

# Risk Assessment and Monitoring of Patients with Cancer Receiving Opioid Therapy

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**Key Words.** Pain • Cancer • Opioids, Substance use disorder • Urine toxicology • Prescription drug monitoring • Risk mitigation

## ABSTRACT

The primary objective of this article is to assist oncologists and advanced practice prescribers to safely and effectively minimize risk when providing opioids for cancer pain relief. The majority of people with cancer are unlikely to misuse or divert opioid medications, yet the prescriber is often unaware of those who are at risk for these behaviors. To provide skillful pain management to each patient in the oncology setting, while limiting harm to the community, all prescribers must consider the potential for risk of misuse, addiction, or diversion. To minimize this risk to the greatest degree possible, it is imperative to include a thorough risk assessment when conducting a comprehensive pain evaluation. This information is

then used to triage pain relief interventions based upon the degree of risk, including whether or not to incorporate opioids into the plan of care. Risk mitigation strategies, incorporating universal precautions, are implemented to assess, monitor, and reduce the potential for opioid misuse. Universal precautions include strategies such as the use of urine toxicology, state prescription drug monitoring programs, and agreements. Ongoing monitoring is conducted with the goal being to identify aberrant behaviors early so that they can be addressed and managed appropriately. Referral to addiction specialists may be warranted when substance use disorder precludes safe use of opioids. *The Oncologist* 2019;24:1294–1298

**Implications for Practice:** Throughout the trajectory of cancer care, opioid use is often indicated, and, in fact, it may be unethical to limit or prohibit the use of opioids when pain is severe. Oncologists face the significant challenge of providing cancer pain control that is safe and effective, while limiting individual risk for abuse or overdose and keeping the community free of diverted substances. Most oncology providers report inadequate training in chronic pain principles and in managing addiction. Risk assessment and mitigation measures can be incorporated within oncology care to enhance effective pain management while reducing the potential for harm.

## INTRODUCTION

Pain in cancer is a complex, bio-psycho-social-spiritual phenomenon. The many causes of cancer pain include direct effects of the tumor, as well as the result of cancer treatment, an evolving source of pain because of the many novel oncologic therapies being introduced daily. Factors that can exacerbate perceptions of cancer pain include negative emotions and mood changes, common responses to receiving the diagnosis of a serious illness. Social isolation and lack of meaning, not restricted to people with cancer but common in our current society, can further reinforce perceptions of pain. Cancer survivors also experience numerous long-term and late treatment effects, notably pain and painful neuropathies but also fatigue, sleep disorders, metabolic syndrome, and osteoporosis, which are all known to affect the pain experience [1].

Contributing to the complexity of cancer pain management is the presence of previous or current substance misuse. The control of cancer pain can be more challenging when compared with other chronic pain states, in which it may be appropriate to limit or prohibit the use of opioids. Throughout the trajectory of cancer care, exposure to opioids is often ethically indicated, in some cases for extended periods. Although many patients can safely use these agents, the intersection of the unprecedented opioid epidemic and cancer pain further complicates care. Although prescription opioids were originally the source of diversion and misuse during the early years of this epidemic, currently monthly initial prescriptions are decreasing [2]. This is in part due to enhanced education of prescribers, but an unintended consequence of

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attention to this epidemic is that a large number of prescribers are no longer prescribing opioids, potentially limiting access to opioids for those in pain. Anecdotally, many of us working in the area of cancer pain relief are seeing people with cancer who were on opioids for chronic painful conditions prior to being diagnosed with a malignancy, now presenting to oncology clinicians and relaying that “my primary care doctor told me their practice no longer prescribes opioids and that you will help me.”

Other significant barriers exist to safe and effective cancer pain management during the time of an opioid epidemic [3–6]. Most oncology and palliative care practitioners report a lack of training in chronic pain principles, particularly crucial in the care of cancer survivors. These clinicians treating cancer pain felt they lacked confidence in managing addiction because of limited training about substance use disorders (SUD) and inadequate access to addiction specialists [7]. The consequences of this lack of preparation and support can contribute to a patient’s misuse of opioids and other tragic sequelae. Although patients with cancer are less likely to die of an opioid overdose when compared with those with chronic nonmalignant pain, the diagnosis of cancer, pain, and mental health disorders increase the risk of suicide [8–10].

To provide safe and effective cancer pain management, it is imperative to include a thorough risk assessment when conducting a comprehensive pain evaluation. This information is then used to triage interventions based upon the degree of risk and implement measures that mitigate the potential for opioid or other substance misuse.

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### RISK ASSESSMENT AND MONITORING

Comprehensive assessment of pain is imperative to ascertain the underlying etiology, when possible, to guide the treatment plan [11]. Function is now integrated into this assessment to assist with goal setting when developing a pain treatment plan. The efficacy of pain interventions is measured by improvement in function individualized to the patient’s performance ability. This is a change from prior goals that were solely based upon reduction in pain intensity. The third arm of a comprehensive assessment is understanding the patient’s risk factors for misuse. Most current history taking and screening routinely conducted in oncology do not include risk for SUD [12]. Although known risk factors such as smoking and alcohol intake are often recorded, other variables believed to increase risk are often neglected. Several factors implicated in a higher risk of opioid misuse are male gender, younger age, reporting higher pain intensity, having a family member with opioid misuse, a history of sexual or physical abuse, the presence of anxiety, depression, posttraumatic stress disorder, or a history of serious psychiatric illness [13–20].

Numerous screening tools are available to help identify those currently misusing, or at risk for misusing opioids, including the SOAPP-SF (Screener and Opioid Assessment for Patients with Pain, Short Form) [13], the Opioid Risk Tool [21], and the Brief Risk Interview [22]. One concern regarding the use of these tools is that many have not been widely tested in the oncology population. The CAGE (Cut Down, Annoyed, Guilty, Eye Opener) has been used

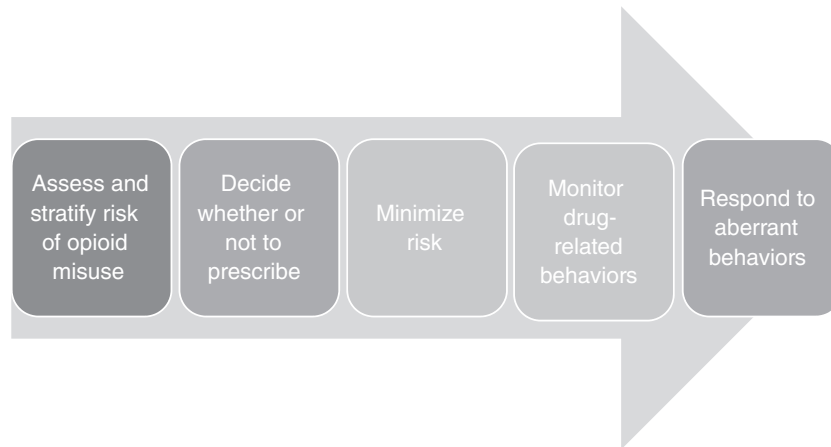
extensively by the palliative care program at the University of Texas M.D. Anderson Cancer Center, identifying predictive factors for misuse and chemical coping [20, 23]. An alternative approach can include the simple question “How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?” [24].

Additional measures, often called “universal precautions,” include obtaining urine drug toxicology, reviewing the results of the state prescription drug monitoring program (PDMP), and using treatment agreements. Universal precautions, based on similar principles to treat blood and body fluids as potentially infectious, are employed to mitigate risk when using opioids and acknowledge that anyone might be at risk for misuse. Approaches that only target those perceived to be “at risk,” rather than screening all patients, will be liable to expose the patient to the clinician’s implicit bias (i.e., assumptions about misuse based on age, socioeconomic status, or race) [25].

Universal precautions may include several strategies, including the use of urine toxicology [21, 26–28], standardized contracts or agreements [29], and review of the data accessed from the state PDMP [30, 31]. More information is needed regarding which of these strategies are most beneficial, as well as cost and time effective, in the oncology setting. Processes would need to be implemented in most oncology practices to streamline the use of these methods, including working with laboratory and internet support.

Accurate interpretation of the results of urine toxicology is crucial. If these findings are not accurately interpreted, patients may be inappropriately accused of inadequate adherence or even misuse. There are two primary urine toxicology tests conducted, an enzyme mediated immunoassay or gas chromatography/mass spectroscopy (GC-MS) or high-performance liquid chromatography (HPLC). Immunoassays, although less expensive and generally available, can yield false positives. GC-MS is more accurate but is less widely available, more expensive, and can take more time to yield results. As a result, many centers use immunoassay techniques for widespread screening, whereas GC-MS or HPLC may be used to confirm questionable findings. There are numerous examples of agents that can lead to false positives for opioids, such as fluoroquinolones or rifampin, and false negatives often occur with synthetic agents, such as fentanyl patches. Several reviews can assist providers as they interpret the findings from urine toxicology testing [21, 26, 27].

Formerly referred to as “contracts,” the preferred term is “agreement,” as this emphasizes the shared responsibilities between patients and providers. Optimal agreements are designed to be educational, alerting patients to their role in ensuring safe opioid use and reducing risks of misuse or diversion [29]. Components may include storage, appropriate use of opioids and controlled substances, and disposal strategies once these agents are no longer indicated. Despite nonstop media attention to the opioid epidemic, patients are often stunned when advised to lock up their medications [32–34]. Optimally, agreements provide an educational opportunity to emphasize our partnership in ensuring safe opioid management. A real threat in our current climate of fear surrounding opioids is to simply have the patient “sign



**Figure 1.** Steps in risk mitigation

**Table 1.** Structure employed in prescribing opioids based on risk

Minimal Structure	High Structure
Annual urine toxicology	Frequent urine toxicology – may be conducted with each refill in some cases
Review of PDMP every 3 months <sup>a</sup>	Review of PDMP with each refill
Clinic appointments every 3 months	Reassess pain, function and aberrant behaviors frequently; reconsider need for controlled substances regularly
Prescriptions provided for 30-day supply – may provide 3 prescriptions and notate earliest fill dates for each prescription to receive a total of up to 90 days (e.g., “may fill on or after June 1, 2019”) <sup>b,c</sup>	Prescriptions provided for short periods (e.g., 1- or 2-week supply)
	Engage family or responsible person to dispense medications
	Taper medications when indicated (e.g., change in pain, aberrant behaviors)
	Refer to addiction specialist

<sup>a</sup>More frequently if mandated by state regulations.

<sup>b</sup>If permissible by state law.

<sup>c</sup>For more information regarding prescribing of controlled substances, see the following: Issuance of multiple prescriptions for Schedule II controlled substances. Web site of the Diversion Control Division, Drug Enforcement Agency, U.S. Department of Justice. Available at [https://www.deadiversion.usdoj.gov/faq/mult\\_rx\\_faq.htm](https://www.deadiversion.usdoj.gov/faq/mult_rx_faq.htm). Accessed April 28, 2019. Abbreviation: PDMP, prescription drug monitoring program.

another form” or to use these tools to “fire” patients or stop prescribing opioids.

State PDMPs provide information about controlled substance prescribing for individual patients within that state, and some programs allow access to data from other states [31, 35]. Although they were developed to detect prescriptions obtained from multiple prescribers, often called “doctor shopping,” PDMPs can be useful tools in the clinical setting. These programs assist prescribers in understanding dispensing dates and the specific pharmacy where the medications were obtained. PDMPs also reveal how many tablets were actually released (in the case of a partial fill because of shortages or insurance limitations). Streamlined integration of PDMPs within the electronic medical record is essential to allow prescribers access to these data quickly and effortlessly.

The data derived from the comprehensive pain, function, and risk assessment are then considered along with findings from the urine toxicology and PDMP. The oncology clinician then makes a determination regarding whether initiating opioids is warranted, given the specific pain syndrome, and whether this approach is safe, given the patient's risk for misuse. And if the patient is already taking opioids, these data contribute to

decisions to either continue their use or institute weaning. Weaning might take place if opioids are no longer needed, ineffective, or producing harm in the form of aberrant behaviors.

### TRIAGE BY RISK

The oncologist will evaluate the information obtained from the comprehensive assessment and triage to either prescribe opioids or elect not to prescribe (Fig. 1). Opioids would be prescribed if the pain syndrome and intensity warrant this class of medications and the risk for misuse or diversion is low. The more complicated decision is when there are few other options for pain control and the risk for misuse is high. An example may be the patient with myeloma with extensive lesions distributed throughout the skeleton causing severe pain that is limiting movement, yet this patient has a current history of SUD. Nonsteroidal anti-inflammatory drugs are contraindicated because of risk of renal dysfunction in this population, and interventional procedures are challenging because of the widespread nature of the pain. In this case, a trial of opioids may be initiated while employing strong, highly structured risk mitigation strategies.

**Table 2.** Cancer pain and addiction resources

<p><b>American Board of Addiction Medicine</b>  <a href="https://www.abam.net/">https://www.abam.net/</a>            Has a search tool for physicians certified in addiction medicine            Links to relevant publications</p>
<p><b>American Society of Addiction Medicine</b>  <a href="https://www.asam.org/">https://www.asam.org/</a>            Has a nationwide search tool for professionals in addiction medicine            Links to relevant publications, podcasts and other tools for professionals            Information for patients, including contact for support groups</p>
<p><b>American Society of Clinical Oncology</b>  <a href="https://www.asco.org/">https://www.asco.org/</a>            Guidelines, including “Management of Chronic Pain in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline”            Training and education, such as live meetings and conferences, webinars, podcasts            Journals            Patient-related information at Cancer.net: <a href="https://www.cancer.net/">https://www.cancer.net/</a></p>
<p><b>National Comprehensive Cancer Network</b>  <a href="https://www.nccn.org/">https://www.nccn.org/</a>            Clinical practice guidelines for professionals and patients            Relevant guidelines: NCCN Guidelines on “Adult Cancer Pain,” “Palliative Care,” “Survivorship”            Educational products including live meetings, webinars, online courses</p>
<p><b>Substance Abuse and Mental Health Services Administration (SAMHSA)</b>  <a href="https://www.samhsa.gov/">https://www.samhsa.gov/</a>            Finding treatment tool            Toolkits and resources related to addiction            Education including buprenorphine waiver course</p>

### RISK MITIGATION

Averting all liability surrounding opioids is impossible, yet careful, ongoing application of risk mitigation strategies will reduce the potential for diversion, misuse, and even overdose [24]. The degree of structure and intensity of the application of risk mitigation strategies will vary by the level of concern for misuse or diversion (Table 1). People with low risk can be seen less often, and monitoring of their PDMP data and urine toxicology can be conducted less frequently. Those at greater risk may require much more aggressive supervision, including engagement of family members to dispense and procure medications when safe to do so.

Unexpected findings on PDMPs or urine toxicology should elicit a conversation between the clinician and patient to better understand the issues, restate the goals of care, and

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discuss challenges. If aberrant drug-related behaviors are identified, weaning or tapering the opioid may be appropriate, as may referral to addiction specialists.

Opioid weaning may be conducted when these drugs no longer provide benefit or are causing harm, including long-term adverse effects or misuse. One strategy that may be helpful is to acknowledge landmarks (e.g., free of disease for a time frame such as 6 months or 1 year), investigate readiness to reduce the opioid dose, and re-examine goals. Some patients are quite anxious when presented with this idea of tapering, fearful of increasing pain. A framework to de-prescribe or wean medications that has been used in palliative care to reduce polypharmacy is “FRAME”: fortify trust, recognize willingness or barriers, align recommendations with goals of care, manage beliefs and attitudes, and empower [36]. Statements such as “I am hearing you wish your life were back to normal. One way we can do that is to very slowly reduce these pain medications, as managing the constipation is troubling you and we want to avoid long-term side effects” may begin the conversation. For patients with SUD and aberrant behaviors indicating misuse, weaning is generally more complicated, and care from addiction specialists is necessary. Table 2 lists resources that may be of benefit to oncologists seeking more information regarding complex pain management and addiction.

### CONCLUSION

Oncologists face the significant challenge of providing cancer pain control that is safe and effective while limiting individual risk for abuse or overdose and keeping the community free of diverted substances. To provide skillful pain management to each patient in the oncology setting while limiting harm to the community, all prescribers must consider the potential for risk of misuse, addiction, or diversion. The comprehensive pain evaluation must include a thorough risk assessment. This information is then used to triage pain relief interventions based upon the degree of risk, including whether or not to incorporate opioids into the plan of care. Universal precautions, strategies such as the use of urine toxicology, state prescription drug monitoring programs, and agreements, are implemented to assess, monitor, and reduce the potential for opioid misuse. The goal of these measures is to identify aberrant behaviors early so that they can be addressed and managed appropriately. Referral to addiction specialists may be warranted when substance use disorder precludes safe use of opioids.

### DISCLOSURES

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