Prescribing naloxone for opioid overdose intervention

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Practice points

- The public-health response to the opioid crisis requires a multifaceted approach that includes guidelines to effect changes in opioid prescribing, interventions to prevent or treat opioid abuse and dependence, and strategies to diminish the harmful effects of opioid misuse.
- Numerous guidelines have advocated use of the opioid antagonist naloxone as a harm-reduction strategy.
- Two naloxone products that include instructions for use by personnel without medical training have been approved by the US FDA for community use: an intranasal spray and an autoinjector for intramuscular or subcutaneous use.
- In primary care and pain medicine, coprescription of naloxone could be considered for patients with opioid prescriptions exceeding a threshold daily dose or patients with other risk factors for overdose.
- Although there are potential opportunities to expand naloxone use in many settings, evidence from current literature suggests these are often missed or underexploited.
- Academic detailing interventions could be used to increase naloxone prescribing for patients receiving opioid prescriptions in a primary care setting.
- Naloxone could be prescribed at discharge from the emergency department to individuals at risk of opioid overdose.
- Wider use of naloxone may also include law enforcement personnel, addiction treatment facilities and individuals newly released from incarceration.
- Most states now permit naloxone prescriptions to be written for third parties (e.g., family or friends, staff of organizations providing services to individuals at risk of overdose).

To provide an update on prescription of naloxone as a harm-reduction strategy, PubMed was searched to identify publications relevant to naloxone prescribing for reversal of opioid overdose. Opportunities now exist to expand naloxone use, although evidence suggests these are often missed or underexploited. The US FDA has approved an intranasal naloxone spray and an autoinjector naloxone formulation for community use. Effective use of naloxone in community settings requires screening to identify patients at risk of opioid overdose, discussing naloxone use with patients and their relatives, and providing appropriate training. The tools exist to expand the use of naloxone more widely into the community, thereby creating an opportunity to reduce opioid overdose fatalities.

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The USA, and to a lesser extent some European countries and Australia, is experiencing an opioid epidemic [1,2]. During the past two decades, opioid sales, admissions for opioid overdoses and opioid-related deaths have dramatically increased [2–4]. Since 2000, the incidence of opioid overdoses has tripled, and deaths from opioid overdose (both prescription analgesics and heroin) have increased by 200% in the USA [4]. In 2015, opioids accounted for 33,091 deaths, corresponding to 63% of all drug overdose deaths [5]. This epidemic has been driven by a number of factors, principally increasing rates of opioid prescriptions – and a corresponding rise in nonmedical use of prescription opioids; a recent increase in deaths from illicit opioid overdose, largely driven by heroin use; and a sharp rise in fentanyl-related overdose deaths, particularly involving illicitly manufactured fentanyl [1,2,4,6]. The public-health response to this epidemic of opioid overdoses requires a multifaceted approach that includes

Box 1. Prescribers of naloxone.

- Addiction medicine specialists
 - Upon discharge from inpatient treatment
 - During outpatient treatment
- Department of corrections
 - Upon release from incarceration
- Emergency departments
- Pain medicine specialists
- Primary care providers
- Pharmacy based (varies by state)
 - Collaborative practice agreement
 - Standing medication order
 - Protocol order
 - Pharmacist prescriptive authority

guidelines to effect changes in opioid prescribing, interventions to prevent or treat opioid abuse and dependence, and strategies to diminish the harmful effects of opioid misuse [3,7].

Naloxone is a competitive opioid antagonist that has been in clinical use since 1967 to reverse respiratory depression caused by opioid overdose [8,9]. The continuing epidemic of opioid-related fatalities has led to the increasing use of naloxone in community-based harm-reduction strategies [8–11]. Whereas naloxone is normally given by injection in the healthcare setting, intranasal formulations are generally used in the community [9] and studies have shown that intranasal naloxone can be used successfully by nonmedical first responders and other laypersons to reverse opioid overdose and prevent overdose-related deaths [12–14]. Initially, naloxone for community use consisted of improvised intranasal kits, which contained a prefilled syringe of naloxone (formulated for injection) that could be modified for intranasal administration by attaching an atomizer [15,16]. Subsequently, two naloxone combination (drug/device) products that include instructions for use for personnel without medical training have been approved by the US FDA for community use: an intranasal spray (NARCAN®; Adapt Pharma, Inc., PA, USA) [17,18] and an autoinjector for intramuscular or subcutaneous use (EVZIO®; Kaléo, Inc., VA, USA) [16]. Recent literature was reviewed to provide an update on prescribing naloxone as a harm-reduction strategy, with the aim of encouraging expanded access to naloxone for individuals at risk of opioid overdose.

Methodology

PubMed searches covering the period from January 2000 to October 2017 were performed using the search terms ‘prescription’ OR ‘prescribing’ OR ‘prescribed’) AND ‘naloxone’. Searches were limited to English language publications. The abstracts of retrieved articles were reviewed to identify publications relevant to the prescription of naloxone for the reversal of opioid overdose.

Settings for naloxone prescribing

The principal channels for naloxone distribution are hospitals, clinics and retail pharmacies. Key settings for prescription of naloxone for community use include emergency departments, physician offices and addiction treatment facilities (see [Box 1](#)) [8–11,19–26]. Other potential avenues include prescription upon release from incarceration and prescription by pharmacists [19,24–26].

Naloxone prescribing in the emergency department

Many patients with opioid exposure, either due to legitimate use of prescription analgesia or illicit opioid use, present to emergency departments. In the USA, between 2008 and 2011, more than one million emergency visits occurred each year for drug poisoning, and 14.0% of visits for unintentional overdose were opioid-related [27]. The national rate of opioid-related emergency department visits nearly doubled between 2005 and 2014 [28]. Data in 2010 from the Nationwide Emergency Department Sample show that 67.8% of emergency department visits for opioid-related overdose involved prescription opioids and 16.1% involved heroin [29]. Chronic opioid use is an important driver of emergency department visits. For example, in a study using administrative claims data (both Medicaid and commercially insured patients), approximately 25.0% of patients receiving chronic (≥ 90 days) opioid therapy had an emergency department visit within the first 12 months of opioid use [30].

A population-based study of two US states (California and Florida) found that 52.8% of emergency department visits for opioid overdose resulted in hospitalization, and 10.0% involved a near-fatal event (i.e., an overdose necessitating mechanical ventilation) [31]. Furthermore, the risk of near-fatal events was significantly increased among patients with frequent (≥ 2) visits to the emergency department, compared with those with only a single visit (odds ratio = 2.27; 95% CI = 1.94–2.66; $p < 0.001$) [31]. This finding is consistent with a case–control study of statewide data (New York) that found that approximately 40% of patients who subsequently died of an unintentional prescription drug overdose had multiple prior emergency department visits [32].

Despite the large number of emergency department visits for opioid overdose [27,29], and the fact that opioids are commonly prescribed in emergency departments for pain control [33], prescribing or dispensing of naloxone in this setting is relatively uncommon. A survey of opioid-related policies in New England emergency departments found that only 12% of departments would prescribe naloxone for patients at risk of opioid overdose after discharge, and the adoption of other opioid-related policies was variable (use a screening tool, 18%; notify primary care providers of opioid prescription, 41%; refer to recovery resources, 70%; access Prescription Drug Monitoring Program, 78%) [34]. Similarly, in a Web-based survey of 200 emergency department physicians, respondents generally expressed a willingness to adopt opioid harm-reduction strategies, but only 1.7% reported previously prescribing naloxone and only 10.3% had referred patients to a naloxone distribution program [35]. In another Web-based survey of 459 Canadian emergency department physicians, although 86% of respondents were willing to prescribe naloxone to patients at risk of opioid overdose, they identified limited time in the clinical encounter, lack of institutional supports and lack of knowledge and training as barriers to implementation of community-based opioid overdose education and naloxone distribution programs [36]. Additional barriers to naloxone access may include financial burden (as prices for some naloxone products have increased in recent years) [37], formulary restrictions and variations among state laws regulating prescribing [38,39]. Another important barrier in emergency departments is federal law that prohibits charging for naloxone dispensed in this setting unless there is an outpatient pharmacy within the medical facility.

Emergency department-based naloxone distribution is widely accepted by patients. In one study, 68.2% of patients receiving opioid therapy at a daily dose of ≥ 100 morphine milligram equivalent (MME; equivalent, e.g., to 20 tablets of hydrocodone 5 mg/acetaminophen 300 mg, ~ 12 tablets of oxycodone 5 mg/acetaminophen 325 mg and ~ 2 tablets of extended-release oxycodone 30 mg [40]) and those with self-reported opioid use (or a prescription for medications commonly used in the treatment of opioid addiction) accepted a naloxone kit and training when this was offered [41].

Naloxone prescribing in outpatient settings

Primary care providers commonly provide healthcare for patients receiving opioid analgesia and patients with illicit opioid use, and thus represent a potentially valuable avenue for naloxone use in the community. Discussing naloxone with primary care patients provides the opportunity to highlight the risks associated with opioid use and offer a harm-reduction strategy. However, the available evidence suggests that although primary care providers generally have favorable attitudes toward the use of naloxone, a relatively low percentage has prescribed naloxone to their patients [42]. In a survey of 97 internal medicine residents at an urban US academic medical center, 86.5% agreed that naloxone is effective for reducing opioid overdose deaths, and a similar percentage (92.1%) did not believe that naloxone prescription would promote increased opioid use [42]. However, only 46.8% had ever discussed overdose risk and prevention with patients and only 15% had previously prescribed naloxone for community use. This lack of prescribing may be due to a lack of confidence in their ability to identify patients at risk of overdose and prescribe naloxone appropriately, as only 16% of respondents indicated that they knew how to prescribe the drug. These findings are consistent with those of a survey of 448 general practitioners in Ireland, in which 66.1% of general practitioners indicated that they were in favor of using naloxone in the community, but only 31.6% were prepared to take part in such a project [43].

By contrast, naloxone prescribing rates are much higher at clinics participating in an overdose prevention program [44]. In a survey of 111 primary care providers offering naloxone prescriptions to patients receiving long-term opioids as part of a US public health department program, 79.3% of respondents had prescribed naloxone since the program began, and 99.1% reported being likely to prescribe naloxone in the future [44]. Most respondents reported that they would prescribe naloxone for patients on either high-dose (> 20 MME per day) or low-dose (< 20 MME per day) opioid therapy (97.7 and 59.8%, respectively), and in patients without a known history of overdose (80.7%) or substance use disorder (73.6%). Nationally, Symphony Health Solutions data (extracted July

2017) showed 101,863,027 prescriptions for opioids and 149,259 prescriptions for naloxone (ratio, 682:1) during the first 6 months of 2017.

Academic detailing programs in primary care

Academic detailing programs use one-on-one educational interventions to deliver evidence-based information to healthcare providers within their own practices. This approach has been used in a number of countries, including Canada and the UK, and has delivered significant behavioral change, for example, in increasing smoking cessation efforts [45]. Such programs may, therefore, increase naloxone prescribing by primary care providers.

An academic detailing program in San Francisco provided 40 primary care providers with written information on prescribing controlled substances, prescription drug-monitoring programs and the effectiveness and cost effectiveness of naloxone, accompanied by a 5–60-min discussion tailored to the interests of the individual provider [45]. The number of naloxone prescriptions was increased to a significantly greater extent in providers who received the detailing intervention, compared with those who did not ($p = 0.01$), and at follow-up, 12 of 24 detailed providers (50.0%) had written at least one naloxone prescription.

To reduce deaths from opioid overdose among US veterans, the US Veterans Health Administration instituted the first nationwide Opioid Overdose Education and Naloxone Distribution (OEND) program in 2014 [46]. The effect of supplementing this program with academic detailing was examined in a retrospective study, in which academic detailing was provided to 750 of 3313 providers (22.6%), almost 91% of whom were in primary care (90.9%) [46]. Naloxone prescription rates were three-times greater after 12 months and seven-times greater after 24 months for providers who received academic detailing, compared with those who did not. However, given the low base rates for naloxone prescribing before the detailing intervention, even such striking increases may have benefited only a modest number of patients.

Naloxone coprescription programs

Naloxone coprescription programs have been developed for both primary care [20,21] and pain medicine [22] practices. In one study [20], naloxone was prescribed in 38.2% of 1985 patients receiving long-term opioid therapy: patients receiving higher opioid doses and those with an opioid-related emergency department visit within the previous 12 months were more likely to be prescribed naloxone. After 12 months, patients who had received a naloxone prescription had made 63% fewer opioid-related emergency department visits per month than those who had not.

The available evidence suggests that patients receiving opioids for pain relief generally have positive attitudes to naloxone coprescription. In a study of 208 patients receiving opioid treatment for chronic noncancer-related pain, 60.6% of participants thought that offering naloxone to opioid-treated patients was a ‘good’ or ‘very good idea’; relatively few would be ‘a little’ (10.1%) or ‘very’ (3.4%) offended if a health professional thought they needed naloxone [47]. Similarly, in an interview study of 60 patients (87% were prescribed opioids for pain) who received naloxone prescriptions in a primary care clinic, most participants had a positive (56.7%) or neutral (21.7%) response to being offered naloxone; 82% of participants successfully filled a naloxone prescription and 36.7% reported positive behavioral changes (e.g., safer opioid dosing or safer timing of dose) after receiving naloxone [48].

Coprescription of naloxone is mandated by law in Vermont (as of 1 July 2017) for patients receiving an opioid prescription that exceeds 90 MME per day or patients receiving an opioid prescription (any dose) concurrent with a prescription for a benzodiazepine. On 15 March 2017, the Virginia Board of Medicine issued regulations requiring coprescription of naloxone with opioids for patients with risk factors, specifically prior overdose, substance abuse, opioid dose in excess of 120 MME or concomitant benzodiazepine prescription. In the 2 months after the Virginia regulation went into effect, naloxone prescribing increased to approximately one naloxone prescription for every 45 opioid prescriptions compared with the national average (in the late May 2017) of approximately one naloxone prescription for every 570 opioid prescriptions (Symphony Health Solutions data).

Naloxone prescribing in addiction treatment settings

Although the ultimate goals of treatment for patients with opioid addiction are treating substance dependence and preventing substance misuse, harm-reduction strategies are essential intermediate steps [49]. Together with syringe-exchange programs and opioid substitution, naloxone distribution is a valuable harm-reduction strategy for opioid users [49], but objections to prescribing naloxone for opioid users have been raised primarily on concerns that naloxone does not address the underlying addiction and may actually encourage opioid use (either

because an antidote is available or by precipitating withdrawal) [49–52]. However, concerns that prescribing naloxone will result in increased opioid use are refuted by the available data [49,51,53].

The potential impact of a naloxone prescription program for opioid users is highlighted by the experience gained in the Drug Overdose Prevention and Education program, which was established in 2003 in collaboration with the San Francisco Department of Public Health and is one of the oldest naloxone prescription programs in the USA [54]. Overall, 11% of individuals who were prescribed naloxone reported using the drug during an overdose event, and 83% of these overdose events were reversed with naloxone.

A recent study has investigated outcomes after providing naloxone overdose reversal kits to patients enrolling in medication-assisted treatment of opioid use disorders [23]. A total of 244 patients were enrolled and received education about opioid overdose and the use of the naloxone autoinjector kit. Of 215 evaluable patients, 31 either experienced or witnessed at least one opioid overdose episode. Interviews of these patients indicated that 39 opioid overdoses had been reversed with naloxone.

Other avenues for naloxone prescribing

Correctional facilities

Opioid users are at increased risk of overdose after a period of abstinence, such as after institutionalization or incarceration [55]. In a US study of former inmates, released between 1999 and 2003, the risk of death within the first 2 weeks after release was 12.7-times that of the general population, and drug overdose was the leading cause of death [56]. A follow-up study of inmates released between 1999 and 2009 found a tenfold increased risk of overdose in former inmates, compared with the general population; opioids were involved in 58.6% of overdose deaths, of which pharmaceutical opioids accounted for 40.5% [57].

An educational program on opioid overdose prevention and naloxone administration designed specifically for inmates before release has been developed and is currently in use in a number of correctional facilities [24]. In what is believed to be the first reported cases of naloxone self-administration to prevent fatal overdose, two former inmates who had undergone this program successfully self-administered intranasal naloxone to treat opioid overdose within 3 weeks of release [25]. In an initiative piloted in 2016 and expanded in January 2017, inmates released from Baltimore area (and other Maryland county) jails are provided naloxone training and two doses of the FDA-approved intranasal naloxone as part of a state-run program [26].

Pharmacy-based naloxone dispensing

Pharmacy-based naloxone dispensing offers an alternative to the traditional prescription process in which a prescription is provided by a licensed provider (e.g., physician, physician assistant, nurse practitioner) to a specific patient. In recent years, 40 states have passed legislation whereby patients and caregivers can receive naloxone from a pharmacy without having a prescription from a healthcare provider (e.g., via standing orders) [58]. These programs are designed to expand community access to naloxone [19,59]. Standing orders, the most common mechanism for pharmacy-based naloxone dispensing, are prescriptions written by a physician or other prescriber that authorize naloxone to be dispensed to any person who meets specific criteria (typically individuals at risk of opioid overdose, in the case of naloxone standing orders), rather than to a specific patient [38,39]. In addition to pharmacy-based naloxone dispensing, some states permit dispensing by nonmedical professionals [38]. In some states, statewide standing orders, issued by a government official such as the Physician General, authorize naloxone dispensing by pharmacists throughout the state [39]. Details about pharmacy-based models vary by state and, in addition to standing medication orders, may include collaborative pharmacy practice agreements, protocol orders and pharmacist prescriptive authority (see Table 1) [19]. Many pharmacy-based models permit third-party prescribing of naloxone, for example, to a friend or family member rather than to the person actually at risk of overdose. This practice is legal in most states, in recognition of the fact that such third parties may be more likely to raise concerns about opioid-related risks and are likely potential witnesses of an overdose [39].

Guidelines & policy statements on naloxone prescribing

The CDC and the WHO along with many additional national and international organizations have issued guidelines or policy statements on naloxone prescribing (see Table 2) [40,60–64]. In addition, a number of state and municipal departments of health have also developed prescribing guidelines for naloxone.

Coprescription of naloxone with opioids is endorsed by large insurers, and an assessment of the legal risk associated with prescribing or dispensing naloxone concluded that coprescribing naloxone for a patient at risk

Table 1. Naloxone distribution models currently in use in the USA.						
Factors	Traditional prescription	Community-based organization	Pharmacy-based naloxone models			
			Collaborative practice agreement	Standing medication order	Protocol order	Pharmacist prescribing
Who issues prescription?	Prescriber	Prescriber via standing order	Nonpharmacist provider	Nonpharmacist provider	Licensing board	Pharmacist
Medical professionals required	Prescriber and pharmacist	Varies by state: prescriber, state/local health department	Prescriber and pharmacist	Prescriber and pharmacist	Pharmacist	Pharmacist
Potential recipients	Patients of the prescriber	Individuals served by the community-based organization	Varies by state	Anyone meeting criteria specified by prescriber	Anyone meeting criteria specified by licensing board	Anyone for whom medication is indicated
Target overdose risk population served	People who misuse/abuse opioids (prescription opioids, heroin) who are in treatment or visit a prescriber ⁱ Patients prescribed opioids who are at risk of overdose ⁱ	People who use drugs (prescription opioids, heroin) who access the community-based organization ⁱ	People who use drugs (prescription opioids, heroin) who visit a pharmacy ^j Patients at risk of overdose who are filling a prescription for opioids at a pharmacy ^j			
Geographic reach	Limited to where the prescriber practices	Limited to where community-based organizations are located and operate	Any practicing pharmacy within the state			Limited to where the pharmacist practices

ⁱMost states now permit prescriptions to be written for third parties (e.g., family or friends, staff of organizations providing services to individuals at risk of overdose), as well as to the person at risk of overdose. Adapted with permission from [19] via a Creative Commons Attribution 4.0 International License.

ⁱMost states now permit prescriptions to be written for third parties (e.g., family or friends, staff of organizations providing services to individuals at risk of overdose), as well as to the person at risk of overdose. Adapted with permission from [19] via a Creative Commons Attribution 4.0 International License.

Table 2. Guidelines and policy statements on naloxone for opioid overdose.

Organization	Guidelines/policy	Key content	Ref.
WHO	Community Management of Opioid Overdose	Contains recommendations on: <ul style="list-style-type: none"> • Naloxone distribution to people likely to witness an overdose • Appropriate formulations and doses of naloxone for community use 	[60]
CDC	Guideline for Prescribing Opioids for Chronic Pain	Clinicians should: <ul style="list-style-type: none"> • Prescribe the lowest effective opioid dosage, use caution increasing to ≥ 50 MME per day and avoid ≥ 90 MME per day (unless carefully justified) • Consider offering naloxone when risk factors are present (i.e., history of overdose or substance use disorder, opioid dose ≥ 50 MME per day, concurrent benzodiazepine use) 	[40]
SAMHSA	Opioid Overdose Prevention Toolkit	<ul style="list-style-type: none"> • Summarizes factors to consider before prescribing opioids, use of PDMPs and patient education/monitoring • Providers should consider prescribing naloxone along with the initial opioid prescription 	[61]
AAPM	Coprescribing of Naloxone in Conjunction with Opioid Therapy	Prescribers of opioid therapy should: <ul style="list-style-type: none"> • Fully assess overdose risk • Discuss risk factors with patients/caregivers • Offer prescription of an FDA-approved naloxone product 	[62]
ASAM	Public Policy Statement on the Use of Naloxone for the Prevention of Drug Overdose Deaths	<ul style="list-style-type: none"> • Supports broadened accessibility to naloxone for community use • Encourages coprescription of naloxone with long-acting opioids and significant total opioid dosage • Recommends training for naloxone recipients in overdose detection and response (including naloxone administration) 	[63]
ASAM	The National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use	<ul style="list-style-type: none"> • Discusses naloxone in the context of other medications used in the treatment of opioid addiction • Prescriptions for naloxone should be provided to patients being treated for opioid use disorder and their family members/significant others 	[64]

AAPM: American Academy of Pain Management; ASAM: American Society of Addiction Medicine; MME: Morphine milligram equivalent; PDMP: Prescription Drug Monitoring Program; SAMHSA: Substance Abuse and Mental Health Services Administration.

of overdose is a ‘reasonable and prudent clinical and legal decision’ and does not increase the provider’s liability risk [65].

Identifying appropriate patients

The identification of patients at risk of opioid overdose is a key challenge in expanding access to naloxone [21]. As might be anticipated, studies of patients on opioid therapy for acute or chronic pain have shown that higher prescribed opioid doses are associated with an increased risk of overdose [66–68]. In addition, the use of long-acting opioids is associated with a significantly increased risk of overdose, compared with short-acting preparations, particularly during the first 2 weeks of treatment [69]. Other factors associated with increased risk of opioid overdose include concomitant benzodiazepine use, co-morbid medical conditions, co-morbid mental disorders and co-morbid substance use disorder [68,70,71].

Having identified individuals at risk of opioid overdose, it might be particularly effective to target OEND interventions to their social network, members of which may be most likely to witness an opioid overdose. However, it should be noted that such individuals may not be interacting with community OEND programs [72].

Clinical best practices in naloxone prescribing

The successful implementation of naloxone prescribing programs requires attention to a number of aspects of clinical practice. Education of providers on all strategies for opioid management should be a priority, and academic detailing programs should be expanded to all providers.

Screening for opioid overdose risk

A number of validated instruments are available to assess the risk of opioid overdose. These include the Opioid Risk Tool, a 5-item measure designed for use with patients in primary care settings [73], and two self-report instruments, the revised Screener and Opioid Assessment for Patients with Pain [74] and the Simple Screening Instrument for Substance Abuse [75]. At this writing, no published data favor the use of one instrument over another in routine clinical practice. Asking about drug use during social history-taking should be part of any encounter with a patient. In addition, a review of the patient’s current medications is essential to assess risk.

Electronic health record alerts

The use of electronic alerts may facilitate effective naloxone prescribing. In a study within an academic health system comprising two hospitals with emergency departments, outpatient clinics, infusion centers and pharmacies, the mean number of naloxone prescriptions per month increased from 4.5 at baseline to 46 during the 3 months after implementing an OEND program with electronic health record alerts [76]. More than half (53%) of these prescriptions were for unapproved (improvised) intranasal naloxone, 43% were for intramuscular naloxone via standard syringe and needle and 4% were for the FDA-approved autoinjector [76]. However, ‘alert fatigue’ may be one limitation to using electronic alerts to increase naloxone prescriptions in patients receiving opioids. Appropriate thresholds should be developed for these communications, particularly with high-risk combinations of medications.

Discussing naloxone with patients

The importance of carefully discussing the use of naloxone with patients or their families or friends cannot be overemphasized. The results of an interview study of 24 patients prescribed high-dose opioid therapy for chronic noncancer-related pain suggested that framing naloxone as relevant for worst-case scenarios (analogous to keeping a fire extinguisher on hand or wearing a seatbelt) was a nonjudgmental, empowering approach that could potentially increase patient acceptance [77].

Training in naloxone use for patients & members of their social network

There is evidence that correct administration of naloxone is more likely with FDA-approved products (intranasal spray and intramuscular/subcutaneous autoinjector) than with unapproved (improvised) intranasal kits [16,18]. Dissemination of naloxone to interested community members and training on its use through a community intervention initiative should be considered. Using local data to target ‘hot spots’ in the community can help identify populations that may benefit from such services. Partnering with community groups, faith-based organizations and local health outreach services could all facilitate harm reduction.

Staying current with state laws & policies regarding naloxone prescribing

The state laws and policies regarding naloxone prescribing have been changing rapidly in response to the epidemic of opioid overdoses [39,78]. As of May 2017, 46 states permit third-party prescription, so that naloxone can be prescribed and dispensed not only to persons at risk but also to potential bystanders [58]. Coprescription of naloxone with opioids is mandated in some states (i.e., Vermont, Virginia), and others are in the process of developing coprescribing guidelines.

Conclusion

Increased access to naloxone as a harm-reduction strategy – both for patients prescribed opioids for pain management and for those using opioids illicitly – is one component of a multifaceted approach to addressing the opioid epidemic. There are potential opportunities to prescribe naloxone to patients at risk of overdose (or to their friends or relatives) in many settings, including emergency departments, primary care office settings, addiction treatment centers, correctional facilities and (depending on the state) pharmacies. However, the current literature suggests these opportunities are often missed or underexploited. Guidelines from many US agencies or organizations consistently recommend the prescription of naloxone for patients at risk, and this approach is supported by insurers. With the FDA approval of two naloxone formulations designed for community use, the tools exist to expand the use of naloxone more widely beyond traditional healthcare settings into the community.

Future perspective

Increased provider awareness of the benefits of community-use naloxone and the availability of easy-to-use naloxone formulations will hopefully lead to increases in naloxone prescription rates. It could, therefore, be anticipated that wider use of naloxone offers the opportunity to attenuate the mortality associated with the current opioid epidemic. Based on the impact of the epidemic, it may be necessary to increase the amount of naloxone dispensed by an order of magnitude or more to make an impact on the rate of opioid-related overdose fatalities. Providers may effect change by screening patients for opioid overdose risk, becoming more familiar with available naloxone formulations, discussing naloxone with patients in a nonjudgmental fashion and staying abreast of state laws and policies related to naloxone prescribing. Additional naloxone products for community use (including instantly disintegrating buccal tablets [79] and additional intranasal spray formulations [80,81]) are currently in development and, if approved by

the FDA, will provide further treatment options. Regulatory approval for over-the-counter purchase, which would remove a significant barrier to naloxone availability, seems unlikely in the near term, highlighting the importance of state laws and regulations that expand access to naloxone.

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