

Přehled poznatků o závislosti na opioidech související s dlouhodobým podáváním opioidních analgetik při léčbě chronické bolesti



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SOUHRN: Článek rekapituluje dosavadní poznatky o problematice diagnostikování závislosti na opioidech u pacientů s chronickou bolestí, kterým jsou podávána opioidní analgetika. Pojednáno je zde rovněž o některých klinických aspektech léčby bolesti u pacientů se závislostí na opioidech, případně těch pacientů trpících chronickou bolestí, kteří se nacházejí ve vysokém riziku závislosti na opioidech. Klinická pozorování a neformální přehled relevantní literatury potvrzují předpoklad, že u pacientů, kterým jsou na tlumení chronické bolesti podávána opioidní analgetika, dochází velmi často k neadekvátní diagnostice závislosti na opioidech. Cílem článku je přispět k snazší identifikaci a lepší prevenci a léčbě závislosti na opioidech u pacientů na opioidní analgesii. Výstupy tohoto článku mohou posloužit jako věrohodný základ pro koncipování studií zaměřených na stanovení prevalence a incidence závislosti na opioidech u pacientů s chronickou bolestí, kterým jsou dlouhodobě podávána opioidní analgetika.

KLÍČOVÁ SLOVA: OPIOID – ZÁVISLOST NA OPIOIDECH – ZNEUŽÍVÁNÍ NÁVYKOVÝCH LÁTEK – LÁTKOVÁ ZÁVISLOST – PORUCHA Z UŽÍVÁNÍ PSYCHOAKTIVNÍCH LÁTEK – ZÁVISLOST – LÉČBA BOLESTI – CHRONICKÁ BOLEST – PODÁVÁNÍ OPIOIDŮ – EPIDEMIOLOGIE – SENZITIVITA – FALEŠNÁ NEGATIVITA

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An Informal Review of Opioid Dependence (Addiction) Associated with Chronic Opioid Analgesic Therapy (COAT) for Chronic Pain



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SUMMARY: The diagnosis of opioid dependence (addiction) in pain patients on chronic opioid analgesic therapy (COAT) is reviewed. Some of the clinical implications of managing pain in opioid-dependent patients, or those pain patients who are at high risk of opioid dependence, are discussed. Clinical observations and an informal review of the pertinent literature support a common failure to make an appropriate opioid addiction diagnosis in pain patients on COAT. The paper aims to help opioid addiction be better recognized, prevented, and treated when pain is managed with COAT. The paper provides an important foundation for justifying and designing studies that establish the prevalence and incidence of opioid addiction in pain patients who receive COAT.

KEY WORDS: OPIOID – OPIOID DEPENDENCE – SUBSTANCE ABUSE – SUBSTANCE DEPENDENCE – SUBSTANCE USE DISORDER – ADDICTION – PAIN MANAGEMENT – CHRONIC PAIN – OPIOID THERAPY – EPIDEMIOLOGY – SENSITIVITY – FALSE NEGATIVE

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● 1 INTRODUCTION

Established and validated criteria for the diagnosis of opioid dependence are available. Opioid addiction is synonymous with opioid dependence, according to the DSM-IV-TR criteria (*Table 1*). Some clinicians confuse physical dependence with drug dependence. Drug dependence is the label for addiction under the DSM-IV terminology. To avoid confusion with physical dependence, the term opioid addiction, rather than the DSM-IV-TR term opioid dependence, will be used in this paper.

Inadequate treatment of pain leads to significant morbidity and mortality (Fine, 2011). The failure to make an opioid addiction diagnosis in pain patients on COAT proba-

bly adds further to this significant morbidity and mortality (Morasco, Corson, Turk, et al., 2011; Centers for Disease Control and Prevention, 2011; Coolen, Best, & Sabel, 2009; Substance Abuse and Mental Health Services Administration, 2012). Multiple studies report that patients addicted to opioids have high levels of mortality and morbidity, regardless of their pain status. Examples include:

- in a 2003 yearlong Swedish study, four out of twenty opioid-addicted controls died, compared to none in the group being treated for opioid addiction with buprenorphine (Kakko, Svanborg, Kreek, et al., 2003);
- a 2009 Norwegian study confirmed the importance of ready access to opioid maintenance therapy (OMT) to

Table 1 / Tabulka 1

DSM-IV criteria for opioid dependence diagnosis: worksheet

Kritéria DSM-IV pro diagnózu závislosti na opioidech: pracovní list

Patient Name:			
Diagnostic Criteria* (Dependence requires meeting 3 or more criteria)	Meets Yes	criteria No	Notes/supporting information
(1) Tolerance, as defined by either of the following: (a) need for markedly increased amounts of the substance to achieve intoxication or the desired effect			
(b) markedly diminished effect with continued use of the same amount of the substance			
(2) Withdrawal, as manifested by either of the following: (a) the characteristic withdrawal syndrome			
(b) the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms			
(3) The substance is often taken in larger amounts or over a longer period of time than intended			
(4) There is a persistent desire or unsuccessful efforts to cut down or control substance use			
(5) A great deal of time is spent on activities necessary to obtain the substance, use the substance, or recover from its effects			
(6) Important social, occupational, or recreational activities are given up or reduced because of substance use			
(7) The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance			

Physician's Signature

Date

* Criteria from American Psychiatric Association (2000). *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*. Washington, DC

* *Kritéria dle čtvrtého upraveného vydání Diagnostického a statistického manuálu duševních poruch Americké psychiatrické společnosti (American Psychiatric Association, 2000. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Washington, DC.)*

prevent high mortality rates from untreated opioid addiction (Clausen, Waal, Thoresen, & Gossop, 2009).

The above studies involved heroin-addicted patients. Hence, it could be argued that these patients represent a more severe spectrum of opioid addiction (Wu, Woody, Yang, et al., 2011). Regardless of the opioid used, unrecognized and untreated opioid addiction can be expected to have serious health consequences. The recent public health crisis of prescription drug overdoses confirms significant mortality risks (CDC, 2011). According to the Centers for Disease Control and Prevention (CDC), multiple drugs were listed in 72.3% of “opioid-related fatality” death certificates (American Pain Society, 2009). While opioid overdose mortality is often associated with mixing opioids with other substances, particularly sedatives, the overall etiology of opioid-related deaths is complex and multi-factorial (Webster, Cochella, Dasgupta, et al., 2011). The varied risk factors and causes do not mitigate the significant mortality from untreated opioid addiction (Morasco et al., 2011; Coolen et al., 2009; SAMSHA, 2012; Kakko et al., 2003; Clausen et al., 2009; Ward, Hall, & Mattick, 1999; Kreek, 2000).

Treatment of substance addiction is both life-saving and cost-effective (Miller & Hendrie, 2008; National Institute on Drug Abuse, 2009). When comorbid conditions, such as complex chronic pain, are present, health benefits and cost savings are expected (Fine, 2011; Dubois, Gallagher, Lippe, et al., 2009). This review of opioid dependence (addiction) associated with COAT for chronic pain aims to further research that will better determine the prevalence of opioid addiction in pain patients on COAT. Perhaps when its prevalence is better appreciated, clinical outcomes will improve?

● 2 BACKGROUND

● 2 / 1 Diagnostic criteria for opioid addiction (dependence)

The criteria in the Diagnostic and Statistical Manual of Mental Disorders, third and fourth editions (DSM-III and IV) are the commonly cited criteria for opioid addiction. Newer DSM-V criteria have eliminated the criteria associated with physical dependence. These newer criteria have not been adequately validated or tested for reliability. On the basis of the DSM-IV-TR criteria, longstanding reliability has been established through structured diagnostic interviews (First, Williams, Spitzer, et al., 2007). While the structured interview provides the “gold standard” for research purposes, clinical judgment remains important in establishing a diagnosis. The worksheet provided in *Table 1* provides a formal evaluation of opioid addiction based on the DSM-IV-TR criteria.

Addiction is a primary, chronic disease of brain reward, motivation, learning, and the related circuitry. It entails brain dysfunction that is not necessarily secondary to another disease. The DSM-IV-TR criteria are consistent with the International Classification of Diseases (ICD-9-CM) guidelines. DSM-IVTR and the upcoming ICD-10 guidelines were revised in a coordinated effort among researchers worldwide to develop criteria that were as consistent with one another as possible (Babor, 1992; Schuckit, 1994). The definitions of addiction such as those established by the consensus of the American Academy of Pain Medicine, American Pain Society, and American Academy of Addiction Medicine are consistent with the DSM-IV-TR criteria.

DSM-V, as already mentioned, changes the criteria, and compared to DSM-IV TR, it groups substance abuse and dependence disorders into substance use disorders (SUDs). This reflects the growing appreciation of a continuum of severity in addictive disorders. These DSM-V changes are expected to make it easier to establish a diagnosis for an opioid use disorder in pain patients on COAT. The merits of this facilitation are likely to be debated for some time. Rather than embrace or wait for these new criteria to be validated, this paper uses the well-established DSM-IV-TR criteria. The research associated with these criteria and the previous similar DSM-III criteria for opioid addiction is significant. Further research, aimed at establishing reliability and validity, is needed to relate current research findings to any new diagnostic labels or criteria. This is especially true given that criteria for opioid addiction are still not without controversy (Babor, 1992; Schuckit, 1994).

In addition to the established criteria for the diagnosis of opioid addiction, there are also addiction screening and assessment tools (National Drug Abuse Treatment Clinical Trials Network, 2004; Miller & Hendrie, 2008). Difficulty or a failure to make an accurate diagnosis of opioid addiction reflects many possible factors, such as poor diagnostic tools or skills, a lack of objective markers, cultural beliefs, legal ambiguities, and a lack of adequate management options, among other factors.

Even when there is a lack of current use, signs, or symptoms, opioid addiction can be diagnosed by a professional interview that focuses on the patient’s history. As is the case with many diseases, serious clinical consequences arise when a patient’s history is not adequately taken.

Perhaps the best readily available definition of addiction is on the American Society of Addiction Medicine’s (ASAM) website at <http://www.asam.org/for-the-public/definition-of-addiction>. ASAM lists five (ABCDE) features common in most addictions:

- a/ Inability to consistently Abstain;
- b/ Impairment in Behavioral control;

- c/ Craving, or increased “hunger” for drugs or rewarding experiences;
- d/ Diminished recognition of significant problems with one’s behaviors and interpersonal relationships; and
- e/ A dysfunctional Emotional response.

Note that these five features are not intended to be used as “diagnostic criteria” for determining if addiction is present or not. Although these characteristic features are widely present in most cases of addiction, regardless of the substance in question, each feature may not be equally prominent in every case. Consequently, ASAM recommends a professional assessment for a diagnosis of addiction.

In the context of COAT for pain, a recent discussion of addiction was offered by Ballantyne, Sullivan, and Kolodny (2012). As already noted, the current criteria for an addiction diagnosis do not include findings from the physical exam, laboratory, or imaging markers. The criteria are, however, well established and have validity and reliability. Furthermore, the diagnosis of opioid addiction is associated with meaningful prognostic and therapeutic findings. Perhaps the physiological basis for opioid addiction is better understood than the majority of chronic diseases. (See below under The Nature & Physiology of Opioid Addiction.) Until improved criteria are supported by the literature, the DSM-IV-TR criteria continue to be recommended.

● 2 / 2 The Nature & Physiology of Opioid Addiction

Addiction correlates with powerfully conditioned behaviors. The development of opioid addiction involves repetitive exposure to opioids, in the context of exposure being contingent on situational variables. The situational variables are associated with pharmacologically induced dopamine surges in the nucleus accumbens (Di Chiara, Bassareo, Fenu, et al., 2004). Potent “memories” are laid down. This physiological “conditioning” is what is thought to be the basis of addiction. This conditioning, and its association with long-term memory, helps explain why addiction, whether treated or not, is expected to be a chronic condition. All addictions, indeed all forms of higher learning, may involve dopamine surges in the nucleus accumbens. Furthermore, all substances demonstrated to be addictive in animal models are thought to pharmacologically induce the release of dopamine in the nucleus accumbens (Willuhn, Wanat, Clark, et al., 2009; Hyman, Malenka, & Nestler, 2006; Koob & Le Moal, 2001).

“The understanding of addiction requires understanding of a broader network of neural connections involving forebrain as well as midbrain structures. Selection of certain rewards, preoccupation with certain rewards, response to triggers to pursue certain rewards, and motivational drives to use alcohol and other drugs and/or pathologically

seek other rewards, involve multiple brain regions outside of reward neurocircuitry itself.” (*ASAM statement on the physiological nature of addiction at <http://www.asam.org/for-the-public/definition-of-addiction>*)

Substance addiction is only considered in remission when the patient has not misused the substance for a twelve-month period. When a patient is being medically managed with opioid agonists and taking their medications as directed, they are considered opioid addicted on agonist therapy.

The disease of addiction is a chronic relapsing disease. Similarly to other mental conditions, relapses are to be expected, and lifetime therapy is indicated to prevent or minimize relapses. Continuing maintenance is indicated even in the context of normal or better-than-normal functioning. Hence, recovery from addiction consists of a “one day at a time” process, as is suggested in twelve-step programs such as Alcoholics Anonymous.

Clinicians may associate the presence of addiction as being reflected in the signs and symptoms of end-stage disease. It is often not appreciated that opioid-addicted patients can be stabilized, even for a lifetime, on a fixed amount of a properly administered agonist agent (Ward et al., 1999; Kreek, 2000; NIDA, 2009; Mattick, Breen, Kimber, & Davoli, 2009). Time in treatment is closely associated with outcomes, and agonist treatment is known to help achieve this objective (Kakko et al., 2003; Clausen et al., 2009; Ward et al., 1999; Kreek, 2000; Mattick et al., 2009).

Similarly to other chronic diseases, the signs and symptoms of untreated opioid addiction may vary significantly over time. The disease may also appear to be cyclic in nature. Indeed, in milder or partially treated cases, there may be extended periods of time with no apparent signs or symptoms of addiction.

All chronic diseases have a continuum of severity based on individual susceptibilities, genetic variables, environmental factors, initiating factors, and the available medical care, as well as other often unrecognized or underappreciated variables. Similarly, opioid addiction has a continuum of severity. The notion of individual susceptibility is highlighted by the estimates that only one in four individuals exposed to heroin eventually becomes opioid-addicted (Anthony & Helzer, 1995).

Compared to alcohol addiction, for which abstinence is generally considered optimal, opioid-addicted patients have a poor prognosis with abstinence-based therapy (Kakko et al., 2003; Clausen et al., 2009; Ward et al., 1999; Anthony & Helzer, 1995; Weiss, Potter, Fiellin, et al., 2011; Ling, Wesson, Charuvastra, et al., 1996; Mattick et al., 2009; Washington State Agency Medical Directors’ Group, 2007). The degree of neuroapoptosis (neural cell death) or mu-opioid receptor degradation that occurs with repeated

opioid administration is still being studied. The full mu-opioid receptor agonist methadone is well known to improve the prognosis in opioid-addicted patients. The partial agonist buprenorphine is also FDA approved for treating opioid addiction. The mu-opioid receptor antagonist naltrexone has also demonstrated its efficacy. These pharmacological therapies are important in predicting a favorable prognosis for opioid-addicted patients (Kakko et al., 2003; Kreek, 2000; Ling, Wesson, Charuvastra, et al., 1996; Mattick et al., 2009; Washington State Agency Medical Directors' Group, 2007; Sees, Delucchi, Masson, et al., 2000; NIDA, 2009; Haastrup & Jepsen, 1988).

For most patients, opioids result in physical dependence when used continuously over time. As previously noted, physical dependence alone does not mean addiction. Conversely, some clinicians assume that addiction requires evidence of physical dependence. This emphasis on physical dependence is misleading. Only two of the seven DSM-IV-TR criteria for addiction involve physical dependence: tolerance and withdrawal. At least three criteria need to be met to establish addiction. Consequently, the diagnosis of opioid addiction can be readily met without evidence of physical dependence. When an opioid-addicted patient is free of symptoms and signs for a period of time, their tolerance does return to normal. It is frequently an addicted patient's loss of tolerance that contributes to drug overdoses (Morse, 2003). Hence, an opioid-addicted patient may die from their disease even when they are not currently physically dependent on an opioid.

Whether receiving agonist therapy (some call it substitution or maintenance therapy) or not, a diagnosed opioid-addicted patient can function normally, as well as feel normal without symptoms or signs. Just as with diabetes and other chronic diseases, the diagnosis of opioid addiction does not establish disability or invariably predict a poor prognosis. This is particularly true when the disease is being adequately treated or is in remission. The lack of current signs and symptoms must not therefore dissuade the clinician from at least entertaining a diagnosis of opioid addiction. Any twelve-month period in the patient's lifetime when three criteria are met is adequate to establish the diagnosis. Addicted patients who are drug-free or sober for years are not to be considered cured. Like a cancer patient, the longer an addicted patient remains without a "relapse," the better their prognosis.

A patient's age and genetic and environmental factors are all known to influence the risk of opioid addiction. What percentage of the population is at risk? Who is at the highest risk? Does third-party coverage matter? This last question may be quite relevant, because in Washington State, more than 50% of the opioid overdose deaths were in Medicaid clients¹ (Coolen et al., 2009). Are there objective

factors to determine or predict severity? Answers to these questions, while clinically relevant, are not well researched.

● 3 OPIOID ADDICTION IN PAIN PATIENTS ON COAT

The preceding introduction of the diagnostic and clinical attributes of opioid addiction has implications for pain patients on COAT. As already mentioned, the lack of apparent signs or symptoms of opioid addiction does not preclude the diagnosis. With regard to addiction in the context of COAT for pain, a brief discussion of pseudo-addiction is warranted. The historical acceptance of the pseudo-addiction concept may partially explain the failure of some clinicians to make an opioid addiction diagnosis in pain patients on COAT.

● 3 / 1 The Issue of Pseudo-Addiction

The term "pseudo-addiction" was coined to describe the behavior of undertreated pain patients with behavior resembling addictive behavior (Weissman & Haddox, 1989). Patients with unrelieved pain may become focused on obtaining medications, watch the clock, and exhibit "drug-seeking" behavior. Even behaviors involving illicit drug use and deception can understandably occur during a pain patient's efforts to obtain adequate pain relief.

Pseudo-addiction is a descriptive term, and not a diagnosis per se (SAMHSA, 2012, p. 56). It is believed that pseudo-addiction can be readily distinguished from true addiction in that the behaviors resolve when the pain is effectively treated. While this common belief is based on what might be considered common sense, clinical dilemmas commonly arise as a result. For example, the average patient who is withdrawing from opioids will start to experience painful muscles. It could be expected, because of the anxiety and sleeplessness associated with the withdrawal, that the pain stemming from any etiology would increase. This "withdrawal pain" would also be relieved by adequate opioid administration. A clinical dilemma arises: does the new or worse pain stem from withdrawal, or is it reflective of another etiology? Does the pain reflect an acute change in nociception? Does it reflect progressive chronic nociception? How can a clinician effectively differentiate the pain of withdrawal from the expected ups and downs of complex chronic pain?

Other problematic clinical questions arise: does this increased pain occur because of opioid-induced hyperalgesia (Mao, 2002)? When does it relate to an unrecognized medical or psychiatric disorder, or even common situational stressors? More to the point, pain can be of a nociceptive origin in addicted patients, as well as non-addicted patients. How, then, could one really be confident that providing a higher dose of an opioid and relieving pain is secondary to pain relief rather than simply a more robust

treatment of an opiate addiction with agonist treatment? It is well established that opioid-addicted patients often require much higher levels of opioids to be stabilized, even when they do not have pain. In my opinion, any patient who requires more than a 60-milligram equivalent of methadone per day for adequate pain management for chronic non-cancerous pain is likely to be opioid-addicted. That is, the patient's brain has been altered significantly in such a way as to require long-term chronic agonist therapy in order to help assure stable brain functioning and optimal outcomes.

Concerns about the concept of pseudo-addiction were recently reviewed in a commentary by Ballantyne et al. (2012). The authors state that a premise of pseudo-addiction is that the drug-seeking behavior will go away when an adequate dose is employed, but that this is not necessarily apparent in the long-term treatment of chronic pain. These authors also discuss the possibility that diagnoses other than opioid addiction must be entertained. They suggest the term "complex persistent opioid dependence" to acknowledge the common dependence seen in COAT for chronic pain. The authors acknowledge that regardless of diagnostic labels, the effective clinical response is likely to be similar to that in the case of an opioid-addicted patient. This would include extra support, structure, and monitoring.

Experienced pain practitioners acknowledge that it is clinically problematic to ascertain a clear etiology for pain behavior in patients with complex pain. The differential diagnosis is even more complex in patients with a substance use disorder.

On the basis of the preceding discussion, any astute clinician must be extremely cautious when applying the label of pseudo-addiction. Nonetheless, there is probably a small subset of patients whose behavior might best be properly attributed to the descriptive term pseudo-addiction. Perhaps the label is particularly valid in patients who have established etiologies for rapidly progressive nociception, such as patients with terminal cancer or in the context of an acutely painful condition.

This discussion also confirms the importance of clinical judgment and professional assessments in complex clinical settings. Pseudo-addiction and a further discussion of its origins and history can be found in an earlier paper by Ballantyne and LaForge, which reviewed opioid addiction in pain patients on COAT (Ballantyne & LaForge, 2007).

The term "problematic opioid use" is a better label for the behavior that could be associated with the concept of pseudo-addiction. The adjective "problematic" has advantages over the terms "aberrant behavior" or "pseudo-addiction." Aberrant behavior may inappropriately shame a patient. In some clinical contexts, "aberrant" behavior can actually be relatively common behavior. The term "problematic opioid use" assumes no etiology and may be less

judgmental. It also encourages effective solutions to be sought. Thankfully, there are effective ways to address problematic behavior associated with COAT and pain management, even when opioid addiction or risk factors for this are present (SAMHSA, 2012; Gourlay & Heit, 2009; Fishman, 2011; Fishbain, Johnson, Webster, et al., 2010; Kircher, Zacny, Apfelbaum, et al., 2011; Passik & Kirsh, 2011; Weaver & Schnoll, 2002).

● 3 / 2 Prognosis and Treatment Recommendations Related to Opioid Addiction in the Context of COAT for Pain

What are the differences in properly managing opioid addiction in association with COAT for pain resulting from opioid addiction stemming from heroin use? Or, in other words, if patient A has pain and is addicted to heroin and patient B has pain and is addicted to prescription opioids, how should the treatment differ for patients A and B? Furthermore, what differences remain between patients A and B once significant confounding variables are eliminated? (Weiss et al., 2007) Until clinical trials are conducted to answer these questions, it is suggested we assume that the differences are negligible.

Variability is common both in the severity and response to treatment for opioid addiction (Ling et al., 1996). In addition to the variables already mentioned, there are other variables to be considered, such as the pharmacology of the substance(s) used, routes of administration, and comorbid conditions. When risk factors for opioid addiction are present and uncertainties about pain etiology exist, a clinical response based on a risk assessment is required (Fishman, 2011; Passik & Kirsh, 2011; Rotchford, 2007). Patients in high-risk groups probably require different therapy compared with low-risk persons (SAMHSA, 2012; Gourlay & Heit, 2009; Fishman, 2011; Fishbain et al., 2010). Which opioids are best? Are long-acting opioids best or only those that are effective for opioid addiction? What is the role for breakthrough or "as needed" opioid prescriptions? In what context can they be prescribed safely? What behavioral support is indicated and when is it necessary or simply better? On what reliable basis can we assess the severity of an addiction? Which clinical factors best determine the nature and intensity of therapeutic options? When acute nociception is present, such as after surgery or a fresh injury, what role do risk factors play in establishing proper pain management? Unfortunately, many of these important clinical questions presently have only expert opinions to guide the clinician.

Therapy based on expert opinions based on understandings of the pathophysiology of complex chronic pain and opioid addiction is likely to have the best outcomes, pending further guiding research. On the basis of the pathophysiology of addiction, outside of an acute nocicep-

tive event, a chronic pain patient who also has opioid addiction would probably do best on agonist therapy with a relatively stable serum level. Avoidance of breakthrough or symptom-contingent dosing is also suggested in the context of chronic pain (Jegu, Gallini, Soler, et al., 2011).

Long-acting medications such as methadone or buprenorphine are the current preferred medications (FDA approved) for agonist therapy for opioid-addicted patients. Perhaps, given their demonstrated efficacy in treating pain, these are the agents of choice for opioid-addicted patients on COAT for pain? In methadone maintenance clinics, the average daily dose of methadone is 80–150 milligrams per day (Ries, Fiellin, Miller, et al., 2009). This range of methadone is also likely to be the one that is effective for stabilizing some complex-pain patients who are also opioid-addicted. However, effective pain management with methadone often requires more than once-daily dosing. Note the possibility that long-acting slow-release morphine (SRM) could be an effective management option for some patients who are mildly addicted to opioids (Jegu et al., 2011).

Unfortunately, barriers to effective management of opioid addiction are common, even outside of the context of COAT for pain (Dubois et al., 2009). Cultural, legal, regulatory, and financial barriers are prevalent. These barriers can also help explain why clinicians often fail to make the diagnosis of opioid addiction in patients on COAT.

● 3 / 3 Prevalence of the Failure to Make a Diagnosis of Opioid Addiction

3 / 3 / 1 Clinical observations

Clinical observations suggest that a high rate of false negatives (failure to make the diagnosis) of opioid addiction is present in pain patients on COAT. Experienced clinicians (Rotchford, 2007) corroborate that establishing or formally excluding the diagnosis of opioid addiction in a pain patient on COAT is problematic, but often the opinion of pain specialists is that opioid addiction is relatively rare. This opinion is formed with little effort to provide a formal and specialized workup for addiction in pain patients on COAT. Consultants expressing concerns regarding the use of opioids will typically use phrases such as “This is a high-risk patient,” “This patient needs further psychiatric evaluations,” “This patient must be taken off of their pain medications,” “This patient is a drug seeker,” “This patient exhibits aberrant behaviors,” or “There is no good reason for this patient to be on this dose of opioids.” In contrast, one rarely encounters a clinical report such as: “This patient meets (or does not meet) the criteria for opioid addiction.”

On occasion, tools that screen for high-risk patients are referenced. However, these tools can only help clinicians predict and assess the likelihood of aberrant drug-related behaviors in patients on chronic opioid therapy. Evi-

dence for the validity of such tools, however, is limited (Chou, Fanciullo, Fine, et al., 2009), and it can be argued that they should not replace efforts to establish or exclude the important diagnosis of opioid addiction.

The contents of current debates about the relevance of morphine-equivalent doses and their relative risks for complications in pain patients on COAT (McCarberg, Hahn, Twillman, et al., 2012) further suggest a denial of the importance of recognizing and effectively managing comorbid conditions, including opioid addiction in pain patients on COAT. In Washington State (USA), legislation was passed that was based on morphine-equivalent doses. In part, this was supported by a linear relationship between doses and the likelihood of complications and high rates of overdose deaths occurring. Nonetheless, 50% of the opioid overdose cases in Washington State were in Medicaid¹ clients (Coolen et al., 2009). This is in the context of probably less than 10% of the prescribed opioids being prescribed to Medicaid clients in Washington State. These factors, with the additional evidence that privately insured patients are prescribed similarly high doses of opioids (Edlund, Martin, Fan, et al., 2010), suggest that undisclosed variables other than morphine-equivalent doses are better primary predictors for opioid complications. Current evidence supports that the numbers of painful conditions, age, mental health conditions, and substance use disorders are good predictors of higher opioid dosing in pain patients (Edlund et al., 2010). It is reasonable to assume these variables are better predictors of opioid use complications than morphine-equivalent doses are. As referenced, they predict who is likely to receive the higher opioid doses in the first place.

The focus on higher morphine-equivalent doses as the primary concern for preventing opioid complications (McCarberg et al., 2012; Washington State Agency Medical Directors' Group, 2010) is consistent with many pain specialists assuming that the diagnosis of opioid addiction is rare. It attributes the risk primarily to the dose of the opioid used rather than attributing the risk to a patient's diagnosis or the proper management of underlying substance use disorders or other co-morbid medical and psychiatric conditions.

Extensive experience in a specialized outpatient pain and addiction clinic (Rotchford, 2007) supports the hypothesis that the diagnosis of opioid addiction is commonly not entertained, let alone established. Furthermore, when such a diagnosis is considered in high-risk patients, the diagnosis of opioid addiction is likely to be established.

3 / 3 / 2 Informal literature review

In addition to the addiction literature, the search included the titles and abstracts of articles published in the pain literature. Some articles were found by reviewing the publications of acknowledged leaders in the field (Ballantyne, Fine,

Katz, Passik, Portenoy, Shnoll, and Webster). Other papers were found through searches that included the terms “chronic pain,” “opioid dependence,” and “addiction.”

None of the literature directly addressed the question “What is the failure rate for making or excluding the diagnosis of opioid addiction (dependence) in pain patients on COAT?” The current literature does, however, attempt to address questions related to incidence or prevalence of opioid use disorders in pain patients on COAT.

- In 1997, in a study of 125 chronic pain clinic patients, 69.6% were on opioid analgesics (including codeine) and 17.6% were on benzodiazepines. 12% of these patients were diagnosed as having psychoactive substance abuse or dependence disorder using the DSM-III-R criteria (Kouyanou, Pither, & Wessely, 1997).

Comment: Because of the mix of prescriptions and the nonspecificity of the findings regarding opioid addiction, little can be gleaned, but this study highlights the lack of formal assessments for opioid addiction in studies reporting prevalence or incidence.

- A 2005 American study demonstrated that 2–5% of chronic pain patients were addicted to opioids (Webster & Webster, 2005). The definition they used for addiction was: “Addiction means the pursuit of such substances for no medical purpose despite resulting physical or psychological harm.”

Comment: The definition of addiction used would probably exclude many patients who are opioid-addicted and are receiving adequate therapy. These “treated” patients on prescribed COAT would not be expected to present with aberrant behavior or overt illicit behavior. Furthermore, by excluding craving and other criteria generally appreciated as being consistent with addiction, the expected sensitivity for establishing opioid addiction would be limited. What is more, since they did not include the use of opioids to help manage opioid addiction, it reflects potentially strong prejudices in the pain community about opioid addiction. Opioids are not only medically helpful for painful conditions, but, as already discussed, are frequently essential and potentially life-saving in patients who are opioid-addicted.

- Mehta and Langford (2006) quote a 3–16% rate of addiction in patients who complain of pain, albeit in diverse pathological conditions, and using different definitions of addiction.

Comment: This group is not formally comparable to patients on COAT for pain. The study does highlight a significant concern about addiction in patients with pain complaints and implies the usefulness of formal assessments

for addiction in patients with chronic pain, regardless of their COAT status.

- Ballantyne and LaForge (2007) review the pain literature as it pertains to the diagnosis of opioid addiction in patients on COAT. The authors provide confirmation that diagnosing iatrogenic opioid addiction is more problematic than when the opioid use is associated with longstanding illicit drug use. The authors express a lack of satisfactory means of differentiating “true addiction” from problematic behavior secondary to factors other than addiction.

Comment: Rather than considering one disorder that presents in a variety of ways and depends on severity and context, the authors suggest additional distinct explanations for the observed “problematic” behavior. In their discussion, no formal diagnosis is typically established to explain the “problematic” behavior. As already discussed, the phenomenon of pseudo-addiction is often provided as a common reason for problematic behavior. In addition to not formally addressing the question of false negatives, the review by Ballantyne and LaForge supports a wide variation in the reported prevalence of opioid addiction in pain patients on COAT. This is consistent with the hypothesis that formal and reliable assessments are lacking.

- In 2007, another study involved 801 chronic pain patients who received opioid therapy from their primary care physician (Fleming, Balouse, Klessig, et al., 2007). The point prevalence of current (DSM-IV criteria in the past 30 days) substance abuse and/or dependence was 9.7% (n=78) and 3.8% for an opioid use disorder.

Comment: This represents a significant number of opioid-addicted patients on chronic opioid therapy for pain. It also limited the assessment to the past 30 days, which, as previously mentioned, would clearly limit the number of potential patients who meet the diagnostic criteria. Such a potential reduction in addiction diagnoses interferes with meaningful prevalence determinations. Indeed, the validity and reliability of the findings are not discussed.

There was no reported attempt to address the rate of false negatives. This lack of determining the “false negative” is typical of the current literature that explores prevalence rates of opiate use disorders in pain patients. False negatives must be important in these populations. It is well recognized that self-reporting is problematic in populations being prescribed opioids (Gourlay, Heit, Ballantyne, et al., 2009). Nonetheless, the diagnosis is most often not entertained, even in specialized pain management settings.

- A 2007 European review paper reported that the prevalence of addiction varied from 0% up to 50% in chronic nonmalignant pain patients, and from 0% to

7.7% in cancer patients. The rates depended upon the subpopulation studied and the criteria used (Hjrted & Sjogren, 2007).

Comment: The variability in prevalence rates reported in this review calls for further studies to formally assess the prevalence of opioid addiction in various subgroups of patients. Note that the findings did not require the patients to be on COAT, but simply to have chronic nonmalignant pain. The findings of addiction were not reported to be specific to opioid addiction. Nonetheless, their findings provide supportive evidence that opioid addiction is likely to be significantly prevalent in patients with chronic nonmalignant pain. It could be argued that those who are on COAT are even more likely to be opioid-dependent. Patients on COAT for pain commonly meet at least two out of the three required DSM-IV-TR criteria.

- In their book *Avoiding Opioid Abuse While Managing Pain*, Webster and Dove (2007) state:

“The prevalence of addiction in pain patients has almost certainly been underestimated in the recent past. In truth, the prevalence of drug abuse and addiction in patients treated with opioids for chronic pain has not been established because of the lack of prospective studies.”

They quote statistics that suggest that having chronic pain, whether managed by opioids or not, is associated with substance abuse in the 10%–18% range. This rate is similar to or slightly higher than the general rate of addiction in the general population.

Comment: There were, admittedly, no studies that directly and formally address opioid addiction prevalence. If 10%–18% of the general population has substance abuse problems, and patients on COAT for pain inevitably meet two (tolerance and withdrawal) out of the three DSM-IV-TR criteria for opioid addiction, a fair percentage of the patients on COAT for pain are probably opioid-addicted. Given the lack of observed opioid addiction diagnoses being made, these statistics support a common failure to make the diagnosis of opioid addiction in pain patients on COAT.

The authors state in the next chapter, “True opioid addiction that results from long-term opioid therapy is relatively rare” (Webster & Dove, 2007, p. 30). One must agree that long-term opioid therapy is not by itself the sole cause. Genetics, age, and environmental and comorbid conditions all contribute to the possibility of disease initiation and progression. The statement, however, is misleading. By focusing on the question of incidence as the direct or unique result of COAT, it sidesteps the more important clinical question of the prevalence and incidence of opioid addiction in pain patients on COAT, regardless of the causes.

- In the 2011 study “Assessment, Stratification, and Monitoring of the Risk for Prescription Opioid Misuse

and Abuse in the Primary Care Setting,” Brown, Setnik, Lee et al. conclude: “There was a tendency for investigators to assign lower risk levels than those that were protocol-specific, suggesting a need for better understanding of factors influencing investigator decisions.”

Comment: While they did not specifically address the question of the prevalence or incidence of opioid addiction, their findings support the hypothesis that even seasoned clinicians tend to minimize the risks of opioid addiction in their patients on COAT.

- In 2011, Morasco, Corson, Turk, et al. wrote in more generic terms of substance use disorders in patients with chronic non-cancer pain.

Comment: While the importance of recognizing morbid SUDs is stressed, they did not formally address the question of prevalence of opioid addiction in patients with chronic non-cancer pain. This study, too, was performed in a primary care setting. Studies to compare incidence and prevalence in primary care setting versus specialized settings such as emergency rooms, orthopedic clinics, or pain management clinics would be helpful.

- In 2012, Minozzi, Amato, and Davoli published “Development of dependence following treatment with opioid analgesics for pain relief: a systematic review”. The studies that qualified for analysis included three systematic reviews, one randomized controlled trial, eight cross-sectional studies, and four uncontrolled case series. Most of the studies involved adult patients with chronic non-cancerous pain; two also included patients with cancer pain, but only one included patients with a previous history of dependence. Minozzi et al. found that the incidence of addiction reported across the various studies ranged from 0% to 24% (median 0.5%), while prevalence ranged from 0% to 31% (median 4.5%). There was a significant variation among the studies in terms of design, definitions of addiction, data collection, and other factors, so a data meta-analysis could not be conducted. The researchers rated the evidence overall as being of very low quality.

Comment: The authors did not comment on how they defined incidence or prevalence, and the tables discussed frequencies. Frequency, particularly in the context of opioid addiction, does not readily translate to standard definitions for incidence or prevalence. The wide ranges of addiction incidence (0–24%) and prevalence (0–31%) reported by the researchers are consistent with a lack of reliability or validity in the methods used to assess opioid addiction. The estimates of median values — 0.5% incidence and 4.5% prevalence — cannot be reliably used to denote the extent of addiction in patients receiving opioid analgesics for pain. The

usefulness of the median statistic can be compromised by its large variation from the established mean. Median values also have limited value in estimating rates when the measures used are not established as being valid or reliable.

The duration of the exposure to opioids varied greatly in the various studies. Only eleven of seventeen studies reported on the length of the opioid treatment, which ranged from three days to eighty-one months. Most of the studies were of short duration. Since the duration and intensity of exposure are related to the likelihood of developing an addiction, studies of short duration are less likely to demonstrate the development of addiction. As previously explained, if attempts were not made to formally assess evidence of opioid addiction in the past, the prevalence data for the diagnosis of opioid addiction are uncertain. As would be predicted, indirect evidence from logistic regression analyses in three studies found that prior substance abuse/dependence was a strong predictor of addiction during opioid analgesic therapy.

- Kevin E. Vowles et al. published in *Pain*: “Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis.” (Vowles, McEntee, Julnes, et al., 2015) The rates of problematic use were quite broad in COAT, ranging from <1% to 81% across the studies. The rates of addiction averaged between 8% and 12% (range, 95% CI: 3%–17%). In none of the studies reviewed were there formal and systematic attempts to diagnose opioid dependence based on the DSM-IV criteria, but rather on some current consensus definitions. In an accompanying commentary Ballantyne commented: “But could rates of addiction have been underestimated because there cannot be clear distinctions between misuse and addiction, despite the apparent clarity of the definitions?” (Ballantyne, 2015), Ballantyne also comments that it may be impossible to understand what addiction actually is when it arises during pain treatment with opioids.

Comment: When it comes to problematic opioid use associated with COAT for pain, it seems that there are significant barriers to using standard and established definitions of addiction based on their established validity and reliability. This resistance was codified in the newer DSM-V criteria, by which the diagnosis of opioid use disorders are to have different criteria in the context of the medical management of pain. While there is little or no literature to support these new criteria and the assumptions are arguably problematic on the basis of our current understandings of the disease of opioid addiction, they are likely to endure until studies are designed and performed to address the questions.

- Most recently, in 2015, Degenhardt, Bruno, Lintzeris, et al. published a most important paper looking at the prevalence of opioid addiction and use disorders in Australian patients on COAT for chronic non-cancer pain.

It was a cohort study and compared the prevalence of opioid dependence and use disorders using the DSM-IV, DSM-V, ICD-10, and proposed ICD-11 criteria. They used the well-established Composite International Diagnostic Interview, a structured interview, to explore the rates of opioid addiction in the population studied. The population was recruited generally with a median duration of pain of ten years, strong opioids used for a median of four years, and a mean age of fifty-eight (1,422 participants).

While their findings are worth reviewing in detail, for the purposes of this review they found in the population studied an 8%–10 % lifetime prevalence of opioid addiction, with a DSM-V rate of 21% if mild opioid use disorder criteria were used, and conditional exclusions present (i.e., tolerance and withdrawal criteria excluded). It is noteworthy that they found men were more likely to meet the criteria for opioid dependence, with an odds ratio of approximately 1.5.

Their discussion of the different criteria and their agreement showed excellent agreement between ICD-10, ICD-11, and DSM-IV. There was only fair to moderate agreement between the ICD-10, DSM-IV, and DSM-V use disorder criteria. According to their “model fit,” the definition of dependence in the draft ICD-11 worked best, and the worst was DSM-V.

Comment: The results of this paper no longer allow a prescriber of COAT for a patient with chronic non-cancerous pain to assume that opioid use disorders are rare. As a result, their findings have huge clinical implications. The intention in writing this review was to promote studies such as this one. The next step is to tease out the rates of opioid use disorders in patients who are likely to be at high risk: those with comorbid major psychiatric diagnoses and substance use disorders, age of onset of opioid use before age 25, disability status, post-traumatic stress disorder (PTSD) or sexual trauma in the past, family history, etc. (See next review.)

It is also likely that the rates are different in different clinical contexts. Even more importantly, it is time we recognized how frequently the diagnoses are missed in the various clinical contexts, that is, to explore formally the failure rates of making an appropriate opioid addiction diagnosis in pain patients on COAT. While Degenhardt et al., on the basis of their findings, would seem to prefer the draft ICD-11 criteria, I would predict that the DSM-IV criteria are equally suitable. The DSM-IV criteria also have a ro-

bust and established research base as it relates to prognosis and effective therapy.

- In conjunction with the large Australian cohort study just discussed, Campbell, Nielsen, et al. published an article in *Pain Medicine* in 2015. This article examines pharmaceutical opioid dose and dependence, and the correlates of each. Multivariate analysis found past-year dependence was independently associated with being younger, male, unemployed, unmarried, exhibiting more aberrant behaviors (most commonly early requests for refills or requests for higher doses), and having a history of benzodiazepine dependence. Patients who were opioid-dependent were also more likely to report past-year depression, generalized anxiety disorder, PTSD, or other substance abuse disorders. A greater daily oral morphine equivalent (OME) consumption was also associated with higher odds of multiple physical and mental health issues, aberrant opioid use, problems associated with opioid medication, and opioid dependence. They, like many reviewers, seemed to be concerned about the opioid doses prescribed and the selection process for these. They commented: “The term ‘adverse selection’ has been coined to describe this apparent contradiction in which the likelihood of a patient receiving opioid therapy increases as the number of risk factors for adverse outcomes increases; this study found strong evidence for this, whereby those consuming higher levels of opioids were clearly those with a more complex picture of physical and mental health problems, as well as social disadvantage.” (Campbell, Nielsen, et al., 2015)

Comments: The correlates that were found confirm clinical experience and the literature (Cochran, Flentje, Heck, et al., 2014; Sullivan, 2010) in terms of higher morbidity and risk factors for having an opioid use disorder. A most pertinent question remains: when patients have one or more established risk factors, what is the actual likelihood that they have a significant opioid use disorder? If multiple risk factors are present, we might expect a greater likelihood of a significant opioid use disorder. If this is true, a possible implication is that the complications seen as the result of higher doses of OMEs may simply be a failure to recognize and properly manage opioid use disorders in COAT patients. As previously noted, opioid-addicted patients, even those who do not have chronic non-cancer pain, require higher doses of stabilizing opioids to avoid complications and ensure the best clinical outcomes. One must appreciate that opioid use disorders must be considered lifetime disorders. The diagnosis must be considered when criteria are met during any twelve-month period, not just the most recent twelve-month period as in this study. So the

8%–10% prevalence of opioid addiction in the past year does not necessarily accurately reflect the true prevalence of the disease in this cohort.

Indeed, the impetus of this paper is the clinical impression that the failure to make the diagnosis and ensure proper care for an opioid use disorder is common amongst COAT patients. Such a failure may well be the primary reason for the greater complications associated with the higher OME doses. Another possibility is the relatively poor management of the other comorbid psychiatric problems, let alone the socio-economic stressors, and the overall adverse selection process (Cochran et al., 2014; Sullivan, 2010; Rogers, Kemp, McLachlan, & Blyth, 2014; Clarke, Soneji, Ko, Yun, & Wijeyesundera, 2014).

With almost all strong pharmaceuticals, when predicting good outcomes, proper patient selection and monitoring for potential side effects and complications are essential. Most often, the selection and monitoring are more important than the actual dose of medicine prescribed.

The author is concerned that the emphasis on OME doses often represents a post hoc fallacy. In other words, the association between higher OME doses and complications does not necessarily imply that higher OMEs are the primary cause of the complications.

● 4 GENERAL COMMENTS ON REVIEW ARTICLES

The reviews by Minozzi et al., along with Vowles et al., were, until the cohort study by Degenhardt et al., the most exhaustive evidence-gathering and review process on this subject to date. With the findings of Degenhardt et al., the contention that addiction is not a “major risk” associated with COAT can be rejected. As already discussed, opioid therapy alone is not likely to be a significant risk, but when it is coupled with other risk factors, the prevalence and incidence of opioid addiction is expected to be even greater than the 9–10% noted in a general cohort of COAT chronic non-cancer pain patients.

Until the findings of Degenhardt et al., there was a deficit in the literature regarding valid and reliable opioid addiction assessments for a large cohort of chronic complex pain patients on COAT. Conclusive evidence regarding the incidence and prevalence of opioid addiction will probably come from prospective clinical studies that use the “gold standard” of structured interviews, as found in the study of Degenhardt et al.

Another possibility is that “objective biomarkers” will soon be able to establish the diagnosis of opioid addiction, as is now being considered with major depressive disorders. Biomarkers might readily overcome subjective biases and other inherent barriers that make the diagnosis of opioid use disorders difficult to formally establish.

This is particularly true when the disease of opioid addiction is clinically mild, intermittent, or in remission, whether as a result of agonist therapy for pain or addiction, or through abstinence-based approaches. Until such biomarkers have been validated and found to be reliable, the patient history, expert clinical evaluation, and the appreciation of risk factors will remain essential to help prevent serious complications in patients with chronic non-cancer pain who receive COAT.

The variable rates of addiction reported above and elsewhere reflect a heterogeneous group of settings and patients who take opioids for chronic pain. Given this, along with the variety of definitions used and the lack of clear objective markers, the challenges and controversies in establishing the prevalence or incidence of the diagnosis of opioid addiction are likely to continue.

Patients at risk of substance abuse are not expected to be reliable reporters. This makes self-reported criteria further suspect. The clinical significance of false negatives in the population of pain patients on COAT has not gone unnoticed. Because of the clinical uncertainties in identifying problematic use, abuse, or dependence, urine drug testing has become standard in specialized clinics prescribing COAT for pain. If not sought or screened for, drug abuse and adherence concerns are commonly missed, even by the most experienced practitioner (American Pain Society, 2009; Gourlay et al., 2009; Minozzi et al., 2012; Heit & Gourlay, 2004).

Clinicians may also falsely label patients as “drug seekers” or “addicts.” In addition to the concept of pseudo-addiction as discussed here, another confounder is that adherence problems are common in most chronic conditions, particularly those with prescribed regimens requiring regular dosing. Hence, problems of adherence do not occur only in pain patients suffering from an addiction or substance abuse. Perhaps the rates of adherence problems in pain patients with addictive disorders are similar in magnitude to those with other chronic diseases such as diabetes, hypertension, or asthma? Indeed, most chronic diseases have similar relapse rates to those of addictive disorders (Savage, Kirsh, & Passik, 2008).

Lastly, one must acknowledge that abuse, addiction, and diversion are not the only possible reasons for adherence problems in a specific COAT patient. Other explanations always need to be entertained by the astute clinician when confronted by an adherence concern, whether for a low- or high-risk patient.

● 5 CONCLUSIONS & SUMMARY DISCUSSION

Three lines of evidence support a common failure to diagnose opioid addiction in pain patients on COAT.

- 1/ the established pathophysiology of opioid addiction and the risks inherent in repeated exposure to potent opioids. In addition to the repeated exposure to opioids, there are a significant number of patients who are known to be at high risk of having or developing addiction;
- 2/ clinical observations;
- 3/ an informal review of the literature.

How common these failures are requires further study, but the findings of Degenhardt et al. have already documented a likely significant failure by prescribers to establish or rule out opioid use disorders. A prevalence of 10%, which is probably much higher in certain subgroups or cohorts, is not a rare or even uncommon diagnosis.

This paper provides support for the importance of clinical research to help resolve the question of the prevalence and incidence of opioid addiction in pain patients receiving COAT. We encourage formal screening for opioid use disorders in all pain patients on COAT, in particular those with risk factors.

On the basis of established morbidity and mortality rates, the consequences of the lack of formal screening for opioid addiction in pain patients prescribed COAT are serious and predictable. Until there are better criteria for establishing the diagnosis of opioid addiction, with research confirming their validity and reliability, the currently established criteria for opioid addiction based on DSM-IV-TR or perhaps with time the new draft ICD-11 criteria will be found to be best.

Once the incidence and prevalence of opioid addiction in pain patients on COAT are more widely appreciated, effective preventive and therapeutic measures are likely to follow. It is hoped, as the new DSM-V criteria for substance use disorders become established, that there will be a further appreciation that opioid addiction, as is the case with most chronic diseases, has a continuum of severity and morbidity. Unrecognized and/or poorly treated opioid addiction may be a common explanation for the recent spate of opioid overdose deaths (Webster et al., 2011).

As physicians better appreciate the common neuropsychological findings present in patients with chronic complex pain and addictive disorders, they will be better prepared to address and treat addictions in patients with chronic pain disorders. Physicians might also better utilize some of what is known in treating addictions to improve their management of complex pain patients (Savage et al., 2008; Passik, Kirsh, Donaghy, & Portenoy, 2006).

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