Abstract
The FDA’s 2012 risk evaluation and mitigation strategy is a major step toward systematically reducing the inherent risks of chronic opioid therapy for pain, but does not distinguish between risks related to sources of pain. This article discusses the effect of risk mitigation in the treatment of cancer pain, with a focus on pretreatment screening and ongoing monitoring in this patient population that often requires pain management at some time during cancer treatment. Experience with screening, risk stratification, and interventions at one cancer center is shared, along with some recommendations for practice. A new screening checklist is proposed that summarizes known risk factors. Patients with cancer are not protected from the problems of opioid abuse/misuse, and the multidisciplinary cancer treatment team should coordinate an evaluation of risk and the monitoring of aberrant behaviors as part of the comprehensive care plan. (JNCCN 2013;11:1023–1031)

Opioid Misuse and Abuse: Risk Assessment and Management in Patients with Cancer Pain

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Treatment of chronic pain with opioids is associated with the risk of abuse, misuse, diversion, and addiction.1 Patients receiving chronic opioid therapy (COT) for malignant or nonmalignant pain should be assessed for risk factors of abuse and misuse, stratified in risk categories and monitored during the duration of therapy.2 The concept of risk evaluation and mitigation strategy (REMS) was developed by the FDA for specific opioids used for chronic pain.2 Currently, long-acting and sustained-release opioids are under the requirement of REMS per the FDA. Nevertheless, any opioid prescription for chronic use should be based on similar principles. The most recent NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Adult Cancer Pain specifically describe the application of REMS for patients with cancer.1

The epidemiology of substance abuse in patients with cancer should be described in the context of the general problem of illicit drug use. One third of the population in the United States has used illicit drugs and 6% to 15% has a substance use disorder of some type.3–5 A lower prevalence of drug abuse has been reported in the cancer population, with 3% of psychiatry consultations in a single cancer center being requested for managing issues related to drug abuse.6 Similarly, a low prevalence of drug abuse was reported by the Psychiatric Collaborative Oncology Group study, in which fewer than 5% of patients in ambulatory care met the criteria for a substance abuse disorder.7 This low prevalence may not be an accurate reflection of the true prevalence because of underreporting. As Pas-sik et al6 suggest, “the epidemiology of substance abuse in cancer patients remains largely understudied and needs clarification.”

Clinicians should consider the implications that arise from specific correlations between cancer, cancer-related chronic pain, and risk of opioid addiction. Cancer survival rates and longevity continue to improve, and the incidence of chronic pain in long-term cancer survivors is not insignificant; therefore, patients with an addiction disease who are diagnosed with cancer may have a longer exposure to opioid therapy.8 The low prevalence of substance abuse disorder diagnoses among patients with cancer may also be a reflection of the older age at the diagnosis of cancer generally, whereas most of the addiction issues are di-
agnosed earlier in life. Younger patients receiving COT are more likely to abuse opioids and use illicit substances. Age younger than 42 years was associated with a greater risk of aberrant drug-related behaviors, whereas age older than 65 years has been negatively associated with opioid misuse and abuse. Therefore, younger patients with cancer, and especially adolescent patients, whose age falls within the “addiction critical period,” should be approached with enhanced awareness of the risk of exposure to opioids.

**COT as a Risk Factor for Opioid Misuse/Abuse**

Evidence shows that COT may represent a risk factor for the development of opioid abuse/misuse behaviors; however, causality is unclear. For example, Edlund et al found that mental health diagnoses mediated the relationship between COT and abuse/misuse behaviors. Regardless, the currently accepted approach for screening and risk stratification of patients undergoing COT is based on the principle of “universal precautions.” No patients are considered risk-free; treatment with opioid medications, which have a potential addictive effect, implies that every patient is exposed to a degree of risk. A system of diagnostic tools should be applied to identify the patients at high risk of opioid misuse, abuse, diversion, and addiction. Specific interventions must be instituted when continuing COT in this population to control and minimize the risks.

**Definitions of Terms**

Table 1 lists the definitions for opioid tolerance; physical dependence; the spectrum of aberrant opioid use behaviors, including abuse, misuse, and dependence; addiction; and pseudoaddiction.

**Risk Assessment at Initiation of Opioid Therapy**

The risk of opioid misuse and/or abuse increases with the introduction of opioid therapy; however, opioid therapy often is essential in the management of pain in patients with cancer. Therefore, when long-term opioid (≥7 days) prescribing is intended or expected, risk for aberrant behaviors (e.g., opioid misuse, abuse, and diversion) should be assessed. In risk assessment, the goal is to identify patients at high risk for future opioid misuse, abuse, and/or diversion and provide them with additional safeguards in an attempt to decrease the likelihood of future aberrant behavior. Turk et al posit that multiple sources of information should be used when determining a patient’s risk potential, such as previously documented history, direct observations of behaviors, health provider’s clinical judgment and intuition, urine toxicology screens, patient-reported history, and information obtained from screening questionnaires.

The use of prescription monitoring programs is strongly encouraged on initiation of COT. Depending on state laws and access to databases, prescribers can potentially investigate for illegal practices, the quantity prescribed to a patient and frequency of refills, and track whether patients are obtaining opioid prescriptions from more than one provider. State laws vary on the requirements for reviewing the database before prescribing opioids to a patient. In Tennessee, prescribers must review the database any time a new prescription is written for opioids or benzodiazepines to last more than 7 days, which meets the definition of COT. The practitioners are encouraged to make their own decisions about opioid therapy based on the database information.

Some practitioners operate under the false assumption that patients with cancer do not develop addiction. The authors’ practice with young patients shows that a cancer diagnosis does not necessarily exclude the possibility of misuse and addiction behaviors. Older patients with cancer may be recovering from addiction or have current addiction problems underlying the cancer diagnosis, and oncologists must be better prepared to manage these complex clinical scenarios, especially as cancer survivorship increases.

A clinical interview completed by a mental health professional is one method of obtaining patient-reported history in the assessment of opioid misuse risk. When a clinical interview is used to identify individuals at high risk, information related to previous and current mental health, sexual abuse, substance use, substance abuse, social functioning, and family history is often obtained. Although use of a clinical
interview has shown superior sensitivity compared with some common screening measures, the extended time necessary to complete the comprehensive clinical interview may impact the feasibility of this method for some prescribers.

In addition to a clinical interview, multiple screening instruments are available. Although no screening instruments were validated for use with patients with cancer at the time of writing, the efficacy of instruments validated for use with patients experiencing nonmalignant pain should not be overlooked. Table 2 outlines some of the readily available opioid misuse screening instruments. Sehgal et al also provide an overview of multiple screening instruments.

In determining which screening instrument to use in clinical practice, health care providers should consider using a tool with high sensitivity. The authors’ institution uses the revised Screen and Opioid Assessment for Patients with Pain (SOAPP-R) tool. With this tool, a cutoff score of 18 is recommended, and commonly cited in the literature; however, the authors intentionally choose a score of 17 at their institution because of its greater sensitivity (0.83 for cutoff of 17; 0.81 for cutoff of 18). Although this will likely lead to overidentification of patients at elevated risk, this result is preferable to underidentification. Screening instruments should never be used in isolation and are not intended to screen patients into or out of consideration for opioid therapy. Rather, screening tools should be used to determine the amount of support and magnitude of safeguards necessary to proceed with opioid therapy.

### Education and Supportive Interventions

Patients should be informed of the purpose of the risk assessment and assured that their risk status will not be used to preclude them from appropriate care. Once risk status is determined, patients should be informed of it and provided with appropriate support to help mitigate the impact of known risk factors. Prescribers must use universal precautions, including obtaining informed consent and providing education about the foreseeable risks of misuse. Prescribers must use universal precautions, including obtaining informed consent and providing education about the foreseeable risks of misuse. Patients should be assisted in using problem-solving approaches to alter, and thus reduce the impact of, modifiable risk factors. For example, when coupled with close monitoring and behavioral accountability, psychological therapy strategies focused on education related to opioid misuse, motivation for avoidance of aberrant behavior, strategies for coping with urges, and guidance in using problem-solving techniques led to increased opioid compliance among patients at high risk for opioid misuse.

Additional education should be provided to patients regarding use, secure storage, and disposal of opioids. All controlled medications must be accounted for in a pain diary, which requires notations for all doses of opioids taken, including as-scheduled and as-

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### Table 1 Glossary of Terms Related to Opioid Use

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Physical dependence</td>
<td>Pharmacologic property of some drugs, defined solely by the occurrence of an abstinence syndrome after abrupt dose reduction, discontinuation of dosing, or administration of an antagonist drug.</td>
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<tr>
<td>Tolerance</td>
<td>Diminution of one or more drug effects (either favorable or adverse effects) caused by exposure to the drug; may be pharmacologic or associative (related to learning).</td>
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<tr>
<td>Substance abuse</td>
<td>Use of a substance in a manner outside of sociocultural conventions. • all use of illicit drugs • use of a licit drug in a manner not dictated by convention (ie, following physician’s orders).</td>
</tr>
<tr>
<td>Addiction</td>
<td>The aberrant use of a substance characterized by • loss of control • compulsive use and preoccupation • continued use despite harm.</td>
</tr>
<tr>
<td>Misuse</td>
<td>The inappropriate use of a prescription opioid agent, whether intentional or unintentional, and regardless of motivation.</td>
</tr>
<tr>
<td>Abuse</td>
<td>A maladaptive pattern of a prescription opioid use leading to considerable impairment and/or distress.</td>
</tr>
<tr>
<td>Pseudoaddiction</td>
<td>Distress and drug-seeking that occurs in the context of unrelieved pain. These behaviors subside when adequate analgesia is achieved.</td>
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</table>
needed doses. The expectations for both the patient and the pain clinician can be outlined in an agreement or “contract,” which notes the risks and benefits, and alternatives or adjuvants to opioid therapy (such as nonpharmacologic interventions and nonopioid interventions), while describing the expectations for physician and patient behaviors. The effectiveness of these patient agreements has been debated.44,45

### Monitoring for Opioid Misuse and Abuse

Once patients have completed a risk assessment, been provided with appropriate education, and initiated long-term opioid therapy, prescribers and multidisciplinary team members should continually monitor for opioid misuse and abuse. Ives et al9 concluded that continual monitoring may lead to improvements in appropriate opioid use and mitigate risks of misuse and diversion. Multiple strategies for opioid monitoring exist. For example, pain medication diaries can be used to assess adherence to opioid regimens.46 These diaries typically ask patients to document the date and time that the prescribed opioids, nonopioids, and adjuvant analgesics are taken. Additionally, patients are commonly asked to document the dose and/or number of tablets taken at each occurrence. Pill counts during outpatient visits can be used to verify information contained within pain medication diaries and to help providers determine appropriate refill needs.

<table>
<thead>
<tr>
<th>Assessment Tool</th>
<th>Purpose and Administration</th>
<th>Validation</th>
<th>Concordance Index/*Sensitivity and Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screener and Opioid Assessment Measure for Patients with Pain – Revised (SOAPP -R)37,38</td>
<td>Assess the risk of opioid abuse in patients with chronic pain Self-report rating scales^a</td>
<td>Adult patients, nonmalignant pain Strong predictive validity, reliability, and internal consistency</td>
<td>≥17 / Sensitivity: 0.83; specificity: 0.65</td>
</tr>
<tr>
<td>Opioid Risk Tool (ORT)27</td>
<td>Assess risk of aberrant behaviors when introduced to opioid therapy Self-report checklist^a</td>
<td>Adult patients, nonmalignant pain</td>
<td>Concordance index considers sensitivity and specificity For men, c=0.82 For women, c=0.85</td>
</tr>
<tr>
<td>Pain Medication Questionnaire (PMQ)64</td>
<td>Assess the risk of opioid misuse Intended for use at start and throughout opioid therapy Self-report rating scale^ab</td>
<td>Adult patients, nonmalignant pain Evidence of construct and concurrent validity Acceptable reliability, strong test–retest reliability</td>
<td>≥25 / Sensitivity: 0.36; specificity: 0.78</td>
</tr>
<tr>
<td>Prescription Drug Use Questionnaire (PDUQ)65,66</td>
<td>Identify opioid abuse/dependence in patients with chronic pain Interview format and self-report questionnaire available^ab</td>
<td>Adult patients, nonmalignant pain Moderate reliability Strong concurrent and predictive validity</td>
<td>≥20 / Sensitivity: 0.67; specificity: 0.60</td>
</tr>
<tr>
<td>Addition Behavior Checklist (ABC)53</td>
<td>Long-term tracking of behaviors consistent with opioid abuse Interview format incorporating observational data^b</td>
<td>Veteran population, chronic nonmalignant pain Strong interrater reliability and concurrent validity</td>
<td>≥3 / Sensitivity: 0.87; specificity: 0.86</td>
</tr>
<tr>
<td>Current Opioid Misuse Measure (COMM)51,52</td>
<td>Monitor aberrant medication-related behaviors for patients already on long-term opioid therapy Self-report rating scale^b</td>
<td>Adult population, chronic nonmalignant pain Strong internal consistency and test–retest reliability Evidence of concurrent and predictive validity</td>
<td>≥9 / Sensitivity: 0.77; specificity: 0.66</td>
</tr>
</tbody>
</table>

\^aTool to be used as a screener, before long-term opioid therapy.

\^bTool to be used to monitor throughout opioid therapy.
The prescription monitoring programs also provide a valuable monitoring tool during ongoing COT. Current practice in the authors’ cancer center pain service is to investigate the data on the prescription monitoring program at the initiation of COT, and as needed thereafter. Individual prescribers of opioids are strongly encouraged to access the database once a month to evaluate their own opioid prescription patterns as recorded in the database, and to review for any fraudulent activity under their own names.

Frequent outpatient visits and urine drug testing (UDT) are also included among commonly recommended opioid adherence monitoring practices. UDT should be used at baseline when prescribing COT and throughout treatment to ensure regimen compliance and/or detect the use of a nonprescribed, illicit substance. Effective use of UDT requires an understanding of physiology, pharmacology, and toxicology, and it should not be used as the sole means of monitoring for aberrant behavior. Interpretation of urine and serum levels of prescribed and illicit drugs is a complex process, which is described in the literature and will not be covered in this manuscript.

As with screening instruments, assessment tools validated for use in monitoring aberrant drug-related behaviors during opioid therapy exist. Table 2 includes common screening tools and instruments that can be used for continued monitoring, and assessment tools intended solely for use in monitoring aberrant drug-related behaviors during COT. The Current Opioid Misuse Measure (COMM) is one validated self-report assessment tool used to detect aberrant drug-related behavior in patients currently receiving COT. The COMM was developed to track patients’ aberrant behaviors over time. It asks patients to rate indicators of current opioid misuse for the previous 30-day period. The Addiction Behavior Checklist (ABC) is another validated instrument solely intended for monitoring aberrant drug-related behavior in patients experiencing chronic nonmalignant pain. This assessment tool relies on both patient report and direct observations. The ABC is intended to be used repeatedly over time.

In addition to these validated measures to assess compliance and risk of misuse, clinicians should be familiar with some behaviors exhibited by patients who do not follow the pain regimens as prescribed. These “red flag” behaviors deserve serious inquiry, because they could not only suggest drug-seeking behavior on the part of the patient but also indicate inadequate analgesia, inadequate control of other troubling symptoms (eg, anxiety, depression), or diversion of the prescriptions by others involved in the patient’s care. The response to the aberrant behavior should address the motivation behind the patient’s behavior.

In a review of opioid misuse risk factors, Pergolizzi et al described common aberrant drug-taking behaviors observed by clinicians, which are potentially attributable to drug misuse and abuse. This list combines the observations of several earlier publications. Table 3 describes the aberrant behaviors that the authors observed in their experience with patients at a cancer center as a comparison with the literature.

Based on the authors’ clinical experience, behaviors that are considered more of a concern than others cannot be identified with confidence. It is generally accepted that the aberrant drug behaviors span over a large spectrum. Nevertheless, addiction research describes the concept of degree of aberrance, suggesting that some behaviors are “less aberrant” (eg, aggressively complaining about the need for medications) than others (eg, injection of an oral formulation; selling, buying, and stealing prescription drugs; prescription forgery).

This article does not review the addiction literature, and the authors’ practice does not solicit information regarding cravings, which would pertain to treatment in an addiction clinic. The literature reports that some degree of craving is reported by 55% of patients on COT, and there is an association seen between craving and a higher incidence of aberrant drug behaviors and abnormal UDT.

**St. Jude Experience**

The authors describe the experience of their cancer center pain service in treating 38 young adults (age range, 16–29 years; median 19 years) referred for chronic pain management and expected to require COT, who underwent assessments of opioid abuse risk and their subsequent opioid use behaviors over 9 months. Referrals to the pain service are made for patients with complex and/or chronic pain. The current practice is that on referral to the pain service, all patients aged 16 years or older are
evaluated for opioid abuse risk by the pain service psychologist using a diagnostic interview and administration of the SOAPP-R diagnostic tool, and a patient contract is completed. Of all 39 patients aged 16 years or older referred to the pain service during this interval, one refused evaluation by the pain service psychologist for assessment of opioid use risk and for nonpharmacologic interventions to treat chronic pain. In the set of 38 patients who completed the initial risk evaluation, all received the diagnostic interview and 13 were also evaluated using the SOAPP-R tool. The risk category was determined based on positive findings during the clinical interview and a score of 17 or higher (increased vs standard risk). Concordance was seen between the psychology interview and the SOAPP-R for identifying risk category in patients who received both assessments. Figure 1 presents the relationship of the risk category to the subsequent aberrant behaviors of opioid misuse/abuse. Of the patients identified as standard risk (23 of 38; 60.5%) based on both the psychology interview and the SOAPP-R assessment, none developed any aberrant opioid use behaviors. Fifteen of the 38 patients (39.5%) were classified as high risk for aberrant opioid use behaviors, and of these, 5 displayed “red flag behaviors” indicative of these behaviors. The classification of high risk was based on either the psychology interview and SOAPP-R together (3 of 7) or the psychology interview alone (2 of 8).

For patients identified to be at high risk of misuse, additional safeguards were subsequently initiated, specifically designed to address the risk identified in the individual patient assessment. For example, a patient may have outpatient visits or medication dispensed as frequently as once a day if needed, and the number of opioid prescribers is limited to the pain clinic providers only. Other interventions could include cognitive behavioral therapy or using medications that have lower potential for diversion, such as methadone. Despite these measures, 5 patients demonstrated red flag behaviors, which are consistent with the literature (Table 3).

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Behaviors Suggestive of Aberrant Drug Use</th>
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<tbody>
<tr>
<td>*<em>Observable Behaviors</em></td>
<td></td>
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<tr>
<td>Missed, canceled, or unscheduled appointments with pain provider</td>
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<tr>
<td>Seeking pain treatments from multiple providers (“doctor shopping”) or urgent care/emergency department</td>
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<tr>
<td>Excessive phone calls or attempts to obtain treatment or refills without office visit</td>
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<tr>
<td>Reporting lost/stolen prescriptions or pills</td>
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<tr>
<td>Pill count discrepancy, with or without explanation</td>
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<tr>
<td>Requesting specific drugs by brand or street name</td>
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<tr>
<td>Resisting changes to regimen</td>
<td></td>
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<tr>
<td>*<em>Medication Noncompliance</em></td>
<td></td>
</tr>
<tr>
<td>Unauthorized change in dose or frequency; unauthorized combinations of medications or substances to achieve additional effect</td>
<td></td>
</tr>
<tr>
<td>Use of other prescriptions or substances for pain relief; use of pain medications or substances to treat nonpain symptoms (eg, anxiety, insomnia)</td>
<td></td>
</tr>
<tr>
<td>Patient admitting to desiring euphoric effects or purposely oversedating oneself</td>
<td></td>
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<tr>
<td>**Interpersonal Behaviors</td>
<td></td>
</tr>
<tr>
<td>Decreased functioning in daily responsibilities related to opioid use</td>
<td></td>
</tr>
<tr>
<td>Third party expressing concern over opioid use or requesting to manage patient’s medications*</td>
<td></td>
</tr>
<tr>
<td>Hoarding drugs</td>
<td></td>
</tr>
<tr>
<td>**Illegal Behaviors</td>
<td></td>
</tr>
<tr>
<td>Illicit drug use*</td>
<td></td>
</tr>
<tr>
<td>Stealing or selling prescription drugs</td>
<td></td>
</tr>
<tr>
<td>Obtaining opioids from nonmedical sources</td>
<td></td>
</tr>
<tr>
<td>Prescription forgery or other tampering</td>
<td></td>
</tr>
</tbody>
</table>

*Behaviors noted in the authors’ cancer center pain service. Data from Refs.10,54–58
The current opioid risk assessment tools (Table 2) are validated for adults; data on opioid abuse risk in adolescents has not generated a validated opioid risk assessment tool. Based on the authors’ experience with young patients with cancer or sickle cell disease and a thorough literature review of adult and adolescent studies, the authors identified risk factors thought to have predictive value for subsequent aberrant behaviors in adolescents and young adults, and are developing a checklist for use with young patients (Screening Tool for Opioid use Aberrant Behavior [SOABR]; Figure 2). The SOABR is unique in the fact that the risk factors included in this tool are supported by both the adolescent and adult literature. Although similar to the Opioid Risk Tool (ORT), SOABR includes questions about a patient’s peer group, excessive impulsivity, and pathologic gambling. Importantly, this checklist is not a validated tool, but has provided useful information in the authors’ clinical practice. Further refinement and formal validation of the SOABR are necessary.

**Conclusions: Recommendations for Practice**

Based on the evidence supporting the need to assess the risk of aberrant opioid-use behavior, the authors recommend patients undergo evaluation through psychology clinical interview and/or SOAPP-R assessment at the initiation of COT for chronic cancer pain, and follow-up risk evaluation with COMM assessment. UDT is recommended at the initiation of COT and periodically throughout treatment to augment objective data about the patient’s behaviors. Education regarding the risks of aberrant opioid use behaviors and use of nonpharmacologic interventions for chronic pain management should be offered to all patients undergoing COT, independent of the risk category, to minimize the risks of aberrant opioid use behaviors.

**References**


![Figure 1](image1.png)

**Figure 1** Risk category and aberrant behaviors observed in 38 patients evaluated for opioid misuse risk over 9 months in one cancer center. Abbreviation: SOAPP-R, revised Screener and Opioid Assessment for Patients with Pain.

![Figure 2](image2.png)

**Figure 2** New screening tool for aberrant opioid-use behavior. Abbreviations: ADHD, attention deficit-hyperactivity disorder; PTSD, posttraumatic stress disorder.


Opioid Misuse and Abuse


