

Clinical Perspective on Opioids in the Context of Suicide Risk

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Psychiatrists are on the front lines of two simultaneous public health crises: the increasing rates of suicide and opioid-related deaths. In this review, the authors discuss ways in which these two classes of preventable deaths may be linked, with an emphasis on identifying and preventing both outcomes through increased understanding of their shared risk factors. As clinicians, it is crucial to maintain awareness of the ways in which opioid use may contribute to depression and suicidality, as well as how mood disorders may complicate opioid use. In light of this interplay, interventions which target risk factors for both suicide and overdose are key. Interventions include

early treatment of substance dependence and depression, as well as harm reduction measures, such as provision of naloxone, medication-assisted treatments for dependency, and multidisciplinary approaches to chronic pain that do not rely solely on escalating opioid doses. It is also important to address social determinants of health, which may increase risk for both accidental and intentional overdose. The roads to overdose and suicide overlap considerably and cannot be considered separately.

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Rates of unintentional overdose and suicide have both climbed during the past 2 decades in the United States, in contrast to other common causes of death, such as cancer and heart disease, rates of which have declined because of improvements in health care. In the United States, overdose and suicide represent the first and second leading causes of death, respectively, among those younger than age 40. In the country, cumulatively, there were 33.7 unintentional overdose or suicide deaths per 100,000 people in 2017 (1). This figure represents 111,968 deaths in total, outnumbering deaths from diabetes (83,564) for that year (1).

In addition to their shared trajectory of increasing mortality rates, overdose and suicide share other similarities. Some of this similarity is conceptual. Evidence from high-risk samples indicates that many (nonfatal) opioid overdoses include some degree of suicide intent or ideation, despite few being outright suicide attempts (2, 3). Additionally, for both overdose and suicide, death rates are higher among men than women and among whites or Native Americans than among blacks or Asian Americans (4). Overdose and suicide also share a number of clinical indicators of elevated risk, such as opioid prescriptions (particularly those for high daily dosages) and diagnosed mental health conditions.

In this article, we aim to provide an overview of the ways in which suicide and unintentional overdose are intertwined problems in the United States, with a focus on implications for mental health clinicians. Mental disorders, particularly depression, have a critical role in the development of risk for

both problems and are discussed here accordingly. Additionally, opioid use has been a primary driver of the rapid rise in overdose deaths and has a less recognized but also important role in suicide risk. However, many tools and strategies, described below, are available to clinicians to address risk of these two problems simultaneously.

MENTAL ILLNESS AND OPIOID USE

Major depressive disorder and other serious mental illnesses are the major contributors to suicide risk. As many as 90% of suicide decedents had a major mental illness, most commonly depression (5, 6). Approximately 6% of patients with major depressive disorder will die by suicide, which is 20 times the rate for those without depression (7, 8). In addition, depressive symptoms and diagnosed depression, as well as most other mental health conditions, have been consistently found to be associated with risk of unintentional overdose (9, 10). However, the degree to which this association varies across the spectrum of intentionality is unknown. Nonetheless, across both suicide and accidental overdose, depression and other mental health conditions have a clear role in either directly causing, or being a useful indicator of, elevated risk.

Opioid use also has been shown to increase risk for suicide and unintentional overdose (4). The majority of unintentional overdoses are caused by consumption of opioids alone or in combination with other substances. Since 2010, heroin has contributed to an increasing proportion of deaths,

and since 2016, synthetic opioids (driven by illegally manufactured fentanyl) have overtaken prescription opioids as the drug type responsible for the most deaths (11). Among individuals prescribed opioids, those receiving higher daily dosages are at the most increased risk for unintentional overdose (12–14). Although only a small number of suicide deaths are ruled intentional opioid overdoses (4), high opioid dosages have been associated with suicide (15). Opioid use disorder has been directly linked to increased risk for suicide, with an estimated 13–14 times greater risk of suicide among patients with the disorder compared with patients without the disorder (16).

Opioid use has a complex and potentially bidirectional relationship with depression, particularly in the context of pain. Individuals with depression are more likely to receive prescriptions for opioids than individuals without the condition (17). In a study of patients at a chronic pain clinic, patients with depression were more likely to take opioids for lower pain levels than patients without depression (18). In studies of patients taking opioids, those with depression have been more likely to take higher daily dosages and to report opioid misuse than those without depression (19) (20). Cumulatively, these studies have established the role of depression in the initiation of opioid use and in escalation to potentially problematic use, but there is also some evidence for the reverse direction of effect—among individuals initiating opioid use, a longer duration of use is associated with new-onset depression (21) and with treatment-resistant depression (22). The Scherrer et al. studies considered diagnoses of depression and other psychiatric disorders when establishing the association of higher opioid dosages with overdose and suicide. Given the relationships between depression and opioid use, however, depression may significantly mediate or moderate the association between opioid use and dosage and suicide and overdose.

Cumulatively, the extant evidence indicates the critical and central roles of depression and opioid use in the development of risk for suicide and overdose in the United States, along with an interaction between these factors that is only beginning to be understood.

In addition to these complex relationships between general opioid use and depression, the acute effects of the opioid itself can contribute proximally to suicide risk. These effects include the disinhibition and impulsivity seen with any intoxication (23, 24), including opioid intoxication, as well as the lethality of these substances when taken in high doses (25, 26). The majority of suicides are impulsive (27), and increased impulsivity as a trait has been linked to suicide risk (28). State impulsivity, conferred by intoxication, may present a similar risk. Decision-making capability itself is hindered by intoxication (29). These effects may partly explain why alcohol and other intoxicants, including opioids, are commonly found in the blood of suicide decedents, even when these agents were not the direct cause of death (30).

A final characteristic of opioids, which directly contributes to their association with suicide, is their lethality in

overdose (26). A large body of work has shown that suicide risk is in many ways a function of access to lethal means (31). In the United States, this finding is particularly salient in regard to firearms, which greatly increase the risk of suicide largely because of their high case fatality rate and easy access (32–34). Although poisoning in general has only a 2% case fatality rate, when the substance used is an opioid, the rate may be much higher, especially with the increasing presence of fentanyl contamination (25, 35). The presence or availability of opioids may be analogous to having a gun in the home. The accessibility of these potentially dangerous substances may play at least a minor role in the increased suicide rates seen among patients with chronic pain and those with opioid dependence (16, 36), and the increased availability via medicine cabinets may contribute to increasing rates of suicide and overdose even among those not prescribed the medications.

DIFFICULTY DETERMINING INTENT IN FATAL OVERDOSES

Death from suicide or opioid overdose can be so closely related that distinguishing between them in even an individual decedent can be challenging. Given the spectrum of intentionality reported by patients who have experienced nonfatal opioid overdose (3), as well as the overlapping risk factors for suicide and unintentional overdose and the limited amount of information available from death scene investigations and autopsies, it is unsurprising that the intentionality of fatal overdoses can be difficult to determine (37). Nationwide during the 21st century, about 8% (range 5%–17%) of poisoning deaths have remained unclassified (38). Classification of deaths varies by region, with some states leaving as many as 80% of overdose deaths labeled as undetermined (39). It has been estimated that about one-third of these undetermined deaths may be due to suicide (40–43). In fact, unintentional and intentional overdoses may be so difficult to distinguish that leading researchers of suicide have proposed a combined category of self-injury mortality as a better alternative for surveillance (44, 45). Such categorization may more accurately portray these deaths, especially for women and people from minority groups, where classification based on estimated intent may be particularly misleading (46). Clinicians should be aware of this potential bias in classification of deaths and not allow tunnel vision to hinder their identification of hazard outside of populations traditionally reported as highest risk, such as white men.

WHAT CLINICIANS CAN DO

Because of the relationships among depression, suicide, and opioids, clinicians must be cognizant of the risks involved in opioid use for potentially vulnerable patients (4, 19). The danger of creating or worsening a mood disorder or of risking intentional or accidental overdose must be

considered. In general, as with any medication, opioid analgesics should be prescribed only when the risks outweigh the benefits. Because poorly managed pain can also increase risk for suicide, pain management is one potential benefit of opioid use. As described below, however, the evidence for benefit from opioids at the population level is limited, with consequently limited guidance on who is likely to benefit from opioids.

Although opioids can be effective for acute pain, including postsurgical management, the effectiveness of opioids in the management of chronic pain is finite (47). In fact, chronic opioid use may modestly lower the pain threshold, increasing pain's impact (48). Given the bidirectional relationships between depression and opioid use problems, poor opioid stewardship has the potential to increase mental health problems (4).

Nonetheless, chronic pain itself is a clear contributor to suicide risk (15, 49) and must be addressed. Several non-opioid approaches for the management of chronic pain are recommended, and each case should be adjudicated on the basis of the nature of the pain, its etiology, and a comprehensive assessment of the patient. The *sine qua non* is the complete medical assessment of the patient. Based on this assessment, further management may be directed for a specific lesion and/or involve alternative pharmacological and nonpharmacological management. In most cases, a combination of treatments involving a multidisciplinary team is optimal (50, 51).

Numerous approaches are available for the management of specific pain syndromes. These approaches may include nerve blocks, trigger-point injections, Botox injections, and local anesthesia to encourage rehabilitation (52). Additional alternatives to opioids include nonsteroidal analgesics, although these have their own potential adverse effects. Topical treatments may also be useful, such as topical capsaicin or salicylate rubefaciants. Other agents that have been found effective in managing chronic pain include serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, anticonvulsants, calcium-channel blockers, and alpha-2 receptor modulators. Several of these approaches have the additional benefit of treating depression, the frequent comorbid of chronic pain (53). Depression should be treated vigorously to ameliorate pain and suffering and to reduce the likelihood of suicide (54).

Nonpharmacological approaches ought to be included as a mainstay of management (55). These include exercise therapy, acupuncture, massage therapy, spinal manipulation, yoga, cognitive-behavioral therapy, progressive relaxation, mindfulness, and patient and caregiver education (56). These approaches should be included regardless of the use of pharmacological treatments, as recommended by several specialty organizations (57). Although some of these approaches have not yet gained sufficient empirical support, this lack should not deter the treatment team from encouraging use of these nonpharmacologic therapies to benefit the patient (58). Insurance restrictions and limited access to

some types of clinicians are likely barriers to some of these modalities, but low-cost, online tools may be able to partially address gaps in access to some of these treatments.

If these first-line approaches fail, opioid treatment may be indicated. In such cases, when pain continues to impair function or quality of life, and the benefit is estimated to outweigh the risks, opioids may be begun judiciously and continued only if they are clearly beneficial in meeting previously established goals for pain control and function (59, 60).

When deciding to prescribe opioids, the dose and duration must be carefully considered with the goal of minimizing risk. Clinicians should counsel patients on the risk of developing depression and on the risks for suicide, in addition to having the critical conversations about accidental overdose, interactions with other respiratory depressants, and dependency (12, 59, 61, 62). Immediate-release formulations are favored when beginning treatment, at low doses and for short periods, to minimize harm. Clinicians should closely monitor and evaluate patients for both benefit and misuse. This supervision should include use of a prescription drug monitoring program when available and urine drug testing as indicated and at least annually. Rescue agents, such as naloxone, should be supplied to be kept at home, at the workplace, or at any potential sites of licit or illicit use. Those caring for the patient, including family, should be informed of the location of the rescue agent and how to use it. Other respiratory depressants, which may work synergistically with opioids, such as benzodiazepines and barbiturates, must be actively avoided. If dependency develops, therapies which incorporate methadone or buprenorphine alongside group-based therapy are usually indicated (59, 63).

Addressing Opioid Use Disorder

Providing appropriate medical management for opioid use disorder is critical. Methadone and buprenorphine are the primary opioid agonists for treatment of the disorder. Naltrexone may also be useful. Unfortunately, these approaches are sorely underused. This underuse can be attributed to patient attitudes, availability of prescribing clinicians, and approaches that shun the use of medication in addiction treatment. However, data for the utility of these medications is overwhelming. There is evidence for their effectiveness in promoting abstinence; reducing recidivism, overdose death, and all-cause mortality; and improving overall functioning (64).

In a recent meta-analysis, the risk of overdose death among patients with opioid use disorder but not receiving treatment with these medications, was 8.1 times that of patients in medication treatment (65). The evidence for this finding has been consistent (66). Moreover, treatment with methadone or buprenorphine has been found to significantly reduce opioid-related deaths after a nonfatal opioid-related overdose (67).

The management of treatment for patients with an opioid use disorder, including patients who develop opioid dependence secondary to chronic pain, is appropriately accomplished with a

psychiatrist leading a multidisciplinary team. Psychiatrists have the advantage of expertise in recognizing and managing the commonly occurring comorbid conditions, such as depression and anxiety. Moreover, they are trained to identify features of temperament and life circumstance that may hinder adherence to the treatment regimen and prognosis. In addition, treatment of an opioid use disorder ultimately requires expertise in behavioral health, including an understanding of the reinforcing factors that maintain the disorder and of approaches available to promote extinction of the behavior. Treatment with methadone or buprenorphine goes beyond solely prescription of the medication and requires an appreciation of the whole patient, including their personality, life story, medical and psychiatric vulnerabilities, and the relevant behavioral triggers, rewards, and consequences around which care and treatment can be structured.

Assessing and Addressing Suicide Risk in the Context of Opioid Use

Acute suicide risk can be difficult to predict. Questionnaires that rely on the presence of current suicidal ideation have poor predictive value and often result in false-positive or false-negative predictions (68, 69). Clinicians who are planning to prescribe opiates should, at a minimum, consider broad risk factors, such as mental illness, substance dependence, history of suicide attempt, family history of suicide, terminal medical conditions, recent significant losses, and access to firearms (70) when deciding whether further evaluation or specialist referral is warranted to better gauge risk.

Patients with a mood or other psychiatric disorder should be considered to be at particularly high risk for adverse outcomes from opioid use. If possible, such patients should be referred to a psychiatrist or other mental health care provider. Once a relationship with such a provider is established, the provider can help identify potential crisis periods as early as possible and refer the patient to higher levels of care, including the emergency department or inpatient psychiatric admission, to prevent suicide. During times of crisis, the opioid medication may be parceled out by a caregiver or prescribed for short periods between visits of increased frequency to prevent the patient from stockpiling medication for a suicide attempt. Safety planning is another crucial suicide prevention measure and may include a written enumeration of personalized warning signs, coping strategies, caregivers and emergency contact plans, and ways to reduce danger in the immediate environment—including the locking up of firearms and dangerous medicines (e.g., opioids) (71).

Because economic factors may play an important part in risk for opioid use disorder, overdose, or suicide, providers must consider social determinants of health, such as socioeconomic status, employment, education, support networks, and access to care. Case management can be a useful tool when available, and patients may not know about the resources that case managers can make available, such

as job training programs, emergency childcare, and connections to social services. Programs that can reduce the socioeconomic burden on our patients can be lifesaving.

CONCLUSIONS

The rising rates of suicide and opioid-related deaths highlight the insufficiency of current practices and policies to address mental health problems, particularly when these co-occur with pain. Mental health clinicians are on the front lines, caring for vulnerable patients and attempting to relieve their suffering. Tools, such as naloxone, medications for opioid use disorders, improved risk screening, and restriction of lethal means, are available to address risk of suicide and overdose in the context of depression and opioid use and should become more commonly implemented in practice.

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