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Opioid Prescribing in an Opioid Crisis: What Basic Skills Should an Oncologist Have Regarding Opioid Therapy?

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Opinion statement

Although clinical evidence supports the use of opioids for cancer-related pain, doing so amidst the current opioid crisis remains a challenge. A proportion of opioid-related deaths in the USA are attributable to prescription opioids, which implicates health care providers as one of the major contributors. It is therefore even more important now for all clinicians to follow safe and effective opioid prescribing practices. Oncologists are often in the frontline of cancer pain management. They are encouraged to use validated tools to screen all patients receiving opioids for high risk behaviors. Those identified as high risk for potential abuse of opioids should be monitored closely. When aberrant behavior is detected, the clinician will need to openly discuss the issue and its possible implications. Oncologists may then implement measures such as limiting the dose and quantity of opioids prescribed, shortening interval between follow-ups for refills to allow for increased monitoring, setting boundaries/limitations, weaning off opioid analgesics, or/and referring to a pain or palliative medicine or drug addiction expert for co-management when necessary. These efforts may aid oncologists in safely managing cancer pain in the environment of national opioid crisis.

Introduction

Opioids are the preferred drugs to treat cancer-related pain [1]. However, the current opioid crisis in the USA makes it challenging to effectively treat cancer pain [2••]. The number of opioid-related deaths has increased considerably in the USA over the past decade [3••]. According to the Center for Disease Control (CDC), over 130 Americans die every day from opioid overdose [3••]. The national opioid epidemic is marked by three distinct waves. The first wave started in the 1990s with the rapid increase in overdose deaths related to prescription opioids. The second wave began in 2010 with heroin-related deaths. The third and most recent wave began in 2013 with a sharp rise in deaths from illicitly manufactured fentanyl sold as counterfeit pills or in combination with cocaine or heroin [3••, 4•]. The US government recently declared the opioid crisis as a nationwide public health emergency [5]. Several other key agencies and stakeholders continue to come up with ways to help mitigate the current crisis [6, 7]. In January 2017, TJC released new public standards for pain management that specifically emphasizes the elements of safe opioid prescribing practices [8]. In this article, we examine the national opioid crisis, its relevance to cancer pain management, and also discuss simple measures that oncologists can implement in treating cancer pain during the current opioid crisis.

Prescription opioids and the opioid crisis

Although a substantial proportion of recent overdose deaths are attributed to non-prescription opioids such as illicitly manufactured fentanyl, prescription opioids are still to be blamed for a considerable proportion of those deaths. Greater than 40% of all opioid-related overdose deaths involved a prescription opioid alone. More than 46 people die from overdoses involving only prescription opioids every day [9]. Over half of the 3.8 million Americans who misuse prescription opioids obtain the medication from a friend or relative [10]. Moreover, a significant number of heroin users first got access to opioids from someone else's prescription [11]. The most common reasons why people aged 12 or older misuse prescription opioids, apart from physical pain relief (62.6%), are to feel good or get high (12.1%), to relax or relieve tension (10.8%), to help with sleep (4.4%), and to help with feelings or emotion (3.3%) [12].

In a study of 14,888 opioid-naive young adult patients who received an opioid prescription from a dentist and an opioid-unexposed cohort of 29,776, exposure to opioids was associated with higher rates of opioid use and subsequent diagnoses associated with opioid abuse or overdose [13]. A similar study among patients who were prescribed opioids after undergoing surgery found that higher quantity of prescribed opioids was significantly associated with higher patient-reported opioid consumption, even after controlling for postoperative pain and other factors [14].

Unfortunately, there is a perception that physicians are mainly responsible for the current rise in prescription opioid-related deaths. According to data from a recent national poll, most people blamed the opioid crisis on physicians (38%), followed by those who illegally sell opioids (28%), and the pharmaceutical industry (13%) [15••]. Moreover, the majority of respondents believed that physicians bear the most responsibility for fighting the opioid epidemic (47%), followed by the pharmaceutical industry (29%), and the law enforcement industry (12%) [15••]. Studies have shown that a positive change in
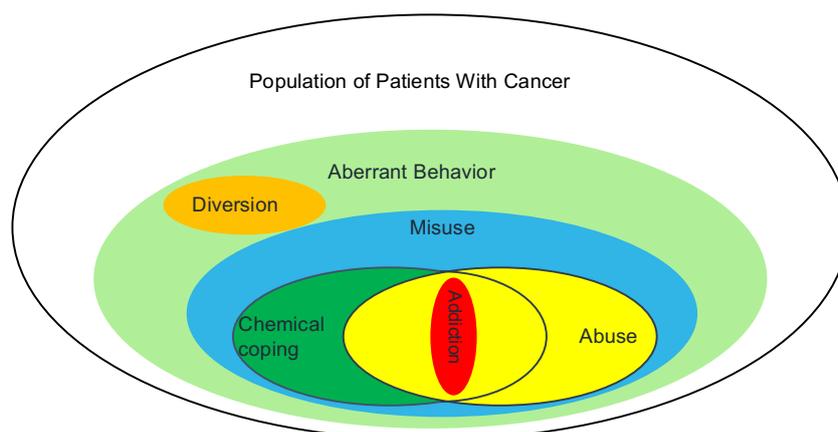
Fig. 1. Spectrum of aberrant opioid-related behavior. Adapted from Arthur J, Hui D. Safe opioid use: management of opioid-related adverse effects and aberrant behaviors. *Hematol Oncol Clin North Am.* 2018;32 (3):387–403, with permission from W.B. Saunders Company/Elsevier.

healthcare provider behavior can have a corresponding positive impact on the situation [16, 17]. The US Surgeon General in 2016 issued an unprecedented letter to all physicians admonishing them to help end the opioid crisis [18]. The Center for Disease Control [19••] and the American Society of Clinical Oncology [20] also released guidelines for pain management with specific emphasis on safe opioid practices. The drop in the rate of prescription opioids from 72.4 opioid prescriptions per 100 persons in 2006 to 66.5 per 100 persons in 2016 [17] suggests that health-care providers are likely more cautious now compared to before in their opioid prescribing practices. However there remains significant room for improvement.

Nonmedical opioid use in the cancer patient

The risk of aberrant opioid use among patients receiving opioids for cancer pain was previously perceived to be very low [21, 22]. However, recent evidence indicates otherwise [23•, 24, 25]. An integrative review by Carmichael et al. found that at least one in five patients with cancer might be at risk for opioid use disorder [25]. In another study, 18% of patients with advanced cancer seen at a supportive care clinic were identified by their physicians as chemically coping (using opioids to help cope with psychosocial distress) [26]. A study by Kwon et al. in patients with head and neck cancer who underwent curative radiation therapy found that patients who were unable to be weaned off opioids within 3 months of treatment completion were at significantly higher risk for aberrant opioid use compared to those who were successfully weaned off (odds ratio [OR], 5.3; $p = 0.014$) [27]. The median duration of opioid use after treatment completion was 261 days for high-risk patients as compared to 93 days for low-risk patients ($p = 0.008$). Several other studies have also shown the prevalence of aberrant behavior among ambulatory cancer patients receiving opioids [23•, 24, 28]. Cancer patients with a pre-existing history of substance abuse pose a higher risk for aberrant opioid use, warranting a closer follow-up [29].

Table 1. Summary of universal precautions in chronic opioid therapy for cancer pain

Step	Precaution	Explanation
1	Pain diagnosis and differential	Make an appropriate diagnosis of pain and/or differentials and determine the need for chronic opioid therapy
2	Initial screening	Prior to starting opioid therapy, screen all patients using clinical interviews, physical examination, and risk assessment questionnaires in order to identify those at risk for nonmedical opioid use; a comprehensive psychological assessment screening is particularly important
3	Informed consent	Discuss with patient the risks, benefits, adverse effects and alternatives of opioid therapy, and provide opioid education on safe use, storage, and disposal
4	Treatment agreement	Obtain a verbal or written treatment agreement (opioid management plan) outlining patient obligations, clinician responsibilities, and treatment expectations.
5	Opioid therapy ± adjuvant analgesics	Individualize opioid selection and dosing based on prevailing conditions (e.g., patient's health status, previous opioid exposure, present contraindications, anticipated complications); supplement therapy with non-opioid and/or adjuvant analgesics when applicable
6	Subsequent monitoring	At subsequent follow up visits, conduct periodic UDS, utilize the PDMP if available, and observe behavioral patterns to help determine treatment adherence and support therapeutic decision making
7	Pain outcome assessment	Conduct pre- and periodic post- intervention assessments of pain intensity and functional level to measure treatment progress and justify the rationale for continual opioid therapy; use the "five A's" of pain management outcome assessment: Analgesia, Activity (function), Adverse effects, Aberrant behavior, and Affect (mood)
8	Comorbid conditions	Periodically review and address the pain diagnosis and other comorbid medical and psychologic conditions including substance use disorders as these may evolve with time.
9	Specialist referral	Consider referral of high risk patients and those with complex opioid regimen to palliative and pain medicine specialists for co-management
10	Documentation	Carefully document all clinical encounters to ensure optimal patient care and minimize any medicolegal ramifications or regulatory scrutiny

UDS, urine drug screen; PDMP, prescription drug monitoring program
Adapted from Arthur J, Bruera E. Balancing opioid analgesia with the risk of nonmedical opioid use in patients with cancer. *Nat Rev Clin Oncol.* 2018, with permission from Nature Publishing Group

Common terminologies regarding opioid-related behaviors

Aberrant opioid-related behaviors range from apparently normal opioid ad-herent behavior to a clear diagnosis of addiction, and most patients fall in between the two extremes [30] (Fig. 1). Several terminologies have been used in literature to describe different behaviors related to opioid use. Misuse is "the use of a medication for a medical purpose other than as directed or indicated, either intentionally or unintentionally. It does not refer to use for mind altering purposes" [31]. Abuse is "the intentional self-administration of a medication

for a non-medical purpose such as altering one's state of consciousness, or the use of any illegal drug" [31]. Chemical coping is "a term used to describe an inappropriate and/or excessive use of opioids to cope with the various stressful events associated with the diagnosis and management of cancer" [32]. Diversion is "the intentional transfer of a controlled substance from legitimate distribution and dispensing channels." [31] Addiction is "a primary, chronic, neurobiologic disease that occurs as result of genetic, psychosocial, and environmental factors. It is characterized by one or more of the following features: impaired control over use, compulsive use, continued use despite harm, and craving." [33]

Some authors discourage the use of terminologies such as abuse, misuse, and addiction which have the tendency to stigmatize patients [34]. Studies have demonstrated that such terms may negatively impact the way patients are perceived [35] and may decrease their access to legitimate opioid therapy and appropriate treatment. In a stigma-reducing initiative, Scholten et al. suggested useful alternatives to some of these terminologies [36•] such as "non-medical opioid use," "substance use disorder," and "opioid agonist therapy" instead of abuse, addiction, and addiction treatment respectively [33]. These terminologies are perceived to be more neutral, precise, and respectful.

Basic approach to opioid prescribing

Because data regarding opioid prescribing and nonmedical opioid use in patients with cancer-related pain is limited, many of the elements underlying best practices are based on evidence from the non-cancer pain population [19••, 20, 37]. Principally, this involes the universal precautions approach, which entails screening of all patients with cancer pain who require opioids by using risk assessment tools to determine their level of risk. Those identified as being at high risk of aberrant behavior will then be monitored more closely on an ongoing basis [2••, 38]. Table 1 presents a summary of the key steps underlying the universal precautionary approach.

Oncologists should notify patients of the risks, benefits, and alternatives to opioid therapy before initiating treatment, and provide education on safe opioid use, storage and disposal strategies [39, 40••]. A study by our team among ambulatory cancer patients receiving opioids found that the use of an educational material resulted in a significant improvement in patient-reported safe opioid use, storage, and disposal outcomes. Patients who received the material were more aware of the proper opioid disposal methods (76% vs. 28%; $p \leq 0.0001$), less likely to share their opioids with someone else (3% vs. 8%; $p = 0.031$), less likely to practice unsafe use of opioids (18% vs. 25%; $p = 0.034$), and more likely to be aware of the danger their opioids pose to others if they take them (94% vs. 89% $p = 0.01$) [40••].

A treatment agreement or opioid management plan helps outline the goals and expectations of treatment as well as the responsibilities of both the patient and healthcare provider regarding opioid prescription and monitoring [37]. It underlines certain key elements such as obtaining opioids from one prescriber, filling prescriptions at one designated pharmacy, adhering to scheduled appointments, random urine drug tests, and the likely actions to be taken for failure to adhere to the policies. When the pain etiology is self-limiting with an

anticipated time of resolution such as oral mucositis from cancer treatments, an early discussion about a definite plan for eventual weaning off of opioids may be helpful.

Initial risk evaluation

Younger age (< 45 years), males, personal or family history of mental health or substance abuse disorders, and alcohol or tobacco use have been identified as risk factors for development of aberrant opioid use [41]. These risk factors may be useful in guiding clinicians to risk stratify and plan for future management.

Although there is no definite test or pathognomonic sign to predict which patient will be adherent to prescribed opioid therapy, certain validated risk evaluation tools (described below) have been found to be useful in detecting the risk for aberrant behaviors in the ambulatory setting. Oncologists are encouraged to adopt one or more such tools to screen their patients for risk of aberrant opioid use.

The "Cut down, Annoyed, Guilty, and Eye opener" (CAGE) questionnaire is a popular validated screening questionnaire that has been extensively used to detect excessive alcohol use, a significant risk factor for aberrant behavior. It can either be administered by the clinician or self-administered by the patient. It consists of the following four questions: (1) Have you ever felt you should Cut down on your drinking? (2) Have people Annoyed you by criticizing your drinking? (3) Have you ever felt bad or Guilty about your drinking? (4) Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover (Eye-opener)? [42] A cutoff score of 2 or greater is considered positive and has a sensitivity of 93% and a specificity of 76% for identifying excessive alcohol use [43]. A variation, the CAGE-Adapted to Include Drugs (CAGE-AID) questionnaire, which substitutes "drink" with "drink or drugs," has been found to have a sensitivity of 88% and a specificity of 55% for a score of 2 or greater [44].

The "Screener and Opioid Assessment for Patients with Pain form" (SOAPP) is a validated patient self-administered screening questionnaire used to help identify patients on opioid therapy at risk for aberrant opioid use [45, 46]. It consists of questions related to the patient's history of substance use, medication-related behaviors, and psychiatric and neurobiologic need for medicine. The responses are based on a 5-point Likert scale ranging from 0 (never) to 4 (very often). There are three main versions commonly used in clinical practice: The original version, SOAPP V.1 is a 14-item questionnaire with scores ranging from 0 to 56 [45] and a cutoff score of ≥ 7 has a sensitiviy of 91% and a specificity of 69%. The SOAPP-revised is a 24-item questionnaire with scores ranging from 0 to 96 and a cutoff score of ≥ 18 has a sensitivity of 81% and specificity of 68% [47]. The SOAPP-short form is a 5-item question-naires with scores ranging from 0 to 20 and a cutoff score of ≥ 7 has a sensitivity of 86% and a specificity of 67% [48].

The "Opioid Risk Tool" (ORT) is a validated patient self-administered questionnaire that assesses five risk factor categories: (1) family history of substance abuse, (2) personal history of substance abuse, (3) age 16–45 years, (4) history of preadolescent sexual abuse, and (5) psychological disease [49]. It consists of 10 items with a possible score from 0 to 26. A score of 0–3 is considered low risk, 4–7 moderate, and ≥ 8 high risk [50]. The ORT has

demonstrated good predictive ability in a prognostic model that simultaneously assesses sensitivity and specificity (c statistic = 0.82 in males and 0.85 in females) [49].

The Pain Medication Questionnaire (PMQ) is a validated 26-item self-administered questionnaire used to predict aberrant opioid use [51]. The items are in the form of statements, to which patients would indicate their degree of agreement or behavioral conformity on 5-point Likert scale. It has a sensitivity and specificity of 92% and 80% respectively for a cutoff score of ≥ 30 [52]. Patients with high scores (> 30.0) were 2.6 times more likely to have a known substance-abuse problem, 3.2 times more likely to request early refills of prescription medication, and 2.3 times more likely to drop out of treatment, as compared to those with lower scores (≤ 20.5) [52].

The "Diagnosis, Intractability, Risk, and Efficacy" (DIRE) inventory is a validated clinician-administered questionnaire that predicts which chronic pain patients will have effective analgesia and be compliant with long-term opioid maintenance treatment. It consists of four categories of risk factors as reflected in the name [46]. Each of the diagnosis, intractibility, and efficacy categories has 3 items. The risk category consists four subcategories. Each subcategory has 3 items. Total scores range from 7 to 21, with lower scores indicating greater risk. A cutoff score of ≤ 13 has a sensitivity of 94% and 87% respectively in predicting patient compliance.

Moore et al. compared a psychologist-led clinical interview with three different risk assessment tools and found that clinical interview (77%) had the highest sensitivity, followed by the SOAPP-R (72%), the ORT (45%), and the DIRE (17%) [46]. The Current Opioid Misuse Measure (COMM), which has sensitivity and specificity scores of 77% and 66% respectively for a cutoff score of 9 or greater [53], and the Addiction Behavior Checklist (ABC) which has sensitivity and specificity scores of 87% and 86% for a cutoff score of 3 or greater are used to monitor patient's ongoing opioid use [54]. In a systematic review, the SOAPP and PMQ had best evidence for predicting aberrant opioid use while the COMM had the best evidence for detecting ongoing aberrant opioid use [55].

Ongoing monitoring

High-risk patients receiving opioid therapy need closer monitoring in order to promptly know if they transition from an opioid-adherent behavior into a pattern of aberrant opioid use. Oncologists must participate in close monitoring by observing certain patient behaviors related to opioids, otherwise known as "red flags" [23•, 56], supplemented by other measures such as urine drug tests (UDT) or prescription drug monitoring programs (PDMP).

Aberrant opioid-related behaviors

Although there are no definitive "gold standard" set of behaviors or clearly defined diagnostic criteria for detecting aberrant behaviors, certain behaviors have been described in literature to be quite indicative of aberrant opioid use. Examples include frequent requests for early opioid refills, frequent opioid self-escalation, reports of lost or stolen opioid prescription/medication, frequent emergency room visits for opioids, seeking opioids from multiple providers ("doctor shopping"), and stealing or selling

prescription opioids. Some behaviors such as "stealing or selling prescription opioids" may be more strongly suggestive than others such as "requests for early medication refills."

Urine drug testing

UDT is an effective risk monitoring tool for patients on chronic opioid therapy [57]. There are two main types of urine drug tests (UDT) routinely used in clinical practice. The screening tests or immunoassays are economical and have a quick turnaround time but cannot distinguish between drugs in the same class, nor detect synthetic opioids [58] The confirmatory tests such as gas chromatography–mass spectrometry or liquid chromatography–mass spectrometry are more specific but relatively more expensive and have a slower turnaround time than screening tests [58]. Interpretation of UDT results have potential drawbacks due to the complexity of the opioid metabolic pathways. Moreover, normal UDT result does not necessarily exclude aberrant behavior because patients with chemical coping may have a normal result despite using their opioids in an exaggerated or maladaptive manner. There is insufficient data regarding the frequency and timing of UDT but most existing guidelines recommend all patients on chronic opioid therapy to receive some form of UDT monitoring regardless of their risk profile since every patient has a degree of risk for opioid abuse [57, 59]. The test appears to be underutilized in the cancer patient population [23•, 24, 28].

Prescription drug monitoring programs

PDMPs are effective resources that aid clinicians in their decision-making during opioid therapy [60]. The programs collect prescriber and pharmacy dispensing information on controlled substances to create a secure electronic database which is made available to authorized users including prescribers, regulatory boards and law enforcement agencies. PDMPs provide objective evidence regarding the source of the prescribed opioid as well as the time and location it was dispensed [61]. This helps identify patients who seek opioids from multiple prescribers (doctor shopping) or fill multiple prescriptions at different pharmacies (pharmacy shopping). Currently, some form of PDMP is available in all US states [62]. A national survey of opioid prescibing practices in ambulatory care settings from 2001 to 2010 revealed a > 30% reduction in the rate of schedule II opioid prescriptions in 24 states immediately after implementation of a PDMP [63].

Management of nonmedical opioid use behavior

Once a patient demonstrates aberrant behavior, the oncologist should have an open dialogue with the patient discussing the issue and possible implications. Measures such as limiting the opioid quantity and doses, shortening interval between follow-ups for refills to allow for more vigilant monitoring, setting

boundaries or limitations, weaning off the opioid analgesics, or referring to a pain and palliative medicine or drug addiction specialist for co-management may be necessary. Elaborate opioid education on safe opioid use, storage and disposal should be provided at each visit [40]. The ultimate goal of opioid therapy in such patients is to achieve satisfactory pain control and improve physical function while preventing possible complications from aberrant opioid use. Occasionally, care should be tailored to the patient's individual prevailing conditions. For example, in patients with advanced cancer who demonstrate aberrant behaviors, the primary emphasis should be on harm reduction with a focus on physical, emotional, and cognitive function because a complete change in behavior might be unachievable due to the high morbidity and expected short lifespan. On the other hand, patients with early stage disease undergoing curative therapy who continue to exhibit aberrant behaviors will need a more aggressive approach including referral to a substance abuse specialist if needed. The following are additional steps that are considered during the management of patients with aberrant opioid use.

1. Carefully consider features of the opioid choice

There is clinical evidence that high-dose opioid prescriptions (usually > 100 mg per day) are associated with an increased risk of abuse liability [64] and/or overdose in patients with both chronic cancer-related pain and non-cancer pain [65]. The CDC guidelines for non-cancer pain recommend that clinicians avoid titrating opioids to > 90 mg daily [19••]. This dose limitation should not be at the expense of achieving optimal analgesia in patients with cancer pain who sometimes require high dosages for extended periods of time. Aim to use the minimum effective opioid dose that will produce the desired analgesia with few or no side effects. Overall, potential for abuse is common for all opioids although oxycodone has been reported to have a relatively higher abuse potential compared with morphine and hydrocodone [66]. Tapentadol [67] and buprenorphine [64] have also shown patterns of relatively low but still existing potential for abuse.

Immediate-release (IR) opioids are associated with elevated risk of abuse as compared with extended-release opioids (ER) [68] because they penetrate the limbic system faster and induce higher levels of reward than extended-release formulations. Conversely, ER opioids are known to be associated with an elevated risk overdose, especially during the initial 2 weeks of therapy [69]. Opioid initiation and titration should therefore be tailored to each individual needs. ER opioid analgesics may be preferred in patients with stable chronic cancer-related pain and known aberrant behavior but its use in acute pain is not recommended [70]. Similarly, faster intravenous opioid infusion rates was associated with increased subjective abuse liability effects compared with slower infusion among healthy volunteers [71]. Caution must be exercised when administering intravenous opioids for pain in the inpatient setting.

Abuse deterrent opioid formulations (ADF) are sometimes used in patients with aberrant opioid use because they make oral opioids less rewarding when used through alternative routes such as injecting or snorting. However, it has certain drawbacks that might limit its usefulness. Despite their relatively higher cost, current evidence is insufficient to support their overall clinical benefit in decreasing non-medical opioid use except for ER oxycodone [72]. They might give a false sense of security and erroneously increase opioid prescribing

because some patients inevitably discover ways to overcome most of the deterrent properties. More importantly, none of the ADFs can prevent aberrant opioid use via the oral route which is the most common route of abuse [73].

2. Beware of combining opioids with benzodiazepines

Clinicians are encouraged to avoid the concurrent use of opioids with benzodiazepines because this has frequently been found to be associated with a high risk of opioid-related deaths and contributes to almost a third of fatal opioid overdoses in the USA [74]. In an observational study among veteran patients receiving opioid therapy, previous or a current benzodiazepine use was associated with a 2.33 or 3.86 times increased risk of opioid-related death respectively [75]. Clinicians should make efforts to minimize, discontinue, or replace them with other agents such as olanzapine in the management of anxiety [76] since there are no reports of increased mortality when these are combined with opioids.

3. Utilize non-opioids and adjuvant analgesics

Non-opioids such as nonsteroidal anti-inflammatory drugs (NSAIDS) and adjuvant analgesics such as gabapentinoids can sometimes be used as part of opioid-sparing or opioid-limiting strategies and are recommended by most opioid prescribing guidelines [19••, 20, 37] for the management of cancer pain in patients in whom there are concerns for excessive opioid use. However, clinicians should be cautious with the concurrent use of opioids and gabapentin especially at increasing doses because this combination has also been found to be associated with a dose-dependent significant increase in opioid-related deaths compared with opioid prescription alone [77••].

4. Consider naloxone co-prescription

The CDC recommends clinicians to consider co-prescribing naloxone with opioids for patients with a history of drug overdose, a history of a substance use disorder, for those requiring large opioid doses (median morphine equivalent daily dose of ≥ 50 mg/day), or concurrently receiving benzodiazepines [19••]. There is further evidence for naloxone use in certain conditions including morphine equivalent daily doses of > 100 mg daily [65], methadone prescription [78], history of chronic pulmonary, renal, or hepatic disease [65], and recent history of incarceration [79, 80•]. In a nonrandomized interventional study of patients receiving long-term opioid therapy for pain, naloxone prescription resulted in 47% fewer opioid-related emergency department visits per month in the 6 months after receiving the prescription (incidence rate ratio (IRR) 0.53 (95% CI 0.34–0.83); $p = 0.005$) and 63% fewer visits after 1 year (IRR 0.37 (95% CI 0.22–0.64); $p < 0.001$) [80•]. It did not cause an increase in the dose of prescribed opioids and might have actually resulted in a possible dose reduction in an alternative analysis [80•]. This is contrary to the perception that naloxone co-prescription can result in risk compensation by encouraging more aberrant behaviors among patients due to a sense of overdose protection with its use.

5. Employ psychological and non-pharmacologic approaches

Patients with aberrant opioid use are known to have underlying coexisting psychiatric conditions such as personality disorder, depression, and anxiety [81] and should therefore be evaluated and treated with interventions such as cognitive behavioral therapy, distraction, mindfulness, relaxation, and guided

imagery whenever appropriate [82]. A specialist pain or palliative care inter-disciplinary team may be helpful in co-managing such patients. These psycho-logical and integrative measures will enhance success in therapy and help minimize the likelihood of relapse. ASCO opioid prescribing guidelines rec-ommend the use of interventions such as physical therapy [83], integrative therapies [84], and pain interventional therapies [85] which have been shown to improve pain-related outcomes when indicated.

6. Involve specialist teams for co-management

Oncologists taking care of patients with aberrant opioid use are encouraged to involve the care of experts such as palliative or pain medicine specialist teams whenever possible. This is because the care of these patients can be complicated by multiple underlying domains, including biomedical, psychosocial, and financial factors. Palliative care interdisciplinary teams which consist of pallia-tive care certified nurses, counselors, social workers, chaplains, pharmacists, physical and occupational therapists, along with physicians are well equipped to manage every patient's unique circumstance and address all the domains above. These interdisciplinary specialist teams also have a relatively higher level of expertise, and adopt more rigorous risk evaluation strategies and established risk mitigation measures to deal with such patients [86]. They provide the primary oncologist with an extra layer of support. A specialized interdisciplinary team intervention implemented in our supportive care clinic for patients with cancer displaying aberrant behaviors resulted in a significant reduction in the frequency of the behaviors from a median of 3 per month prior to the inter-vention to 0.4 post-intervention ($p < 0.0001$). Opioid use also decreased sig-nificantly from a median morphine equivalent daily dose of 165 mg daily at the first intervention visit to 112 mg daily at the last clinic follow-up ($p = 0.02$), although pain intensity remained unchanged [87••].

Conclusion

Oncologists are encouraged to pursue efforts to promote safe and effective opioid-related practices when prescribing opioids to cancer patients experienc-ing pain. The key approach to opioid prescribing involves the adoption of validated risk screening tools as a universal precaution in all patients with cancer-related pain. Those identified as being at high risk of aberrant behaviors should then be monitored more closely for any "red flags," supplemented by other measures such as the use of UDT and PDMPs. Once aberrant behavior is detected, important measures may be implemented such as limiting the opioid quantity and doses at each visit, or referring patients to specialist teams for co-management when necessary. These efforts will aid in achieving the right shift in the risk-benefit paradigm for opioid therapy in cancer patients.

Compliance With Ethical Standards

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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