[42] Perrone and Nelson described limited use of PDMPs among some practitioners because of time constraints and access issues, along with the belief that using the system will not change their patients' behaviors.[43] Nevertheless, an analysis of PDMP data indicated that a state's implementation of the program was associated with an average reduction of 1.12 opioid-related overdose deaths per 10,000 population, which could be increased if programs monitored a greater number of drugs with abuse potential and data were updated at least weekly.[44]

Urine Drug Monitoring

UDM is an important tool for managing patients' opioid use. Testing helps determine whether patients are taking their prescribed medications appropriately and whether they are taking other substances not prescribed or illegal. Guidelines and consensus recommendations suggest UDM at baseline and at least yearly during chronic opioid therapy with increased frequency of UDM based on the patient's level of risk.[11,14,45]

TABLE 3. FDA-Approved Abuse-Deterrent Formulations of Opioid Products[29-38]

Drug	Abuse-Deterrent Formulation Mechanisms	Deterrence Label
Morphine extended-release (Arymo ER)	• Contains proprietary polymer matrix technology that makes the tablet resistant to physical and chemical manipulation • When dissolved, the inner active drug forms a viscous hydrogel that is difficult to snort or inject	IV
Morphine and naltrexone extended-release (Embeda)	• Pellets in capsules consist of opioid around a core of sequestered naltrexone. If pellets undergo physical manipulation, naltrexone is released from the core	Nasal, oral
Hydrocodone extended-release (Hysingla ER)	• Opioid is dispersed within a polyethylene oxide polymer matrix that is composed of long molecular chains to deter dissolution in water. The molecular chains are formed into a firm, interlocked matrix that makes the tablets hard and difficult to crush • When dissolved in aqueous solution, it forms a viscous liquid that is difficult to snort or inject	IV, nasal, oral
Morphine extended-release (MorphaBond)	• Inactive ingredients increase tablet resistance to cutting, crushing, or breaking • Maintains extended-release characteristics when subjected to physical manipulation and/or chemical extraction • Forms a viscous mass that resists passage through a needle when placed in a liquid environment	IV, nasal
Oxycodone extended-release (OxyContin)	• Resists crushing, breaking, and dissolution • In an aqueous environment, the tablet gradually forms a viscous hydrogel that resists passage through a needle	IV, nasal
Oxycodone hydrochloride (RoxyBond)[a]	• Increased resistance to cutting, crushing, grinding, or breaking relative to oxycodone immediate-release tablets • Intact and manipulated tablet resists extraction in various solvents under various conditions • The formulation forms a viscous material that resists passage through a needle	IV, nasal
Oxycodone hydrochloride extended-release; naloxone hydrochloride (Targiniq ER)	• Resists crushing, breaking, and dissolution • In an aqueous environment, the tablet gradually forms a viscous hydrogel that resists passage through a needle • Naloxone is released if tablet is crushed or broken	IV, nasal, oral
Oxycodone hydrochloride extended-release; naltrexone hydrochloride (Troxyca ER)	• Capsules are filled with extended-release pellets of oxycodone with a sequestered core of naltrexone that is released if the pellets are crushed or manipulated • Crushing and mixing the pellets in a variety of solvents results in simultaneous extraction of oxycodone hydrochloride and naltrexone hydrochloride	IV, nasal
Hydrocodone bitartrate extended-release (Vantrela ER)	• Resists crushing, breaking, and dissolution, and retains some extended-release properties despite manipulation • Small volume extraction attempts result in a viscous material that resists passage through a needle	IV
Oxycodone extended-release (Xtampza ER)	• Capsules contain microspheres with inactive ingredients that form a lipophilic salt. Microspheres are crush resistant, cannot be readily dissolved in common household solvents, and will solidify within a needle	IV, nasal

ER indicates extended release; IV, intravenous.
[a]Immediate-release formulation.

A new consensus document released in July 2017 by the American Society of Addiction Medicine provides practical guidance on the appropriate use of drug testing for the identification, diagnosis, treatment, and monitoring of patients with or at risk for SUDs.[46] The value of drug testing depends on using it correctly—selecting the right test for the right patient at the right time.[46] As part of the multidisciplinary team, pharmacists can be helpful in ensuring that healthcare providers understand the principles of drug tests and testing limitations. According to an interdisciplinary group of clinicians with expertise in pain, SUDs, and primary care, evidence on the efficacy of UDM in preventing OUD, overdose, and diversion is limited; however, UDM should be included as part of ongoing risk monitoring in patients who have been prescribed opioids for chronic pain.[45]

Naloxone

Although several screening instruments are available to assess the risk of misuse, abuse, or addiction in patients being treated with prescription opioids, an instrument to assess the likelihood of opioid-induced overdose or life-threatening respiratory or central nervous system depression has only recently been developed.[47,48]

The Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression is a screening tool that can provide valuable decision support to clinicians so they are able to manage pain more effectively in their patients.[47,48] Patients identified as having increased risk are most likely to benefit from preventive and potentially life-saving interventions, including education, increased attention to opioid selection and dose escalation, referral to a pain management specialist, and heightened vigilance for opioid-related AEs.

Naloxone, a highly effective opioid antagonist, is recommended for patients who are at increased risk for opioid overdose, including those on chronic opioid therapy. Until a few years ago, naloxone was available only as an injection, with the potential for accidental needlesticks and transmission of hepatitis or HIV infection. Some emergency workers had been using an adapter placed at the tip of the syringe to convert the injectable into a spray. In April 2014, the FDA approved a naloxone autoinjector product, the first naloxone product specifically approved for administration for suspected opioid overdose outside a medically supervised setting.[49] In November 2015, a ready-to-use, needle-free nasal device was approved by the FDA and is now commercially available.[50] Naloxone injections and nasal spray can be administered easily and safely by a first responder with no prior training and are recommended for use in the revised Substance Abuse and Mental Health Services Administration (SAMHSA) Opioid Overdose Toolkit.[51]

Although some states and cities embrace the life-saving potential of naloxone, a few law-enforcement individuals question whether its availability is helping to enable the opioid epidemic rather than to prevent it. The CDC credits naloxone for saving 26,000 lives between 1996 and 2014.[52] But some officers report that naloxone allows the addiction cycle to continue because often they are saving the same individual multiple times, without long-term treatment options. Yet, others say that naloxone ultimately saves lives and helps people stay alive until, hopefully, they can be successfully treated.[53] Nonetheless, on April 5, 2018, the Office of the Surgeon General released an advisory encouraging increased access in the community to naloxone for those and their friends and families who are at increased risk for overdose, including those on opioids for chronic pain.[54]

Identifying Patients at Risk for Prescription Opioid Abuse

Evaluating a patient's level of risk is important. There are several risk assessment tools available to assist providers. These include the Screen and Opioid Assessment for Patients with Pain–Revised (SOAPP-R); Opioid Risk Tool (ORT); and Diagnosis, Intractability, Risk, Efficacy Tool (DIRE). Additionally, there are tools to assess opioid misuse. Examples include Pain Assessment and Documentation Tool (PADT), Current Opioid Misuse Measure (COMM), and Addiction Behaviors Checklist.[55,56] The tools vary in their studied setting, format, number of items, time involved, scoring, advantages, disadvantages, and whether or not they have been validated. Although these tools are not lie detectors, they can assist with identifying those who are high risk and require increased follow-up and monitoring. At least one from each category should be used before initiating opioid therapy.[55,56]

Guidelines vary regarding recommendations for the use of risk assessment or opioid misuse tools. Literature reviews of the outcomes of screening tools have found inconsistent results and reliability issues.[12,21] Thus, the CDC guideline makes no recommendation regarding the use of screening tools.[12] However, the Interagency Guideline on Prescribing Opioid for Pain recommends using a validated tool to screen for opioid misuse including ORT, SOAPP-R, DIRE, or CAGE-AID combined with information from the patient's medical record and their support system.[57] The American Society of Interventional Pain Physicians includes substance abuse evaluation as part of a comprehensive assessment and providers may consider the use of screening tools for assistance.[21]

Treatment of Opioid Use Disorders

Medication-assisted treatment (MAT) is the use of medications, in combination with counseling and behavioral therapies, to provide a holistic approach to the treatment of SUDs. Research shows that a combination of medication and therapy can successfully treat these disorders, and MAT can help sustain recovery for some people struggling with addiction.[58] Medications used in MAT include methadone, buprenorphine (with or without naloxone), and naltrexone. Methadone and buprenorphine relieve the withdrawal symptoms and psychological cravings that cause chemical imbalances while naltrexone blocks the effects of opioids and decreases cravings. When used correctly, these medications allow individuals to function in society and maintain employment.[58] Qualified physicians may apply for a waiver to dispense and prescribe buprenorphine following specialized training. As a result of CARA, these privileges have been expanded to nurse practitioners and physician assistants until 2021.[2]

Opioid treatment programs use tools such as the Addiction Severity Index (ASI), an interview-based modality, to measure addiction severity and treatment needs.[59] Used as a baseline measurement of the severity of issues relating to substance abuse, the ASI is useful to help create a comprehensive treatment plan that addresses 6 primary categories:

- Medical issues relating to drug use
- Employment/support status
- Levels of alcohol and drug use
- Legal issues arising from substance abuse
- Family/social factors
- Psychiatric/mental health status

The ASI is one tool for developing an individualized treatment plan that includes ending substance abuse, finding work, improving

overall mental and physical health, and addressing relationship issues. Recent studies have investigated the validity of the tool to predict the need for enhanced intervention. Simoneau and Brochu compared ASI profiles of those who re-enter treatment with profiles of individuals entering treatment for the first time.[60] They found that individuals re-entering treatment had higher composite scores, which indicated a need for more intensive treatment. The use of ASI composite scores as a predictor of suicide and psychiatric care after residential treatment for drug use was recently assessed, and it was found to be useful in identifying patients with drug use disorders who could benefit from additional mental health treatment.[61] Comorbid mental health problems are thought to increase the already high risk of suicide among individuals with SUDs. Identifying patients with drug use disorders who are also at high risk of suicide is an important public health task, and using data that are available as part of the routine intake assessment may lead to faster and more effective interventions that improve patients' quality of life and reduce risk of early death and disability.[61]

Opioid Treatment Alternatives

Chronic pain affects more than 100 million Americans, according to the Institute of Medicine.[62] Treatment needs to be individualized and there may be several alternatives to opioids, some of which are not covered by insurance reimbursement. Oral and topical therapies may include nonsteroidal anti-inflammatory drugs, acetaminophen, antidepressants, anticonvulsants, muscle relaxants, and lidocaine patches. Nonpharmacologic options include exercise, acupuncture, and transcutaneous electro-nerve stimulator units. Interventional techniques involving injections into or around various levels of the spinal cord may include epidural steroid injections and nerve blocks.

As a result, renewed interest in opioids that act on receptors other than μ-opioid receptors, nonopioid medications, and early intervention strategies to prevent chronic pain have emerged.[63,64] Novel nonopioid therapies are in various stages of clinical development, and adjunct cannabinoid therapies have the potential to produce opioid-sparing synergistic analgesia.[65] States with medical marijuana dispensaries have reported fewer opioid overdose deaths than states without them.[66] However, in a national survey, cannabis use in adults with pain was associated with subsequent increases in nonmedical prescription opioid use and OUDs.[67]

Evidence for the efficacy of nonpharmacologic interventions for chronic pain management, such as cognitive behavioral therapy and mindfulness meditation practice, has also grown over the last several years. Mindfulness meditation has been shown to reduce the intensity of pain as well as the perception of pain control through neural mechanisms that are distinct from those of placebo effects.[68,69] Unfortunately, these interventions are difficult to access in areas in which OUDs have a high prevalence, and they are less likely to be covered by health insurance, creating socioeconomic disparities in pain management.[70,71]

Conclusions

Numerous factors contribute to the current opioid epidemic, and although some attempts have failed, other efforts to mitigate the crisis in the United States have been effective. Risk mitigation for all patients prior to prescribing opioids is recommended and includes the use of screening tools, treatment agreements, and regular urine monitoring. Unfortunately, risk mitigation strategies have not reduced overall rates of opioid misuse or overdose. According to Schatman and Webster, although most efforts are well intended and may have prevented overdose deaths and diversion, evidence exists that the production of ADFs may work to reduce real-world abuse.[72] Insurance coverage for therapies that reduce the harm associated with opioid prescribing may have the potential to substantially ameliorate the nation's persisting prescription opioid crisis.[72] ■

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