REVIEW ARTICLE

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Prevention of Opioid Overdose

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In the time it takes to read this article, at least one person in the United States will have died from an opioid overdose.[1] From 1999 through 2017, more than 700,000 U.S. residents died from a drug overdose; the majority of these events involved an opioid.[2] Among persons between the ages of 24 and 34 years, one in five deaths is now related to opioid use.[3]

Every opioid-related death represents a missed opportunity for prevention. In this review, we focus on prescriber strategies for overdose prevention in three groups of patients: those who have not received previous opioid therapy, those receiving long-term opioid therapy, and those with an opioid use disorder.

Reducing Overdose Risk in Initial Opioid Therapy

All opioid overdoses share a common characteristic: a first opioid exposure. Although this exposure often occurs independent of a health care interaction (e.g., experimentation with a medication prescribed to a friend or relative), prescribers should strive "to keep opioid-naive patients opioid-naive."[4] For mild or moderate acute pain, nonopioid regimens are the preferred first-line therapy.

Limiting the Initial Dose and Duration

When acute moderate or severe pain necessitates the use of opioids, prescribers should limit the course to the lowest dose and shortest duration possible. Even brief opioid courses have potential long-term consequences. In some patients, physical dependence develops quickly, making cessation difficult.[5] In patients who have not received previous opioid therapy, the risk of transitioning from short-term to long-term use begins to increase after the fifth day of exposure,[6] especially in those receiving high doses or long-acting formulations.[7] Yet, at their first primary care visit for pain, 46% of patients who were prescribed an opioid received enough for 7 days, and 10% received enough for 30 days.[8] Prescribers are advised to be particularly cautious with adolescent patients. Receiving a provider-prescribed opioid before the 12th grade is independently associated with a 33% increase in the risk of nonmedical opioid use by the age of 23 years.[9]

New, persistent opioid use is increasingly recognized as one of the most common complications after elective surgery.[10] In postoperative prescribing, adequate analgesia should be balanced against the risks that come with prolonged treatment and provision of excessive quantities of the drug. Patients receiving an opioid prescription after short-stay surgery were 44% more likely to use opioids at 1 year than were patients who did not receive a prescription.[11] Among adolescents and young adults who had not received previous opioid therapy, approximately 5% of those who were administered opioids postoperatively continued to receive them 90 days later.[12] Moreover, up to 71% of prescribed postoperative doses go unused.[13]

After laparoscopic cholecystectomy or herniorrhaphy, more than 80% of patients used fewer than 15 opioid doses (each typically containing 5 mg of oxycodone or hydrocodone).[14]

Simply lowering the default prescription quantity from 30 tablets to 12 reduced postprocedural opioid prescribing by 15% in one hospital system. This reduction was equivalent to approximately 25,000 fewer oxycodone tablets over a 3-month period, with no significant increase in opioid refills, which suggested an absence of undertreated pain.[15] An innovative and patient-centered approach tailored the dose of analgesic drugs to individual opioid requirements during the 24 hours before hospital discharge, which obviated the need for an opioid prescription in 41% of surgical patients.[16]

ASSESSING THE RISKS OF OPIOID INITIATION

In theory, all patients who are treated with opioids incur a risk of overdose. However, several factors increase that risk, including sleep-disordered breathing, end-organ dysfunction leading to impaired medication clearance, pulmonary disease, and concomitant use of sedating medications. (Details are provided in the Supplementary Appendix, available with the full text of this article at NEJM.org.)

The number and severity of risk factors need to be considered to ensure that the benefits of prescription opioids clearly outweigh the risk of overdose. The revised Risk Index for Overdose or Severe Opioid-Induced Respiratory Depression (RIOSORD) is a validated instrument used to estimate the risk of overdose in opioid-treated patients (Table 1).[17,18] The predicted probability of opioid-induced respiratory depression within 6 months after initiation ranges from 1.9% in the lowest-risk group to 83.4% in the highest-risk group (Table 2).[17] Despite several practical limitations (including the length of the index and a lack of clinician familiarity), the use of RIOSORD can guide risk–benefit decisions and facilitate reassessment of risk over time.

Prescription drug monitoring programs (PDMPs) allow the assessment of a patient's prescription opioid history, and a patient-specific query is required before opioid initiation in several states. In areas without a legislative mandate, PDMP inquiries are infrequently completed; recognized obstacles include time, workload, and poor integration into existing electronic medical records.[19] However, PDMPs can identify doctor shopping, concomitant benzodiazepine prescriptions, and evidence of an undisclosed opioid use

Table 1. Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression (RIOSORD).*

Question	Points for Positive Response
In the past 6 mo, has the patient had a health care visit (outpatient, inpatient, or emergency department) involving any of the following health conditions?†	
Substance use disorder (abuse or dependence), including alcohol, amphetamines, antidepressants, cannabis, cocaine, hallucinogens, opioids, and sedatives	25
Bipolar disorder or schizophrenia	10
Stroke or other cerebrovascular disease	9
Kidney disease with clinically significant renal impairment	8
Heart failure	7
Nonmalignant pancreatic disease (e.g., acute or chronic pancreatitis)	7
Chronic pulmonary disease (e.g., emphysema, chronic bronchitis, asthma, pneumoconiosis, asbestosis)	5
Recurrent headache (e.g., migraine)	5
Does the patient use any of the following substances?	
Fentanyl	13
Morphine	11
Methadone	10
Hydromorphone	7
Does the patient use an extended-release or long-acting formulation of any prescription opioid?‡	5
Prescription benzodiazepine (e.g., diazepam, alprazolam)	9
Prescription antidepressant (e.g., fluoxetine, citalopram, venlafaxine, amitriptyline)	8
Is the patient's current maximum prescribed daily morphine-equivalent dose ≥100 mg for all opioids used on a regular basis?	7
Total possible score	**146**

* This questionnaire was adapted from Zedler et al.[17] with permission from Oxford University Press. The index was validated in 36,166 patients (7234 cases and 28,932 controls) who received an opioid prescription from 2009 to 2013, as recorded in a claims database of a commercially insured health plan. Data on how scores were used to calculate the probability of respiratory depression are provided in Table 2.

† The condition does not have to be the primary reason for the visit, but it should be entered in the chart or electronic health record as one of the reasons for the visit or diagnosis.

‡ Extended-release or long-acting formulations and certain opioid active ingredients were significantly and independently associated with the likelihood of overdose. As such, each formulation and each active ingredient are included and scored as independent factors in the risk index. For example, methadone and an extended-release formulation of fentanyl receive risk points for both the active ingredient and the formulation. A short-acting formulation of fentanyl receives points for the active ingredient only. Risk points for formulations are counted only once, regardless of the number of opioid products that the patient consumes.

Table 2. Risk Classes and Predicted Probability of Serious Opioid-Induced Respiratory Depression during the Next 6 Months.*

Risk Class	RIOSORD Score	Average Predicted Probability	Actual Observed Incidence
		percent	
1	<5	1.9	2.1
2	5–7	4.8	5.4
3	8–9	6.8	6.3
4	10–17	15.1	14.2
5	18–25	29.8	32.2
6	26–41	55.1	58.8
7	≥42	83.4	82.4

* Data are from the study by Zedler et al.[17] The study resulted in a model for scoring of the risk of opioid-induced respiratory depression with a C-statistic of 0.90.

disorder, such as previous receipt of buprenorphine prescriptions. These signals should prompt clinicians to screen for an opioid use disorder and offer treatment when present. This evaluation can be accomplished through the Rapid Opioid Dependence Screen, which can be administered in under 2 minutes.[20]

PROMOTING DISPOSAL OF UNUSED DOSES

Diverted prescription opioids represent a common initial exposure for those with an opioid use disorder.[21,22] Among adolescents and young adults, the risk of heroin initiation is 13 times as high in those with a history of nonmedical use of prescription opioids as in those without such a history.[6] Counseling patients regarding recommended options for discarding their excess tablets improves safe disposal and reduces the risk of misuse by others.[23] Medication disposal boxes and community-based drug take-back events offer alternatives to storing unused opioids at home.[24] Flushing unused opioids down the toilet is practical and introduces negligible amounts of opioids into the environment relative to that contributed by human waste, although the practice is sometimes opposed on environmental grounds.[25]

REDUCING OVERDOSE RISK IN LONG-TERM OPIOID THERAPY

The prescribing of opioids for chronic pain is not supported by strong evidence.[26,27] For some patients, long-term opioid therapy delays recovery, hinders functional improvement, or worsens pain through opioid-induced hyperalgesia.[28-30] Moreover, long-term opioid therapy carries clinically significant risks, including sedation, depression, constipation, reduced libido, motor-vehicle collisions, sleep-disordered breathing, and accidental overdose. Nonetheless, many patients and clinicians view opioids as a beneficial (and sometimes essential) element of chronic pain management. An underappreciated challenge with respect to such patients, particularly those receiving high doses, is ascertaining the extent to which the perceived benefits represent a genuinely salutary effect of opioids rather than the desire to avoid opioid withdrawal, which itself can produce pain and functional impairment.[31]

For patients with chronic pain, opioids should be an intervention of last resort when other drug and nondrug therapies have failed.[27] When opioids are prescribed, the functional objectives of treatment should be established at the outset of therapy, with a clear plan to taper opioids if these goals are not met.

AVOIDING DOSE ESCALATION

Most adverse effects of opioids are related to dose, and guidelines caution against excessive dose escalation in the management of chronic pain except during end-of-life care.[27] Morphine-equivalent doses approximate equianalgesic doses of opioids of varying potency. Guidelines of both the Centers for Disease Control and Prevention (CDC)[27] and its Canadian counterpart[32] encourage maintaining the total daily morphine-equivalent dose below 90 mg (and ideally <50 mg) in patients who are initiating long-term opioid therapy. A dose-dependent increase in the risk of a fatal overdose during long-term opioid therapy is well described[33-37]; death from opioid-related causes occurs in up to 3.8% of men and 2.2% of women who are prescribed a daily morphine-equivalent dose of more than 200 mg.[35]

DECREASING HIGH-DOSE OPIOID USE IN PATIENTS WITH CHRONIC PAIN

Before the publication of guidelines on opioid prescribing for chronic pain, countless "legacy patients" had prescriptions that were progressively escalated to high-dose opioids in an effort to overcome persistent pain. Abrupt dose reduction in these patients can lead to withdrawal-

Table 3. Tapering Strategies and Rotation to Buprenorphine for Patients Receiving Opioids for Chronic Pain.*

Process	Tapering	Rotation to Buprenorphine
Indication	Patient requests dose reduction, no clinically significant improvement in pain or function despite opioid treatment, >90 mg MED or lower dose in conjunction with benzodiazepine or other sedating medication, having opioid-related adverse events, nonadherence to treatment plan, medical conditions conferring increased risk of overdose	Patient requests transition to buprenorphine, no clinically significant improvement in pain or function despite opioid treatment, concern that opioid-induced hyperalgesia is contributing to pain, nonadherence to treatment plan, medical conditions conferring increased risk of overdose, coexisting chronic pain and opioid use disorder
Strategy	Option A: If the patient is receiving multiple opioids, consolidate and switch all opioids to one new, extended-release oral opioid; decrease the dose to account for incomplete cross-tolerance Option B: If the patient is receiving multiple opioids, ask which opioid the patient would feel more comfortable tapering first	Patients must abstain from opioid agonists for at least 8 to 12 hr (best accomplished overnight) and be in mild-to-moderate withdrawal (a score of ≥8 on the Clinical Opiate Withdrawal Scale)†
Speed	Rapid taper: Reduce dose by 5 to 10% every 2 to 4 wk; continue taper over weeks to months Slow taper: Reduce dose by 2 to 10% every 4 to 8 wk with pauses in taper, as needed; continue taper over months to years	Once a patient is having mild-to-moderate withdrawal, administer 2 to 4 mg of sublingual buprenorphine or buprenorphine plus naloxone. If patient has no unacceptable side effects, administer an additional 4–8 mg sublingually at 1–2 hr, followed by adjustment according to response up to 32 mg daily in divided doses

* Listed are strategies for deciding between dose tapering or rotation to buprenorphine in patients who are receiving opioids for the treatment of chronic pain. Details regarding requirements for prescribing of buprenorphine in patients with opioid use disorder in the United States are provided in Table 4. MED denotes morphine-equivalent dose.

† Scores on the 11-item Clinical Opiate Withdrawal Scale indicate the following severity of symptoms: a score of 5 to 12, mild; 13 to 24, moderate; 25 to 36, moderately severe; and more than 36, severe.

associated worsening of pain, insomnia, dysphoria, a protracted abstinence syndrome, and even suicidality.[38] Patients in whom doses are tapered too rapidly may seek alternate sources to alleviate withdrawal symptoms. Given the profusion of highly potent fentanyl analogues in the illicit drug supply, such rapid tapering could be fatal.[38]

In one study, more than 70% of the patients who were receiving long-term opioid therapy voluntarily participated in tapering when offered.[39] Clinicians should engage patients receiving high-dose opioids in shared decision making about the merits of gradual dose reduction — specifically, a more favorable balance of benefits versus harms. These discussions are frequently difficult. However, it can be helpful to explain that for many patients who taper gradually, pain does not worsen and often decreases.[40,41] Explanations for this finding include improvements in opioid-induced hyperalgesia, sedation, and mood.[40] Some patients are able to taper quickly, whereas others struggle with even minor dose reductions, which highlights the importance of an individualized approach that tapers at the patient's pace.[42,43] Adjunctive therapies (e.g., clonidine) can be used to minimize withdrawal symptoms.

An alternative to gradual tapering involves transitioning patients from high-dose opioids to buprenorphine, a medication commonly used for the treatment of opioid use disorder (Table 3).[44,45] Buprenorphine is a high-affinity partial agonist at mu-opioid receptors that has a ceiling effect on sedation and respiratory depression without a clinically relevant ceiling on analgesia.[46] As is the case with full opioid agonists, buprenorphine causes modest reductions in chronic pain, as compared with placebo,[47] whereas its anxiolytic and antidepressant effects may reflect antagonism at kappa-opioid receptors.[48] Transitioning from full agonists to buprenorphine not only reduces the risk of accidental overdose but frequently imparts subjective improvements in pain, function, sleep, and constipation.[49]

Two buprenorphine formulations (transdermal and buccal) have been approved by the Food and Drug Administration for chronic pain, and other formulations have been used off-label for this indication. In the United States, any practitioner can prescribe buprenorphine for chronic pain without additional designation. However, specialized training (8 hours of online or in-person training for physicians; 24 hours for advanced

Table 4. Medications for the Treatment of Opioid Use Disorder.*

Drug	Pharmacology	Route of Administration	Typical Daily Dose Range	Comments
Buprenorphine	Partial opioid-receptor agonist	Oral, sublingual, transdermal, intramuscular	For opioid use disorder: sublingual 8 to 24 mg once daily or intramuscular 100–300 mg; for chronic pain: sublingual 4 to 32 mg in divided doses	In the U.S., a waiver is required to prescribe buprenorphine for opioid use disorder (8 hr of online or in-person training for physicians; 24 hr for advanced practice providers); absent a waiver, can be administered (but not prescribed) for opioid use disorder on an emergency basis for up to 72 hr Buprenorphine is often coformulated with naloxone to deter diversion for injection use (naloxone is inactive orally) Buprenorphine should only be initiated once symptoms of mild-to-moderate withdrawal are present (score of ≥8 on the Clinical Opiate Withdrawal Scale) Adherence to therapy associated with marked reduction in mortality
Methadone	Full opioid-receptor agonist; NMDA-receptor antagonist	Oral	Varies; often 40 to 120 mg per day	In the U.S., methadone must be administered by an opioid treatment program when used for opioid use disorder; does not require abstinence before initiation Long elimination half-life; initial dose escalation should proceed cautiously; multiple drug–drug interactions; dose-dependent increase in QT interval Adherence to therapy associated with marked reduction in mortality
Naltrexone	Opioid-receptor antagonist	Oral, intramuscular	Oral, 50 mg daily; intramuscular (gluteal), 380 mg every 4 wk	Prolonged abstinence (≥7 days) is required before initiation Little evidence of mortality benefit relative to methadone and buprenorphine As compared with standard care at discharge from incarceration, decreased number of overdose events

* NMDA denotes *N*-methyl-D-aspartate.

practice providers) and Drug Enforcement Agency registration are required to prescribe buprenorphine for opioid use disorder (Table 4).[50-52]

MINIMIZING THE USE OF OTHER SEDATING MEDICATIONS

In patients receiving long-term opioid therapy, the risk of overdose increases dramatically when benzodiazepines, muscle relaxants, gabapentinoids, or other central nervous system depressants are coprescribed.[53,54] There is now widespread recognition that coprescribing of opioids and benzodiazepines is hazardous. Nevertheless, 27% of veterans who received opioids also received benzodiazepines, and the risk of overdose death was nearly four times as high in those using the two concurrently.[53] Although gabapentinoids are frequently used in an "opioid-sparing" approach, the concomitant use of gabapentin with opioids doubles the risk of fatal overdose as compared with the use of opioids alone.[54] A similar dose-dependent risk is seen with pregabalin.[55] When opioids must be prescribed with other sedating medications, doses of all agents should be kept as low as possible to minimize the risk of overdose.

MONITORING FOR EVIDENCE OF OPIOID USE DISORDER

Opioid use disorder is a recognized complication of long-term opioid therapy. Several studies suggest that features of opioid use disorder are present in more than 25% of patients receiving opioids for chronic pain.[56-58] Hallmarks of opioid use disorder include emotional volatility and signs of problematic medication use, such as taking more medication than prescribed, using opioids for reasons other than pain, and frequent loss of medication or early refills. Some patients with chronic pain may conceal or disavow features of opioid use disorder because of stigma or fear of losing access to prescribed opioids. Surveillance for opioid use disorder in patients with chronic pain includes pill counts, PDMP checks, and urine screening to assess adherence and check for the presence of unexpected drugs.

Several instruments are used clinically to screen for opioid use disorder.[59] One of the simplest is a validated, single-question instrument that asks, "How many times in the past year have you used an illegal drug or a prescription

medication for nonmedical reasons?" Any number greater than zero is considered a positive result.[60] Prescribers can then opt for a more in-depth survey instrument, such as the Current Opioid Misuse Measure, to further characterize features of opioid use disorder in patients receiving long-term opioids.[61]

Patients who have positive results on screening for features of opioid use disorder should not be denied opioid analgesia when other therapies are inappropriate. When the initiation of prescription opioids in patients with opioid use disorder is unavoidable, prescribers should have a very careful risk–benefit discussion, acknowledging the risks of problematic medication use, establishing the goals of care, and planning follow-up with addiction or pain-management specialists whenever available. In these cases, buprenorphine may be an ideal choice for both analgesia and treatment of opioid use disorder.[42]

Clinicians sometimes find that providing treatment for this patient population is challenging, but opioid use disorder in patients with chronic pain is an indication for more care rather than less. A punitive approach, such as dismissal from care, is counterproductive and places patients at greater risk for overdose if they transition from pharmaceutical opioids to illicit ones. Instead, recognizing the underlying opioid use disorder and arranging appropriate treatment are essential.

NALOXONE FOR PATIENTS WITH CHRONIC PAIN

Coprescribing of naloxone is increasingly accepted as a valuable tool in patients who are taking opioids for chronic pain. In a large observational study involving patients who were receiving long-term opioid therapy, those who were prescribed naloxone and provided with information on the risk of overdose had 63% fewer emergency department visits at 1 year than those who did not receive such treatment.[62] Naloxone is generally well received by patients and prescribers in the primary care setting.[63,64] The CDC guideline recommends coprescription of naloxone when patients who have a history of overdose or substance use disorder are prescribed opioids; it is also recommended in patients who are receiving a daily morphine-equivalent dose of more than 50 mg and in those receiving benzodiazepines concurrently.[27]

Several naloxone formulations that differ in dose, route of administration, and cost are available (see the Supplementary Appendix). Of these formulations, intranasal naloxone (at a dose of 4 mg) offers effectiveness and ease of administration for patients receiving long-term opioid therapy. Excellent resources for guiding patient and family conversations on naloxone coprescribing are available online.[65]

REDUCING OVERDOSE RISK IN OPIOID USE DISORDER

In 2016, the Substance Abuse and Mental Health Services Administration indicated that an estimated 2.1 million U.S. residents had an opioid use disorder.[66] Several strategies have been shown to decrease the risk of fatal overdose in these patients, including medications for the treatment of opioid use disorder and community efforts to distribute naloxone.

MEDICATIONS FOR OPIOID USE DISORDER

Methadone and buprenorphine are the primary opioid agonists for the treatment of opioid use disorder, and their importance in overdose prevention cannot be overstated. They promote retention in treatment, reduce the use of illicit drugs, and consistently decrease mortality in patients with opioid use disorder.[67-69] The choice of opioid agonist is based on a patient's history, preferences, and access to care. Retention in a medication-based treatment program is better with methadone (a full opioid agonist) than with buprenorphine (a partial agonist).[70,71] In the United States, special requirements exist regarding the prescribing of methadone and buprenorphine for opioid use disorder (Table 4).

When patients discontinue opioid use (e.g., detoxification with so-called drug-free protocols or during incarceration), the risk of death rises abruptly owing to loss of tolerance if they resume drug use.[72] As such, both the initiation of medications for opioid use disorder and subsequent efforts to maintain engagement with treatment are essential to overdose prevention.[67] A prolonged period without opioid use (including methadone and buprenorphine) is both a sign of recovery and a risk factor for fatal overdose. Although some patients with opioid use disorder avoid using drugs for extended periods, resumption of drug use is common and extremely perilous, a factor that underlines the importance of

treatment with agonists such as methadone or buprenorphine. Both of these drugs mitigate cravings, and buprenorphine also lessens the risk of respiratory depression. The emphasis by practitioners on abstinence-based recovery and the erroneous perception that opioid-agonist treatment replaces one addiction with another are not based on evidence and pose potentially fatal risks to patients with opioid use disorder. In addition, patients' engagement with treatment for opioid use disorder facilitates improved health care more generally, including screening and treatment for hepatitis C and human immunodeficiency virus infection.

Extended-release naltrexone, which is administered as a monthly intramuscular injection, is another option for patients with opioid use disorder. However, both the evidence base and clinical experience with this formulation are limited.[69] In contrast to buprenorphine and methadone, naltrexone blocks mu-opioid receptors and consequently the euphoric effects of opioids. The primary barriers to the use of extended-release naltrexone include the prolonged period of opioid abstinence before initiation (typically, 7 to 10 days) to avoid precipitation of withdrawal and the inability to later use opioids for analgesia, if necessary. As compared with buprenorphine or methadone, naltrexone is not associated with a reduced risk of opioid-related or all-cause death.[68] However, in persons who were recently released from incarceration, administration of extended-release naltrexone was associated with a marked reduction in overdose events.[73] Naltrexone remains an important option for patients who decline, or do not have access to, opioid agonist treatment.

COMMUNITY PROGRAMS FOR NALOXONE DISTRIBUTION

In 2018, the U.S. Surgeon General called on residents to carry naloxone with the goal of increasing the availability of the antidote.[1] Naloxone-distribution programs for bystanders are safe and cost-effective interventions to decrease overdose deaths.[74] Good Samaritan laws that offer legal protection to bystanders who give assistance during an overdose are associated with lower rates of death from opioid overdose.[75]

Patients with an opioid overdose require immediate restoration of ventilation and oxygenation through artificial means (e.g., rescue breathing and endotracheal intubation) or reversal of opioid-induced respiratory depression with naloxone.[76] In many cases, the timely administration of naloxone is sufficient to counter life-threatening respiratory depression. The effect of high-potency fentanyl analogues is reflected in the evolution of bystander naloxone kits to include the provision of higher doses (up to 8 mg administered intranasally) than were historically supplied (see the Supplementary Appendix). After naloxone administration, respiratory depression will recur if the opioid effects outlast those of naloxone (typically, 30 to 90 minutes).[76] Thus, persons who receive naloxone should be transported to the hospital for immediate follow-up care, as well as for qualified addiction care after overdose.

CARE OF PATIENTS AFTER OVERDOSE

Nonfatal opioid overdose is a strong predictor of increased short-term mortality. From 2011 through 2015, among persons in Massachusetts who had a nonfatal overdose, 6.2% died of an opioid-related overdose within 1 year and 9.3% within 2 years.[77] Patients who see a clinician after an opioid overdose should be screened for suicidal ideation, since the association between opioid use disorder and suicidality remains underrecognized.[78] After a nonfatal overdose, treatment with methadone or buprenorphine reduced opioid-related mortality by 59% and 38%, respectively; however, the majority of patients received neither drug.[68] Initiation of buprenorphine in the emergency department represents a key opportunity to treat opioid use disorder and to decrease mortality.[59] In addition, emergency initiation of buprenorphine increases engagement with addiction treatment, as compared with brief intervention and referral to treatment.[79] Although buprenorphine diversion occurs frequently among patients who are being treated for opioid use disorder, typical motivations for diversion include the treatment of withdrawal symptoms and self-treatment of opioid use disorder; both motivations are more common than use with the intent of "getting high."[80]

PUBLIC POLICY AND HARM-REDUCTION STRATEGIES

Strategies for reducing harm aim to decrease the adverse health and social consequences associated with drug use. For example, several countries have embraced supervised injection facili-

ties to prevent overdose, engage high-risk drug users, reduce health care use, decrease criminal activity, and reduce public drug use, needle sharing, and the associated litter.[81,82] For a subgroup of entrenched drug users, additional strategies to decrease opioid-associated deaths include supervised injection of heroin (diacetylmorphine)[83] and decriminalization of small amounts of drugs for personal use in conjunction with expanded access to addiction treatment. These strategies sensibly approach drug use as a health problem rather than a criminal one. (Details about this strategy are provided in the Supplementary Appendix.)

CONCLUSIONS

Several strategies reduce the risk of opioid overdose in diverse patient populations. Prescribers must carefully weigh potential benefits against the risks of opioid-related adverse events and overdose for all encounters involving prescription opioids. Patients receiving long-term high-dose opioid treatment should be counseled about steps to reduce the risk of overdose. Patients with an opioid use disorder require specialized treatment, including ready access to opioid-agonist therapy, qualified addiction care, and a much greater emphasis on harm reduction, in the recognition that drug use is a common, yet treatable, health issue.

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