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RESEARCH ARTICLE

# Doctors Diagnosing Addiction – Are the Blind Leading the Blind?

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## ABSTRACT

This paper addresses the questions, "are clinicians who treat patients in pain – or even specialists in addiction medicine -- appropriately prepared to accurately diagnose opioid use disorder? Further, is prevailing public policy on pain management employing opioid analgesics firmly grounded in science?"

The author summarizes key findings from reviews of pertinent medical literature on pain treatment and diagnosis of substance use disorder.

- Medical doctors are widely understood to be inadequately trained in diagnosis of both pain and addiction among their patients.
- There is currently no consensus standard of practice to guide clinicians in either prescription of opioids or diagnosis of "substance use disorder" among patients treated for pain.
- Available medical literature and clinical experience do not support the thesis that clinicians prescribing in a continuing relationship with pain patients have contributed measurably to the widely discussed US "opioid crisis".
- Even lacking authoritative education and training in the treatment of pain with prescription opioids or the diagnosis of substance use disorder, general principles do exist and are widely recognized among practicing clinicians.

Entry of a "substance use disorder" or "addiction" code in patient electronic medical records can be a literal "kiss of death" for ongoing treatment of severe pain. Thus it seems necessary to caution clinicians who treat pain - and policy makers who oversee them - that much of what they think they "know" about substance use disorder and its causes may no longer be current or may have been wrong in the first place.

## Introduction

The United States is currently embroiled in a contentious public debate about addiction-related mortality, chronic pain, and government regulation of clinicians who employ opioid analgesic pain relievers in treating pain. A central element in this debate is the question of whether clinicians prescribing to pain patients have contributed to addiction, hospitalizations for opioid toxicity or increasing rates of mortality attributed to drug overdose. Ample published data directly contradict assertions widely prevalent in popular media concerning cause-and-effect relationships[1, 2, 3, 4].

However, medical literature is not yet definitive concerning the incidence of either physiological dependence or iatrogenic substance use disorder in patients who are treated for pain by means of prescription opioid pain relievers. A significant and largely unrecognized confound in estimating such incidence is that substance use disorder is rare in clinical patients and is often confused with physiologic dependence. Medical literature also provides evidence of multiple confounds in clinicians' assignment of diagnostic codes in electronic health records[5].

This paper begins with an overview of the current sorry state of clinician training with regard to diagnosis and treatment of severe chronic pain, as well as a summary of systemic problems in clinician training for diagnosis of addiction. Neither the 2022 US Centers for Disease Control and Prevention (CDC) guidelines on prescription of opioids, nor the 5th edition of the Diagnostic and Statistical Manual offers a useful framework for clinicians in pain medicine, who are directed to explicitly assess "risks versus benefits" for their individual patients before deciding on a therapy plan.

The 2022 revised CDC opioid prescribing practice guidelines are critically reviewed. Major weaknesses of science, misrepresentation of existing trials data and pre-existing biases of the guideline writers, are identified. The magnitude of these errors appears sufficient to justify public repudiation of both CDC guidelines and derivative Veterans Administration/Department of Defense guidelines also published in 2022. Moreover, the author suggests that because of these embedded errors, the entire trials literature for evaluating effectiveness and safety of prescription opioids must be thrown out and done over with trials protocols that explicitly address genetically mediated opioid metabolism. Pending this needed correction, pain doctors are advised that too often, if they enter a diagnostic code of opioid dependence or addiction in a patient's records, they are becoming "the blind leading the blind."

## Methods

This paper offers a critical review and analysis of existing medical literature on clinical diagnosis and treatment of severe pain, and estimation of the incidence of dependence, tolerance, substance use disorder, overdose or death in clinical patients. Findings of key papers are reviewed, compared, and evaluated, to establish central trends. Of particular importance in this review is establishment of a central principle: there is presently no basis in science for estimating risk of iatrogenic opioid addiction in individual patients. This reality effectively invalidates almost the entire rationale for the 2022 CDC

practice guidelines for prescription of opioid analgesics.

## Discussion

Pain is the symptom that most often brings patients to a doctor's office.

"Over one-quarter of United States citizens suffer from chronic pain. It is among the most common complaints seen in an outpatient clinic and in the emergency department. The failure to manage chronic pain, as well as the possible complication of opioid dependence related to treatment, can result in significant morbidity and mortality... It is paramount that providers have a firm grasp on the management of patients with chronic pain[6]."

However, it is also widely recognized that…

"unfortunately, studies have revealed an inherent lack of education regarding pain management in most professional schools and training programs."

Despite this lack of clinical education, prescription opioid analgesics have long been recognized as an indispensable therapy for moderate to severe pain.

"Appropriate opioid prescribing includes prescribing sufficient opioid medication through regular assessment, treatment planning, and monitoring to provide effective pain control while avoiding addiction, abuse, overdose, diversion, and misuse. To be successful, clinicians must understand appropriate opioid prescribing, assessment, the potential for abuse and addiction, and potential psychological problems. Inappropriate opioid prescribing typically involves not prescribing, under prescribing, overprescribing, or continuing to prescribe opioids when they are no longer effective"[6].

*CONTROVERSIES IN OPIOID PRESCRIBING PRACTICE*

To borrow a phrase from Shakespeare's *Hamlet*, "therein lies the rub." How are clinicians to administer opioids in an "appropriate" way, while avoiding harms to their patients (or themselves)? Multiple US and non-US clinical specialty organizations have attempted to develop practice standards or guidelines for their members. The non-uniformity among these guidelines led the US Congress to pass the "Comprehensive Addiction and Recovery Act" in 2016, establishing a Pain Management Best Practices Inter-Agency Task Force in 2016.

"The goal was to propose best practices and issue recommendations that address gaps or inconsistencies for managing chronic and acute pain. The task force released its draft report in December 2018 and allowed 90 days for open comment, for which HHS received more than 6,000 written responses. In early May 2019, the task force gathered for two days of public meetings, wherein they adopted and released a final draft report[7]."

Unfortunately, after a panel of 20 clinical contributors and patient advocates deliberated for 18 months, results were still largely inconclusive. A central reason for this outcome may have been that the Task Force worked in parallel with a major competing effort in the US Centers for Disease Control and Prevention (CDC) that proceeded from 2016 publication of yet another set of opioid prescribing guidelines[8].

CDC practice guidelines for prescription of opioids have been problematic and controversial since even before initial publication in 2016, on multiple

grounds[9,10,11,12,13,14] In 2019, CDC was forced by widespread clinician criticism to release a disclaimer, advising that their prescribing guidelines were never intended to become an inflexible "practice standard" made mandatory under State laws[15, 16, 17]. Criticism of the CDC opioid guidelines process and findings continued unabated thereafter.

A major and potentially disqualifying characteristic of both the original 2016 guidelines and a revision published in November 2022 is that both were founded on the unproven assumption that medical prescribing has contributed significantly to the so-called "opioid crisis" in the US. This assumption is now understood to be unfounded[1,18,19,20,21,22,23].

In 2019, six US clinical professional associations representing over 560,000 doctors and medical students advocated for "removal of political reference from the practice of evidence-based medicine[23]." The American Medical Association (among many others) continued and expanded its earlier criticisms, leading the CDC to announce a two-year-long revision and update to their 2016 guidelines[24,25].

Arguably – and despite conciliatory language proclaiming that patient pain care must be individualized and informed by the experience of clinicians -- the updated 2022 revised CDC opioid prescribing guidelines are now widely recognized to be fatally flawed for many of the same reasons as their effort in 2016:

- Strong recommendations were based on very weak or misinterpreted evidence[26]
- Rarity of long-term trials for opioid effectiveness was conflated with a claimed lack of effectiveness[9]
- Non-opioid and non-pharmaceutical therapies were naively advocated as "preferable" to opioids, despite a complete absence of any trials directly comparing these modalities[27]
- "Risks" of opioid therapy were persistently over-emphasized, as evidenced by over 400 instances of the word in 2022 updated guidelines[9], reflecting pre-existing but unacknowledged anti-opioid bias on the part of guideline writers[28]
- One-size-fits-all thinking generated an asserted "threshold of diminishing returns" at doses exceeding 90 Morphine Milligram Equivalent Daily Dose (MMEDD)[9]
- The guidelines failed to recognize that MMEDD is itself widely understood to be "junk science", lacking any published trials data and prone to inconsistencies in practice[29],
- The document places highly inappropriate over-emphasis on tapering of legacy patients[30,31,32,33]
- The CDC authors failed even to discuss the wide variability of minimum effective opioid dose levels and side effects caused by genetically mediated opioid metabolism[34,35,36]. Arguably, this omission disqualifies much of the existing medical trials literature on pain management, as well as both versions of the CDC opioid guidelines and derivative US Veterans Administration / Department of Defense guidelines published in 2022.

The scope and magnitude of these failings becomes particularly alarming in the context of government regulation of controlled substances and clinicians who employ them in pain management. There is ample evidence that policies of the US Drug Enforcement Administration, State legislatures, and State Medical Boards now constitute a vast over-

reach that is destroying the practice of pain medicine[37,38]. Misdirected and erroneous public health guidelines on prescription of opioids have become major contributors to this destruction[39,40,41,42].

*CONTROVERSIES IN DIAGNOSING "SUBSTANCE ABUSE DISORDER"*

Definitions of Addiction -- or in more recent years Substance Abuse Disorder -- have been under almost continuous evolution since the first edition of the American Psychiatric Association's (APA) *Diagnostic and Statistical Manual of Mental Disorders (DSM)* in 1952[43]. The number and nature of mental disorders has elaborated steadily despite complaints of psychiatrist financial self-interest and poor research scholarship44. Dr Allen Francis, APA Workgroup Chair for development of the fourth edition of the DSM, became one of the most prominent critics of the 5th edition in 2013[45,46]. Two weeks before the DSM-5 was scheduled for publication, the US National Institute for Mental Health announced that they would no longer fund projects that rely on DSM criteria[47,48,49].

It is thus no wonder that relatively few clinicians have had extensive training in the use of the DSM-5's eleven symptoms and three degrees of severity[50] in diagnosing Substance Use Disorder. Likewise, it is highly doubtful that this elaborate classification system has any particular relevance in clinician choices for a course of therapy for pain that also balances concerns for possible undesired outcomes in iatrogenic physiological dependency, tolerance or addiction[27].

The American Society for Addiction Medicine also publishes a National Practice Guideline for Treatment of Opioid Use Disorder. This Guideline describes physical signs and symptoms of opioid intoxication or withdrawal, with the following cautionary note:

"Opioid use disorder is primarily diagnosed on the basis of the history provided by the patient and a comprehensive assessment that includes a physical examination and laboratory testing, including drug testing. Corroborating information reported by significant others can be used to confirm the diagnosis, especially when there is lack of clarity or inconsistency in information. Other clinicians may make a diagnosis of opioid use disorder; however, prescriber confirmation of the diagnosis is required before medications are prescribed[51]."

Unless a clinician treats pain or addiction as a primary practice, it is doubtful that he or she will actually read the ASAM Guidelines or receive in-depth training in similar content.

*HOW PREVALENT IS ADDICTION AS AN OUTCOME OF CLINICAL TREATMENT OF PAIN?*

There are many claims and counter-claims in the medical and popular literature concerning the incidence of opioid dependence, tolerance, addiction (also termed "opioid abuse disorder"), overdose, or death[5,52]. However, multiple sources establish that actual incidence of these outcomes is quite low[53,54,55,56,57].

Volkow and McClellan[5] inform us that opioid addiction is "not a predictable outcome" of clinician prescribing and is rare even in patients who have factors in their medical histories that are thought to be associated with elevated risk of opioid misuse. They also point out that physical dependence is not the same medical entity as addiction, and

possibly on the order of 40% of patient vulnerability to addiction is genetically mediated.

Dependence is characterized by the occurrence of withdrawal symptoms when an existing opioid therapy is tapered too rapidly after a sustained period of use. Addiction involves other physiological mechanisms that require much longer exposure and may be very much more persistent. Volkow and McClellan note that "published estimates of iatrogenic addiction vary substantially from less than 1% to more than 26% of cases." They attribute much of this variation to confusion in definitions -- a view shared by the author.

Other definitive studies provide important insights, even when they do not avoid the confounds that have led to such wide ranges of estimated incidence in iatrogenic addiction. For instance, Oliva, Bowe, Tavikoli et al.[54] developed the Stratification Tool for Opioid Risk Mitigation (STORM) -- a highly accurate predictive model to identify Veterans Administration patients prescribed opioid analgesics, who might be at elevated risk of drug overdose, suicide-related events (ideation or attempt) or death. The model was applied to a population of 1,135,601 patients followed from Fiscal Year 2010 to 2011, employing Veterans Administration electronic health record data. Several types of short-acting and long-acting opioid analgesics were included.

In this population, 2.1% (23,790) of patient records followed from 2010 had codes for a drug overdose, suicide-related event, or death during Fiscal Year 2011. Among the 1,000 patients deemed to be at highest risk in the predictive model, only one of 11 risk factors (e.g., number of classes of sedating medications other than opioids) was related to medical treatment choices per se. The remaining 10 major risk factors related to prior attempted suicides, inpatient mental health treatment, previous drug or alcohol abuse, or diagnoses of major depressive disorder. Medical co-morbidities were also tracked in the analysis -- but risk factors associated with these co-morbidities were substantially lower than the top eleven. Risk factors for the cataloged negative outcomes varied over a relatively small range (1.1 to 1.5) versus the types and strengths of opioids used.

Papers by Sun et al [56] and Brat et al [57] also offer significant insight into demographic risks of opioid therapy.

Sun and colleagues sought to "characterize the risk of chronic opioid use among opioid-naive patients following 1 of 11 surgical procedures compared with nonsurgical patients." The study included 641,941 opioid-naive surgical patients and 18,011,137 opioid-naive nonsurgical patients.

"…Retrospective analysis of administrative health claims [was conducted] to determine the association between chronic opioid use and surgery among privately insured patients between January 1, 2001, and December 31, 2013. The data included "11 surgical procedures" (total knee arthroplasty [TKA], total hip arthroplasty, laparoscopic cholecystectomy, open cholecystectomy, laparoscopic appendectomy, open appendectomy, cesarean delivery, functional endoscopic sinus surgery [FESS], cataract surgery, transurethral prostate resection [TURP], and simple mastectomy)…"

Chronic opioid use was defined as "having filled 10 or more prescriptions or more than 120 days' supply of an opioid in the first year

after surgery, excluding the first 90 postoperative days. For nonsurgical patients, chronic opioid use was defined as having filled 10 or more prescriptions or more than 120 days' supply following a randomly assigned "surgery date."

Sun and his colleagues found that

"…among the surgical patients, the incidence of chronic opioid use in the first preoperative year ranged from 0.119% for Cesarean delivery (95% CI, 0.104%-0.134%) to 1.41% for TKA (95% CI, 1.29%-1.53%). The baseline incidence of chronic opioid use among the nonsurgical patients was 0.136% (95% CI, 0.134% -0.137%)."

"Except for cataract surgery, laparoscopic appendectomy, FESS, and TURP, all of the surgical procedures were associated with an increased risk of chronic opioid use, with odds ratios ranging from 1.28 (95% CI, 1.12-1.46) for cesarean delivery to 5.10 (95% CI, 4.67-5.58) for TKA. Male sex, age older than 50 years, and preoperative history of drug abuse, alcohol abuse, depression, benzodiazepine use, or antidepressant use were associated with chronic opioid use among surgical patients."

From the perspectives of the current paper, these findings might be rephrased. Four of eleven procedures showed no elevated incidence of persistent opioid prescribing following surgery – which would have been expected if exposure to opioids is of itself a predisposing factor for opioid addiction. The highest odds ratio for ongoing chronic use of prescription opioids was found for Total Knee Arthroplasty -- a procedure well known to be associated with higher surgical failure rates. Incidence of protracted prescribing was actually lower in patients who underwent Caesarean Section (all female) relative to those who did not undergo surgery (male and female).

These results directly contradict the widely prevalent perception that all patients treated with opioids are rapidly at risk for opioid dependence or addiction. It is indeed plausible that continuing prescription of opioids following initial post-surgical treatment is at least as much related to procedure failure and emergence of chronic pain as it may be a result of any inherent addictive potential for prescription opioids per se.

Brat et al [57] conducted a retrospective cohort study of "surgical claims from a linked medical and pharmacy administrative database" for over 37 million commercially insured patients between 2008 and 2016. They identified just over a million "opioid-naïve" patients undergoing surgery during that period. Of these, 568,612 (56.0%) patients received postoperative opioids. "Misuse" was defined as the occurrence of a medical record code for opioid dependence, abuse, or overdose. One or more of these codes was subsequently identified for 5906 patients from the million-plus who underwent surgery (0.6%).

Patients were defined as "opioid-naïve" if their total recorded opioid use in the 60 days before surgery was seven days or less. Postsurgical opioid use was indicated if the member filled a prescription for an included opioid within 30 days of discharge. Use was considered to have stopped when either 30 days elapsed without a filled opioid prescription or a "misuse" diagnosis was observed.

Several issues arise in this source. First, it is unclear why Brat et al combined three codes under the single term "misuse", used nearly

100 times in their paper. Long-term clinically supervised prescription use does not equate to opioid misuse. As noted by Sun, et al, prolonged post-surgical prescription may occur among patients for whom a surgical procedure has failed and pain has transitioned from acute to chronic. Outcomes for different types of surgery (Figure 3C and 3D in the reference) confirm such outcomes. Brat et al reported a 4-to-1 spread in mean duration of initial use and a 6-to-1 spread in mean total dose between categories of surgery, suggesting that the type of surgery is more important in the outcomes than exposure to opioids per se.

Even including dependence (which is not a misuse of opioids), the reported rate of "misuse" signaled by post-surgical medical record entries was only weakly sensitive to daily dose, varying from 0.13% to about 0.35% as daily dose varied from less than 20 MME to over 150 MME. There was no noticeable threshold (knee in the curve) of increased "risk" of bad outcomes within this range.

The aggregate incidence of undesired outcomes was reported for a non-homogenous population: 44% of the million-plus opioid-naïve post-operative patients were not prescribed opioids for post-surgical pain, versus 56% who were prescribed. Thus part of the gradual rise in "misuse" should be attributed not to misuse associated with post-surgical prescription opioids, but rather to physiological dependence arising from prolonged use of opioids to manage surgical failures, or attributable to other conditions unrelated to surgery and not tracked in the data analysis.

Findings of Brat et al are thus consistent with those of Volkow and McClellan. Opioid dependence or addiction are not predictable outcomes of clinical prescribing and are relatively rare. Moreover, it seems entirely plausible that extended use of opioids in post-surgical pain may reflect more on failure of surgery than on any inherent patient vulnerability to misuse.

## PSEUDO-ADDICTION AND DENIAL OF CARE

The work of Volkow, Sun, Brat, and others[58] leads us to understand that relatively few clinically managed patients are vulnerable to iatrogenic addiction or overdose – and their vulnerability is only marginally affected by opioid dose levels. However, the US CDC has continued to advocate for restriction of patient access to opioid therapy, and the US regulatory environment for clinicians continues to worsen[59].

Despite FDA warnings confirming significantly increased risk of medical crisis or overdose among patients tapered off opioid therapy, there is a strong emphasis on tapering in the November 2022 revised CDC guidelines. Social media continue to be inundated with reports of involuntary tapers and consequent disability due to sustained and sometimes unbearable agony[60,61].

### *THE ROLE OF "PSEUDO-ADDICTION"*

When a patient reports to their clinician that they are not obtaining adequate pain relief from present dose levels, a poorly trained or defensive clinician may be naively tempted to enter the term "drug seeking behavior" in the patient's medical records. Some who feel especially exposed to possible sanctions by State Medical Boards or the Drug Enforcement Administration may choose to further taper the patient below 50 Morphine Milligram

Equivalent Daily Dose, or to outright discharge them without referral or support for managing withdrawal symptoms. Such action can become a literal "kiss of death[41]."

It can be argued compellingly that "pseudo-addiction" is an iatrogenic syndrome[65,66] and that the poorly trained clinician who enters a diagnostic code of addiction or opioid dependence in the patient's medical records may be one of its victims. As suggested by Nadeau, Wu and Lawhern[53],

"The extent to which clinicians make the diagnosis of OUD on the basis of perception of suspicious behavior, e.g., requests for increased opioid dosage to ease pain… as opposed to DSM criteria, is unknown, and diagnoses based solely on clinician judgment must therefore be questioned."

There is enormous variability in reported estimates of the incidence of iatrogenic opioid addiction. Much of this variability may stem from inappropriate definitions of "opioid misuse".

AGAIN FROM NADEAU WU AND LAWHERN: "The definitions of … outcome measures provide some clues to potential sources of the variability. Misuse was defined, according to widely accepted criteria, as opioid use contrary to the directed or prescribed pattern of use, regardless of the presence or absence of harm or adverse effects. This definition could be applied in several ways unrelated to abuse: patient use of the opioid at times of the day at odds with those recommended by the prescriber, taking extra pills of short acting drugs on bad days and less than the prescribed amount on good days (pain may fluctuate substantially from day to day), urine drug screens that were either falsely positive or turned up marijuana use, requests for an increase in opioid supply to cover inter-current surgery, accidents (however rare), or single instances of use of a different opioid diverted from a family member. We suggest that in good clinical practice, a judgment of misuse should hinge on patterns of behavior extending over repeated clinic visits…

Addiction is an extraordinarily complex disorder and is operationally very difficult to define... A diagnosis of addiction could be correct. However, practicing clinicians are rarely in a position to apply DSM criteria for addiction in a fully informed manner. We suggest that in the present US regulatory environment, "potential for harm" may be as much in the eye of the prescriber or the pharmacist as in any observable behaviors of the patient. Physician concern is often dosage-related [e.g., >90 MMED since CDC 2016]. "Compulsive" use might simply reflect the severity of the pain and the inadequacy of pain control. "Craving" might actually reflect pseudo-addiction—the patient craves higher doses because pain control is inadequate."

A question directly implied by this conundrum is "what should a clinician do when a patient requests increased doses of opioid analgesics?" The answer -- from the author's perspective as a patient advocate -- is to "trust the patient's reports while verifying and documenting details." Urine or blood tests can confirm whether expected values of opioid metabolites are present. Genomic testing may help explain unexpected levels of such metabolites. Prescription Drug Monitoring Programs can indicate doctor shopping or current prescriptions from multiple providers. One report of lost or

stolen medications is an event, while two or more reports suggest a pattern where consultation with a specialist in addiction may be in order.

In the larger context of ongoing treatment, general principles of appropriate clinical management of severe chronic pain are well established, independently of the fatally flawed CDC practice guidelines of 2016 and 2022[67,68,69,70]. Given the state of current regulatory policy regarding prescription opioids, some of these principles are necessarily legal rather than medical.

1. There should be no distinction in principle between the objectives of treating pain which is acute, chronic, or associated with advanced medical conditions assessed to be terminal. The objectives in all three cases are to alleviate suffering, promote patient functioning and improve quality of life. In this sense, treatment of pain is always "palliative". To deny treatment of pain when effective means exist to manage it, is a fundamental violation of human rights.

2. There is no one-size-fits-all patient or therapy plan. Pain management and treatment modalities must be tailored to the individual and guided by the judgment and experience of the clinician. Morphine Milligram Equivalent Daily Dose (MMED) is not a useful metric save for estimating approximately equivalent doses when one opioid medication is to be replaced by another opioid medication. Restriction of patient access to prescription opioids has no serious prospect of contributing to solution of America's "opioid crisis".

3. The volume of opioids prescribed in a medical practice is not a one-size-fits-all criterion to justify confiscation of a doctor's medical records or imposition of sanctions prior to review by State medical boards or courts. Prescribing patterns must be assessed in the context of the numbers of patients served, the nature of their underlying medical issues, and the availability of other nearby practitioners formally accredited to prescribe.

4. In the existing hostile regulatory environment, it is important for clinicians to document the basis for their diagnostic and treatment decisions in managing acute, sub-acute, or chronic severe pain -- and for patients and resident care givers to acknowledge these decisions in a documented therapy plan.

5. Multiple published practice guidelines of clinical specialty academies offer appropriate guidance on selection of pharmaceutical pain relievers for acute, sub-acute, and chronic pain. As one example, the Ladder of Pain Management of the World Health Organization is backed by 40 years of clinical experience as a framework for clinical education and practice.

6. All chronic pain practice guidelines begin with the principle "start low and titrate up to effective dose" while monitoring for and actively managing side effects. If one pharmaceutical treatment fails to produce adequate relief or tolerance develops, then that therapy may be tapered down and replaced with another treatment agent or poly-therapy, employing a different mechanism of action. Clinicians should be aware of the wide range of minimum effective opioid dose between individuals due genetic polymorphism in liver enzymes that mediate opioid metabolism.

7. Some patients receive adequate pain relief from non-opioid therapies (e.g. nonsteroidal anti-inflammatory drugs – NSAIDs -- anti-seizure medications, or anti-depressants). NSAIDs are not risk-free, particularly at high doses[71], and anti-seizure medications are used off-label primarily in neuropathic pain. The record of outcomes for "opioid sparing" on acute pain is decidedly mixed. Similarly, "fail first" treatment policies may have the disadvantage of delaying effective treatments and increasing probability of patient transition from acute to chronic pain conditions.

8. There is little validated medical evidence for what is called "opioid-induced hyperalgesia" (increasing sensitivity to pain over time due to opioid exposure, requiring increasing doses of opioids for effective pain control)[72,73]. There are no documented diagnostic protocols for this supposed medical entity, and there is no generally accepted protocol for treatment, other than tapering down present medications and titrating up others. Given these observations, when drug tolerance or increased pain are reported by patients, development of hyperalgesia or opioid use disorder should not be a default assumption.

9. Opioid medications are clinically indicated and indispensable for a wide range of pain conditions. But they are not the default therapy of choice for all patients; nor are they a fire-and-forget solution for pain. Safe use of opioids requires an on-going and candid in-person relationship between patient, clinician, and resident caregivers. Education of the patient and their caregivers in opioid safety and secure storage is an essential element in safe prescribing and avoidance of drug diversion.

10. Patient health and welfare may be compromised by depression or anxiety; clinicians should monitor for and treat both conditions aggressively.

11. Physiologic dependence is an expected and manageable outcome of prolonged patient exposure to opioid analgesics. Given that the alternative may be a life of disablement and agony, dependence for control of pain is properly viewed as an acceptable outcome in chronic patients.

12. Non-pharmaceutical / Non-invasive treatment modalities help some patients some of the time, when employed as adjuncts to a program of pharmaceutical therapy. However, measures such as Rational Cognitive Therapy, massage, and psychological counseling provide only temporary and marginal pain reduction; they are not "preferable" and cannot replace opioids. It remains to be demonstrated in clinical trials whether this class of treatments can contribute to pain control at lower opioid dose levels.

13. Given major potential negative consequences to the patient, no clinician who is not recently trained or Board Certified in addiction medicine should assign a diagnostic code of "addiction" or "opioid dependency" to a patient's record. To do so may place the clinician among "the blind leading the blind" and the patient in the large group of US citizens who have been deserted by their doctors.

## Conclusions

This critical review has examined the state of current knowledge concerning diagnosis and treatment of chronic pain, versus diagnosis of

opioid dependence or addiction. Key findings are as follows:

1. Despite repeated CDC assertions to the contrary, it is now clear that there is no statistically significant cause-and-effect relationship between clinical treatment of pain versus hospitalizations for opioid toxicity or mortalities in which narcotic overdose is a factor. Prescribed opioid pain relievers are only one of multiple factors that have contributed to the widely hyped "US opioid crisis". Prescriptions have never been the dominant factor in US mortality statistics, even during the pill mill era. In 2023, opioid overdose related mortality is dominated by illegally imported fentanyl.

2. There is a developing consensus among clinicians and clinical researchers that iatrogenic addiction is rare and unpredictable in individuals. However, several factors in medical history reasonably prompt clinician concern during initial or subsequent patient workups. A history of mental health issues, previous diagnoses of substance use disorder or clinical depression should prompt clinicians to monitor some patients more closely or to consult a specialist in addiction medicine to determine whether additional support may be warranted. The only treatment-specific risk factor that rises above noise level in bad medical outcomes is patient exposure to multiple sedating medications.

3. When post-surgical patients are prescribed opioids for pain, the primary factor associated with extended prescribing thereafter is the type of surgery and its failure statistics, not the dose or type of opioid employed. At least one large retrospective cohort study estimates incidence of later opioid dependence abuse or overdose in medically managed patients on the order of 0.6% for a period of up to one year. The prevailing confusion of opioid dependence with opioid abuse suggests that incidence of actual iatrogenic addiction is likely much less than 0.6% -- in a range where inadequate training of clinicians calls the diagnosis itself into question.

4. Among patients who are otherwise stable and benefitting from opioid analgesic therapy, involuntary tapering to meet an arbitrary MMED threshold is never clinically or ethically appropriate. Such tapering is associated with elevated risk of medical crisis or collapse, and may drive patients into dangerous street markets to obtain relief from their pain. Case reports indicate that substantial numbers of patients may benefit from long-term prescription opioid analgesics even at high doses, without unacceptable side effects[74,75]. Selection of dose levels must reflect individual tailoring of therapy to the patient and their response to medication.

5. Multiple guidelines on prescription of opioids are available from sources other than US CDC and general principles are well known. Adherence to these guidelines and thorough documentation of patient therapy plans and response to therapy offers enhanced medical safety to the patient, and legal security to the clinician.

Clinicians treating chronic pain should refrain from assigning diagnostic labels of opioid dependency or addiction in patient electronic health records. Many clinicians are inadequately trained to assign such labels or to manage ongoing addiction therapy. In many cases, distinctions applied by sources

such as DSM-5 or the International Classification of Diseases (ICD) do not substantially contribute to either pain management or effective treatment of addiction.

## Conflict of Interest Statement:

The author has no conflicts of interest to declare.

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## About the Author

Richard A Lawhern, PhD, has 26 years' experience as healthcare writer and subject matter expert on public health policy for treatment of pain, and as a moderator and research analyst in social media patient support groups. He has authored or co-authored 200+ published papers, articles and interviews in this field, in a mixture of peer reviewed medical journals and mass media.

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