First Do No Harm

The Indiana Healthcare Providers Guide to the Safe, Effective Management of Chronic Non-Terminal Pain

Version 1.0

Foreword

With more people dying from drug overdoses – driven primarily by prescription narcotics—than traffic crashes, it is vitally important that we do what is necessary to prevent this abuse from taking place. It is estimated that one person dies of a prescription drug overdose every 25 minutes in our country. The considerable public health and safety consequences of prescription drug abuse underscore the need for action. That is why I established Indiana's first and only statewide Prescription Drug Abuse Prevention Task Force to identify the best strategies and tools to reduce the diversion and abuse of prescription medications and improve public health and safety in our Hoosier communities.

Our Prescription Drug Abuse Task Force brings together federal, state and local law enforcement officials, health officials, pharmacists, lawmakers and social services agencies. Members formed committees focused on education, treatment and recovery, prescription drug monitoring, prescription disposal and enforcement. The task force is taking a comprehensive approach to make recommendations for new rules, regulations and state statutes.

One of the primary causes for the increase in prescription drug abuse is due to the overprescribing of opioid painkillers. As a result, there is a heightened risk of patient addiction and diversion, making it critical that physicians be diligent about prescribing opioids in a safe and responsible manner. The task force has developed this toolkit as a protocol for primary care physicians and pain physicians in assessing pain. This toolkit will serve to assist physicians treating pain patients in getting a clear diagnosis to assess the pain and understand clearly what the problem is before prescribing pain medication.

As your Attorney General, I am attacking this epidemic on several fronts. The medical licensing section of my office is working on several cases involving physicians alleged to have overprescribed and are seeking appropriate disciplinary actions before the state's Medical Licensing Board. We investigate complaints and aggressively pursue any medical providers and pharmacists who divert prescription drugs. My office has also worked with federal, state, and local law

Greg Zoeller

Greg Zoeller was elected Indiana's 42nd Attorney General on Nov. 4, 2008 and is serving his second term in office. As an advocate for prevention, Zoeller has made education a cornerstone of his administration, establishing an outreach services section dedicated to meeting and educating Hoosiers about scams, abuse and privacy. In September 2012, Zoeller established the Indiana Attorney General's Prescription Drug Abuse Task Force. In creating the Task Force it was Zoeller's mission to significantly reduce the abuse of controlled prescription drugs and to decrease the number of deaths associated with these drugs in Indiana.

enforcement on promoting drug take-back sites where the public can safely dispose of unneeded medications so they will not be diverted.

These are solid steps, but it will require more awareness and responsible prescribing by healthcare providers to slow this escalating problem. Physicians can do their part by following the recommendations outlined in this toolkit. It is our hope that with your help, we may reduce abuse and diversion and also begin to recognize the signs of possible prescription drug abuse in patients, so that dependency and addiction can be averted.

Greg Zoeller
Indiana Attorney General

About the Indiana Prescription Drug Abuse Task Force

Established in 2012, the Indiana Prescription Drug Abuse Task Force works to significantly reduce the misuse and abuse of controlled prescription drugs, thereby decreasing the number of addictions and deaths associated with these drugs in the state of Indiana. The task force is made up of more than 80 people, including legislators, law enforcement officials, healthcare providers, educators and representatives from state and local agencies.

Introduction

The Problem

In 2011, at least 718 Hoosiers died from unintentional drug poisoning, the majority of which involved opioids. In fact, between 1999 and 2009, Indiana witnessed more than a 500% increase in the rate of unintentional poisoning deaths, and that number continues to increase. Like the U.S., Indiana loses more citizens to prescription opioid overdoses annually than to cocaine and heroin combined. The Centers for Disease Control and Prevention estimates that for every person who died due to opioid overdose in 2010, there were 15 abuse treatment admissions, 26 emergency department visits, 115 people who abuse or are dependent on opioids, and 733 non-medical opioid users. Data from the 2011 and 2012 National Survey on Drug Use and Health showed that while 20% of the time these drugs were prescribed to the user, more than 75% of the time they were prescribed to someone else, like a friend or family member. In 2011, the Indiana Youth Risk Behavior Survey found that 21% of high school students surveyed had taken a controlled substance without a prescription. The striking increase in opioid overdose deaths in the U.S. since 1999 parallels the 400% increase in the number of prescriptions for these drugs written during that time, without a commensurate reduction in pain or improvement in pain satisfaction scores.

Indiana Prescription Drug Abuse Task Force

The Indiana Prescription Drug Abuse Task Force was established in September 2012 to help fight the growing prescription drug abuse epidemic. Task force members include state legislators, law enforcement, physicians, nurses, health officials, pharmacists, mental health providers, education professionals and representatives of state and local agencies who serve on five committees: Education, Enforcement, INSPECT, Take-Back, and Treatment & Recovery. Although the committees often have overlapping responsibilities, a brief description of the individual committee charges and accomplishments since inception of the task force is included here:

> The **Education** committee has been tasked with provider and public education and awareness around the issues of

Joan Duwve, MD MPH

Joan Duwve, MD, MPH, is honored to serve as the Chief Medical Officer at the Indiana State Department of HealthPrior to joining ISDH in 2008, Dr. Duwve spent 11 years in private practice. She received her bachelor's degree in International Studies from Ohio State University, a Masters of Public Health degree from the University of Michigan and a medical degree from The Johns Hopkins School of Medicine.

controlled substance prescribing, appropriate use, abuse, diversion and overdose. Accomplishments to date include public awareness campaigns, launch of the Bitterpill.IN.gov website, and this toolkit for providers who treat patients with chronic, non-terminal pain to help them comply with the rules developed by the Indiana Medical Licensing Board for appropriate treatment of these patients (Medical Licensing Board Emergency Rules: Page 91 of this document, Effective: December 15, 2013).

The **Enforcement** committee is responsible for expanding the working knowledge of law enforcement and working with the Office of the Attorney General to develop effective legislation to prevent the establishment of "pill mills" in Indiana (IC 35-48-3-1.5). This committee has worked with the Indiana General Assembly to enact requirements for licensure for owners of pain clinics in Indiana. Medical providers licensed by the state of Indiana have already met this requirement. Pain clinic owners who are not licensed medical providers in Indiana must now become licensed as Pain Clinic Owners. They have also sponsored educational seminars for law enforcement throughout the state.

The **INSPECT** (Indiana Scheduled Prescription Electronic Collection & Tracking Program) committee was challenged with ensuring sustainability of INSPECT and improving provider access to Indiana's prescription drug monitoring program. Their accomplishments include legislation dedicating 100% of Controlled Substance Registration funding to provide ongoing support for INSPECT and pilot projects to test a model integrating INSPECT seamlessly into electronic medical records with tools for enhanced physician decision making support.

The **Take-Back** committee was responsible for exploring opportunities for patients to dispose of unused controlled substances in a convenient, safe and environmentally-friendly way. Reducing the quantities of controlled substances stored unsecured in medicine cabinets throughout Indiana will prevent them from being diverted by family members, friends, or others with access to homes (Rule 856 IAC 7).

The **Treatment & Recovery** committee is responsible for exploring issues around access to treatment for those with existing dependence or addiction to controlled substances, including identifying areas with a shortage of mental health and addiction service providers, ensuring reimbursement for addiction and recovery screening and treatment services, exploring opportunities for prescribing Naloxone to patients at risk of overdose to prevent death, and developing tools to better understand the impact of prescription drug abuse on newborn infants and families in Indiana.

The Provider Toolkit

I am pleased to introduce *First Do No Harm: The Indiana Healthcare Providers Guide to the Safe, Effective Management of Chronic Non-Terminal Pain* developed by the task force's Education Committee under the leadership of Dr. Deborah McMahan. This provider toolkit, based on expert opinion and recognized standards of care, was developed over many months with the input of healthcare providers representing multiple specialties and all corners of the state. *First*

Do No Harm provides options for the safe and responsible treatment of chronic pain, including prescriptions for opioids when indicated, with the ultimate goals of patient safety and functional improvement. It was developed as an interactive compendium to the new Medical Licensing Board rule addressing Opioid Prescribing for Chronic, Non-terminal Pain to give healthcare providers tools they can use to comply with the rule.

We welcome your helpful comments and feedback on this document as we work to change the paradigm for pain management in Indiana from one that relies heavily on opioids to a comprehensive assessment and treatment plan with a focus on patient safety and functional improvement.

Joan Duwve, MD, MPH
Chief Medical Officer
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Acknowledgements

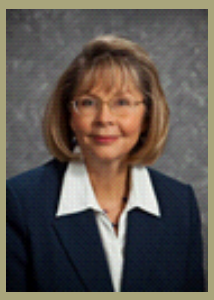
It was an honor to be asked to be the chair of the Education Committee for the Indiana Prescription Drug Abuse Task Force. This is an informed and motivated group of people who have a goal of raising awareness of the dangers of prescription drug abuse and misuse through the education of parents, youth, patients and healthcare providers. Our first initiative was to develop an educational toolkit, *First Do No Harm*, for healthcare providers.

To create the most relevant and robust set of recommendations, we expanded our group of contributors. The working group includes a diverse team of providers from both private practice and academic settings, both specialty and primary care. Included are physicians, nurse practitioners, nurses, laboratory experts, public health and pharmacy professionals located throughout the state. This dedicated group of clinicians and academicians reviewed existing guidelines and recommendations, best practices and current literature to identify ten key recommendations that will assist clinicians in assessing, risk-stratifying, prescribing and monitoring chronic pain patients on long-term opioid therapy.

Resources to facilitate implementation of the recommendations were identified and assembled into a toolkit that will assist our busy providers in putting into operation these vital recommendations. We believe that, in combination with a strong, community message on the safe use of opioids, our toolkit will help reduce the significant number of adverse outcomes associated with long-term opioid use.

Deborah A. McMahan, MD
Chair of Education Committee

Deborah McMahan, MD



Dr. Deborah McMahan has been the Health Commissioner for Allen County since 2000. Prior to becomeing Health Officer, she spent a year with the Roudenbush V.A. Medical Center in in Indianapolis and three years as an Internist with the Medical Group of Fort Wayne. She earned her B.S. from Purdue University in 1986 and her medical degree from Indiana University School of Medicine in 1990.

The Office of the Indiana Attorney General and the Indiana Prescription Drug Abuse Task Force would like to acknowledge the following individuals who contributed their time, talent and experience to this toolkit. Their contributions were invaluable.

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Allen County Health Commissioner Dr. Deborah McMahan joins Indiana Attorney General Greg Zoeller and Allen County Sheriff Ken Fries at a press conference in Fort Wayne to promote the task force's work.

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Members of the Indiana Prescription Drug Abuse Task Force; From left: Philip Zahm; Dr. Deborah McMahan; Attorney General Greg Zoeller; Dr. Greg Eigner; Tracy L. Brooks; and Dr. Rudy Kachmann.

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A Story of Prescription Drug Addiction

Please understand my background is picture perfect in many ways. My family is amazing and would be described as "highly successful." They are all college-educated, happy family members with stable careers and no history or evidence of addictions or substance abuse of any kind. This is true even of alcohol; no one had any history of abuse. I too was on this same path. My honors in school showed great promise.

My grandfather is a well-respected man, a State Senator. Like many, I look to him for advice. After a work-related injury led me to need serious medical direction, he sought to find me a highly-recommended neurosurgeon. It was comforting to be referred to a doctor who was considered among the top in his field.

Because of his reputation, I did not feel a need to validate his recommendations. The pain was troublesome for me. He prescribed a 5mg Percocet®. It was helpful. After some time, it stopped being effective. After a visit to the physician, he increased the dosage. Because of lack of exposure to addictions, it did not cross my mind at first what was transpiring. I was truly unaware of risk factors for prescription drugs. I, like many, felt that addicts were formed by their environment and I was sort of "above" that risk factor because I had a great upbringing.

As my concern grew, I spoke with my family who encouraged me to talk with this doctor. It was the first thing out of my mouth when speaking with the nurse. I told the nurse I felt like I could not function without them and found great anxiety when not on them. She met with the doctor, and then we discussed it. The physician then prescribed me Xanax®. I was hooked.

I now knew addiction. I wanted more Percocet. He then refused and stopped treating me. My life became a spiral downward for a long time. I sought less legitimate prescription-writing environments, then illegal means of prescription drugs, then other opioid drugs such as heroin. I lost ten years of my life and relationships to this dark corner. I also came to pay a serious price legally.

My life is on the upward spiral now. However, I now dedicate it mainly to prevention of these risks to others. I often wonder how a neurosurgeon with so much success and training could have missed the signs of brain addiction. Please know that patients of all backgrounds can become addicted. Warn them and understand they need to be monitored. I am lucky enough to be regaining my life and helping others now. Not everyone has this luxury.

—Alec S.
Hoosier resident

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Section 1: Summary Materials for Office Management of Chronic Non-Terminal Pain: A Ten-Step Approach

Accidental drug overdose is currently the leading cause of injury-related death in the United States for people between the ages of 35-54.[1]

Overview

Chronic pain and its attendant opioid use has become an enormous burden to patients, medical institutions and our society. There are over 50 million estimated chronic pain patients in the United States. Medical expense data places the cost of chronic pain, including direct and indirect costs, at well over $100 billion per year. As many as 15-20% of primary care visits result in a prescription being given for opioids. However, despite the increased use of pain interventions, including opioids, many patients are dissatisfied and report inadequate pain control. Therefore, this aggressive use of resources has occurred without commensurate clinical benefit. A robust increase in pain expenditures from 1997 to 2005 did not translate into improvements in self-assessed health status and pain.[2]

As caregivers, we grow increasingly frustrated and unhappy in our efforts to offer meaningful and acceptable outcomes to patients in pain. Understanding and educating patients is pivotal in transitioning from acute care (pain relief that is primarily pill-based) to comprehensive meaningful treatment that improves function and productivity. Persistent pain, like all chronic illnesses, is managed

In this Section

optimally with the bio-psychosocial model and not with the opio-centric practices of the past. Data from a large population-based study suggests that those on chronic high-dose opioids may fare worse over time than those on lower doses or none at all. Quality of life measures for patients in the study using high-dose opioids were lower than those on a low dose regimen, and they were four times less likely to "recover" significantly during the five years of the study.[3]

Between 1997 and 2010, opioid use increased dramatically. Concomitantly, opioid-related overdoses, substance abuse and prescription costs to society have escalated to unacceptable levels. Leonard J. Paulozzi, a Medical Epidemiologist at the Center for Disease Control and Prevention (CDC), during congressional testimony reported that "the number of deaths in the narcotics category that involved prescription opioid analgesics increased from 2,900 in 1999 to at least 7,500 in 2004, an increase of 160% in just five years." In addition to nearly 16,000 prescription opioid-related deaths in 2010, the rise in opioid use also fueled a substantial increase in substance use disorders. Approximately nine people are admitted for prescription opioid abuse treatment for every one opioid prescription-related death.[4]

Mental illness and opioid-related morbidity and mortality are intimately coupled. A 2009 national survey found that of the 45 million chronic pain patients with mental illness, 8.9 million (or almost 20%) met criteria for substance abuse or dependency. This national data reflects Indiana's experience. We have an obligation to combat this iatrogenic opioid epidemic. Of those who died of an overdose during a 12-month period in West Virginia, researchers found: (1) greater than 90% had substance abuse indicators; (2) greater than 90% had ingested opioids; (3) 79% had ingested multiple substances (often including benzodiazepines); and (4) 78% were known to have a history of substance abuse.[5]

An analysis on 2006 data related to the cost of nonmedical use of prescription opioids placed the total at $53.4 billion.[6] The CDC's estimate on those same costs in 2009 was over $70 billion. Lost productivity was the largest single contributing factor, contributing to 79% of this cost. Clearly, suboptimal risk stratification and monitoring of patients prior to opioid therapy, combined with current practices of prescription writing, are creating enormous emotional and financial burdens.

First Do No Harm: The Indiana Healthcare Providers Guide to the Safe, Effective Management of Non-Terminal Pain Recommendations echoes the content and concern emphasized with the universal precautions proposed by Gurlay and Heit's 2005 Pain Medicine article and the 2009 American Pain Society opioid guidelines. The *First Do No Harm* guidelines and accompanying toolkit inform and support the practitioner, while prioritizing patient safety. While the method and documentation suggested will possibly require some additional time to implement, the upfront time investment will reduce confusion, frustration, liability, morbidity and mortality, while improving patient outcomes. This comprehensive set of practices will allow healthcare providers to provide a consistent, structured and patient-centered approach to all patients being treated for chronic pain.

Recommendations

1. Do your own evaluation. Perform a thorough history and targeted physical exam, together with appropriate tests, as indicated. Obtain and review records from previous caregivers to supplement

your understanding of the patient's chronic pain problem, including past treatments. Ask your patient to complete a Brief Pain Inventory (BPI) survey or other objective pain assessment tool to document and better understand their specific pain concerns. After completing your initial evaluation, attempt to establish a working diagnosis and tailor a treatment plan to functional goals that your patient identifies with you, reviewing them from time to time. **4 Required by Section 4 of Emergency Medical Rules**

2. Risk Stratification for all. Assess both the mental health status and risk for substance abuse in each patient with a diagnosis of chronic pain. Mental health metrics such as PHQ-2 or PHQ-9 (for depression) and GAD-7 (for anxiety) are useful screening tools. Ask patients about any past or current history of substance abuse (alcohol, prescription medications or illicit drugs) prior to initiating treatment for chronic pain. A risk assessment survey (e.g. Opioid Risk Tool, SOAPP or COMM) should be completed at intake for every patient seeking treatment for chronic pain. Since risk levels may vary over time, repeat these assessments accordingly at follow-up visits. The use of chronic opioids in "high risk" patients is strongly discouraged. **4 Required by Section 4(a)(3 & 4) of Emergency Medical Rules**

3. Set functional goals with your patients that include achievable targets for pain management. In general, it is unrealistic for patients to expect complete resolution of their chronic pain with any specific treatment or combination of therapies. Nevertheless, it is important to have a conversation with your patient about their treatment plan and set realistic goals for improvement. Work together towards improving pain control and achieving specific functional goals, as both are key outcomes. Functional goals might include increasing physical activity level, resuming a job/hobby or improving the quality of sleep. A multifaceted plan, focusing on function and utilizing appropriate medications together with non-pharmacologic treatment modalities will usually provide the optimal balance of risk and benefit for most patients. It is recommended that you review functional assessment tools periodically with your patients at follow-up visits. **5 Required by Section 5 of Emergency Medical Rules**

4. Utilize evidence-based treatments, including non-opioid options initially, where possible. Refer to the flowchart entitled *"An Approach to Managing Chronic Non-Terminal Pain"* (Appendix A) for details regarding a broad range of possible treatment options for your patients, based on their specific pain diagnosis. Give strong consideration to non-pharmacologic therapies, in addition to the various medications available. Also utilize available first-line pharmacologic options before prescribing opioids. When you believe that an opioid trial is warranted, use the lowest dose of medication required to reduce pain and improve functioning. This will help to reduce the risk of overuse and also minimize the adverse effects that typically arise with this class of medication. Also explain from the outset that opiates will be discontinued if pain does not improve or if functional goals are not met. Do not begin a treatment that you are not prepared to stop.

"Our story is a nightmare. I have lost a brother to overdose and now have an addicted son. Pain pill addiction tears a family apart. Doctors understand that pain medications can be addictive. They understand mixing pills can be fatal. It is important they understand that other people do not always understand. "

– Joyce G.

There is a lack of evidence-based support for the use of opioid therapy in general, and specifically for several chronic conditions including: chronic headache, low back pain and pelvic pain, as well as fibromyalgia and functional bowel disorders such as Irritable Bowel Syndrome. Use non-opioid pharmacologic agents and other available treatment modalities for pain management in these situations. Also, avoid prescribing ingredients of known "drug abuse combinations" such as alprazolam (Xanax®) and carisoprodol (Soma®, now a Schedule IV controlled substance) together with opioids, as safer alternatives exist.

Avoid Poly–pharmacy combinations that contribute to morbidity, mortality, and diversion. Certain medications combos are known to depress respiration and lead to acute death. Care must be exercised when prescribing opiates and sedatives in cases of COPD, asthma, sleep apnea, or CHF. Additionally, signature combos have high street value and are also contributory to death from respiratory depression and/or heart failure. These would include:

- The "Holy Trinity": benzodiazepine (Xanax®), opiate (hydrocodone), muscle relaxer (SOMA)
- Methadone plus any sedative/hypnotic (eg Xanax®)
- Amphetamine (eg Adderall) plus opiate (any narcotic). This is known as a *prescriptive speedball.*
- Multiple opiates (easy to exceed risky MED levels)
- Opiates plus *enhancer* medications (antidepressants, neuropathic medications, cannabis, alcohol, testosterone/anabolic steroid preparations.)

In summary, be aware of respiratory and cardiac co-morbidities in the presence of dangerous drug combinations when defining the opiate portion of a drug treatment plan. Be very aware of the dangerous consequence of mixing uppers and downers. 4 **See Section 4(b) of Emergency Medical Rules**

5. Discuss the potential risks and benefits of opioid treatment for chronic pain, as well as expectations related to prescription requests and proper medication use. Provide a simple and clear explanation to help patients understand the key elements of their treatment plan. Together, review and sign a "Treatment Agreement," which includes the details of this discussion for all patients that are prescribed controlled substances (opioids, benzodiazepines, stimulants) on an ongoing basis. 5 **See Section 5 of Emergency Medical Rules**

6. When prescribing opioid medications for patients, periodic scheduled visits are required. Evaluate patient progress and compliance with their treatment plan regularly and set clear expectations along the way (e.g. attending physical therapy, counseling or other treatment options). Follow-up visits for patients with a stable treatment plan and receiving regular controlled substance prescriptions should probably occur at least once every 3-4 months. For patients working with you to achieve optimal management, more frequent visits would be appropriate. "High-risk" patients and patients receiving high doses of opioids require closer monitoring. 6 **Required by Section 6 (a) of Emergency Medical Rules**

There is no obligation to prescribe controlled substances on an initial visit for new patients unless you have all of the information that you require to prescribe safely. This includes obtaining records of past treatments from primary care providers, imaging centers, pain clinics and other specialists. Review your patient's past medical history (including an INSPECT report), and perform your own medical/psychosocial assessment. Then determine if your patient is an appropriate candidate for an opioid trial, to supplement their other treatments. 5 **See Section 5 (4)(D) of Emergency Medical Rules**

7. Remember the 5 A's when managing your chronic pain patients with opioids: Assess ***Affect*** (and screen for mental illness in general), ask about ***Activities of Daily Living*** (ADLs), provide ***Analgesia*** to assist patients in meeting their functional goals, minimize ***Adverse effects*** of treatment, and monitor for ***Aberrant*** drug use behaviors.

8. Use INSPECT. Indiana's prescription drug monitoring program (PDMP) helps us all. Use INSPECT regularly for both new and established patients. This system tracks all controlled substance prescriptions filled by patients state-wide. Links have been established with neighboring states as well. INSPECT is easy to use and there is no cost, so please register with the state at www.in.gov/inspect. You will derive valuable information that impacts decision-making at the point of care. INSPECT reports should be run at least once every 3-6 months or more often as desired or appropriate. Use of this essential resource will help to protect you, your practice, and most importantly, your patients from unsafe patterns of medication use. 7 11 **Required by Section 7 & 11(a) of Emergency Medical Rules**

9. Urine drug monitoring (UDM) protects you and your patients. Like PDMPs, urine drug monitoring has evolved to become a standard of care when prescribing opioids for chronic pain. This is a useful tool that complements your other risk assessments; it will help you to identify patients using illicit substances and assist in monitoring patient adherence to their prescribed medications. UDM should be performed at the initiation of an opioid trial and also periodically thereafter. The actual frequency may vary depending on past UDM results and the level of risk for a particular patient, if known. Higher risk patients and patients receiving high doses of opioids (including those receiving other controlled substances) should have UDM performed more frequently. It is important that you fully understand the specifications and limitations of the particular drug tests that are available to you. Ensure that confirmatory testing (by mass spectrometry technique) is performed if screening (immunoassay) results are inconsistent or not acknowledged to be accurate by your patient. Discussion with patients regarding the need for UDM should be appropriately framed around their

safety. When UDM suggests "inconsistent" medication use patterns or the presence of illicit substances, review these findings with your patient to determine an appropriate plan going forward. This may include discontinuing medication(s). Document your plan and the details of your discussion in the patient's record. Saliva testing is an acceptable alternative if urine testing is not available. 8 11 **Required by Section 8 & 11(b) of Emergency Medical Rules**

10. Action is required as a patient's Morphine Equivalent Dose (MED) escalates above 30 mg per day. Take the time to see your patient for a complete review if they continue to report intolerable pain or if they demonstrate lack of functional improvement over time. Based on your assessment, consider these possible actions:

a) Institute a slow, compassionate therapeutic wean of the opioid (or rotate to another opioid, if appropriate).

b) Refer patients to an addiction specialist for evaluation when a substance use disorder is suspected.

c) Enhance mental health support and physical well-being with a modified treatment plan that you monitor, in collaboration with a mental health professional, when indicated.

d) Refer to a pain management specialist for consultation and/or ongoing care.

Taper or discontinue opioids when your patient's pain is poorly controlled on appropriate doses of medication OR if there is no functional improvement with opioid treatment. The increased risk for adverse outcomes (including death) are more frequently observed when the MED of medication prescribed is > 50-60 mg/day. Patient mortality risk is more pronounced for patients treated with opioids that have any of the following active co-morbid issues: benzodiazepine use, illicit substance use/abuse, alcohol overuse, untreated mental health issues (e.g. depression) or chronic respiratory problems such as obstructive sleep apnea or COPD. 9 **See Section 9 of Emergency Medical Rules**

Equianalgesic Comparisons

Commonly used opioids that correspond to a Morphine Equivalent Dose (MED) of 60 mg include:

Hydrocodone (short-acting): 50 mg daily (e.g. Vicodin® 10/300 mg)
one tablet q4-6h = 5 tabs per day

Oxycodone (short-acting): 40 mg daily (e.g. Percocet® 10/325 mg)
one tablet q6h = 4 tabs per day

Oxycodone (long-acting): 40 mg daily (e.g. Oxycontin® 20 mg) one tablet twice daily

Fentanyl (transdermal patch): 25 mcg daily (e.g. Duragesic® patch)
25 mcg applied once every 3 days)

	Equianalgesic to **50-100** mg Oral Morphine (mg)/day[a]
Fentanyl Patch[b]	25 mcg/hour
Hydromorphone (Dilaudid®)	12.5-25 mg
Oxycodone/acetaminophen	35-70 mg
Hydrocodone/acetaminophen[c]	45-90 mg

Keep in mind:

a.) Equianalgesic tables should only serve as a general guideline to estimate equivalent opioid doses. These tables do not address critical individual factors (gender differences, organ dysfunction, bidirectional differences in equivalence with certain opioids, drug interactions, and large inter/intra-individual differences in pharmacokinetics and pharmacodynamics that may alter equianalgesia.

b.) When used in chronic pain, transdermal fentanyl patches (dosed in mcg) are roughly equivalent to 50% of the total daily dose of oral morphine in milligrams.

c.) It is difficult to provide calculated equivalences between an opioid and a compounded analgesic that contains an opioid together with an adjuvant analgesic.

Talking Points

- *"During this check-up, I would like you to fill out this brief questionnaire. It will help me to organize your treatment plan."*
- *"A comprehensive evaluation is very important in any chronic disease and evaluating for depression or anxiety is a routine part of our assessment"*
- *"I understand you are experiencing pain. I probably can't make all of your pain disappear so let's talk about some coping strategies."*

If a patient responds that collecting a drug test is a form of spying on them:

- *"It may seem like that to you, but it's a standard part of care for all my patients. Any level of substance use can affect a patient's life and the management of the pain. Is there something we need to talk about?"*

If a patient says you are treating me like a drug addict:

- *"I'm sorry if this gives you the impression that I am judging you. As your doctor, I have a job to identify and resolve any issues that may interfere with your pain treatment, sooner rather than later. The drug screen helps me do that."*

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[1] http://www.drugpolicy.org/drug-overdose
[2] JAMA 2008; 299(6):656-664
[3] Clin J Pain Vol 26 No 9, 2010
[4] CDC MMWR, 60:43, 2011
[5] JAMA. 2008;300(22):2613-2620
[6] Clin J Pain 2011, 27; 194-202

Section 2: Elements of the Initial Exam

One of every 50 prescriptions for addictive prescription painkillers in the United States is filled for so-called "doctor shoppers" who obtain the drugs for recreational use or resale on the street.[1]

Overview

As patients move along the continuum from acute pain to chronic pain, you will need to perform a comprehensive assessment. This is also true when patients present with an existing diagnosis of chronic pain and you are considering initiation or continuation of opioids.

Such an evaluation should be completed before a decision is made as to whether to prescribe an opioid analgesic.

Chronic pain assessment should include a general history and physical. Spending time on taking a good history, including identifying the onset and progression of the problem may help to focus how a problem developed from localized pain to a more generalized or multifocal pain experience for the patient. Of course you will also want to identify the location, quality, intensity, duration, aggravating and relieving factors of the pain. You will also want to determine the effect of the pain on the patient's physical and psychological functioning, especially mood and sleep habits. It is also important to identify comorbid disorders and conditions, especially those that could be negatively impacted by narcotics, such as sleep apnea or heart failure.

Other important information includes the response to previous pain treatments, including complementary and alternative treatments and interventional treatments.

Routine review of systems and social/vocational assessments can be very important in your evaluation. There are a number of templates you can use in your office including some from Partners Against Pain® (see sidebar Page 25).

In this Section

Rule Highlight

"Chronic Pain" is defined the by Medical Licensing Board as a state in which pain persists beyond the usual course of an acute disease or healing of an injury, or that may or may not be associated with an acute or chronic pathologic process that causes continuous or intermittent pain over months or years. Section 2 of Emergency Medical Rules

Assesment Tools

Partners Against Pain Initial Assesment forms:

- Initial Pain Assessment Tool
- Initial Pain Assessment
- Brief Pain Inventory (Short Form)

A good mental health assessment should also be completed and is addressed in more detail in the section on Risk Stratification. Past or current physical, sexual, or emotional abuse may be informative. Be sure to query the patient about sleep habits, exercise habits and other activities of daily living that can influence the perception of pain. Chronic pain may also have had an impact on cognition in terms of memory or ability to concentrate.

There are a number of validated screening tools to use in your office with minimal disruption to your workflow. The most widely used and best-validated instruments in the primary care setting are the Patient Health Questionnaire (PHQ)-9 and its two-item version, the PHQ-2.

The GAD-7, a 7-item anxiety scale, is a useful screening tool for generalized anxiety disorder (GAD).

It is also important to assess a patient for a personal or family history of substance abuse. If the initial assessment reveals a current or past history of substance abuse, the guidelines of the Federation of State Medical Boards recommend, if possible, a consultation with an addiction specialist before opioid therapy is initiated (and follow-up as needed). Patients who have an active substance use disorder should not receive opioid therapy until they are established in a treatment/recovery program or alternatives are established such as co-management with an addiction professional.[2]

To identify addictions specialists in your area, visit the Substance Abuse Treatment Facility Locator.

For the physical exam you will want to focus on the musculoskeletal and neurological systems. Muscle strength, sensation, and muscle stretch reflexes are all important elements of the exam and findings of allodynia and hyperalgesia are useful in any pain syndrome.[3] Of course joint exams should center on signs of effusion, instability, and ligament or cartilage pathology. Posture and gait can also be significant clues to pathology. Unfortunately, you will also want to look for signs of substance abuse (e.g., track marks, hepatomegaly, residua of skin infections, nasal and oropharyngeal pathology).

There is no one diagnostic test for chronic pain. But with any diagnostic tests that you order, it is important to remember that finding pathology on diagnostic tests does not necessarily prove that the identified pathology is causing the patient's pain.

As part of your routine data collection you will want to obtain data from state electronic prescription monitoring programs– INSPECT if

the patient has lived in Indiana. You will also want to check a baseline urine drug screening test to ensure no other illicit drugs are being used or controlled substances that might be prescribed by another provider. Prior medical records are important for assessing for other comorbid conditions such as hepatic, renal, cardiovascular or metabolic disorders that may influence opioid risks.

Finally, collateral information from family members and other healthcare providers is an important part of the assessment.[4] Of course you need patient consent to proceed with these discussions. It is a potential red flag if the patient declines to give consent, and you will want to keep this in mind when developing a treatment plan for this patient. From a legal perspective, a clinician who prescribes narcotics to a patient who refuses to permit access to outside information could be considered to be ignoring evidence of addiction or substance misuse and, therefore, to be trafficking.

The Institute for Clinical Systems Improvement (ICSI) has a very thoughtful assessment and management algorithm that provides clear guidance on determining the biological mechanism of pain including neuropathic, muscle, inflammatory and mechanical, as well as the key elements of management strategies. Appendix B and Appendix C provide a snapshot of the assessment and management algorithms, but for more information, look through the entire Health Care Guideline: Assessment and Management of Chronic Pain, from the Institute for Clinical Systems Improvement.

Finally, the Opioid Manager is another great tool to capture your initial assessment and treatment strategies for your patient and can be completed and placed into the medical record for review at follow-up appointments.

Recommendations

1. A thorough history and physical should be completed before a decision is made as to whether to prescribe an opioid analgesic. 4 **Required by Section 4(a)(1) of Emergency Medical Rules**
2. All patients should have an adequate pain assessment recorded in the medical record that includes documentation of pain location, intensity, quality, onset/duration/variations/rhythms, and manner of expressing pain, pain relief, what makes it worse, effects of pain, and a pain plan. 4 **Required by Section 4(a)(3) of Emergency Medical Rules**
3. All patients should be screened for depression and other mental health disorders, as well as substance use disorder as part of risk evaluation. 4 **Required by Section 4(a)(4) of Emergency Medical Rules**
4. The medical record shall document opioid risk factors, contraindicated medical conditions, history of drug abuse or addiction, and current or past psychiatric illnesses.
5. A list of co-existent diseases should also be included in the medical record.
6. The exam and evaluation shall be in support of the pain diagnosis.
7. The diagnosis shall be for a recognized medical condition that qualifies for treatment with controlled substances.

Talking Points

- *"Mr. Smith, I understand that your former physician prescribed daily Vicodin® for you, but as a healthcare professional I have an obligation to perform my own assessment after which you and I will work together to identify a safe treatment plan that will serve to improve the quality of your life."*

Resources

ICSI Health Care Guideline: Assessment and Management of Chronic Pain

Partners Against Pain®; Pain Management Tools

PainEDU.org Clinician Tools

Advances in Opioid Analgesics: Maximizing Benefit While Minimizing Risk

Managing Chronic Pain in Adults with or in Recovery from Substance Use Disorders

Prescribe Responsibly; Assessing Patients with Pain and Using Evaluation Tools

ACP Internist Extra: Chronic Pain Management, An Appropriate Use of Opioid Analgesics

[1] http://www.medicinenet.com/script/main/art.asp?articlekey=171692
[2] Federation of State Medical Boards, 2013
[3] http://www.guideline.gov/content.aspx?id=36064
[4] http://www.ncbi.nlm.nih.gov/books/NBK92053/

Section 3: Risk Stratification

Nearly 40 percent of older suicide victims see a doctor during the week before killing themselves[1]

Overview

The above statistic is startling and reflects that we are often ineffective at identifying mental illness in the absence of an overt plea for help or the regular use of a screening tool. At least 75% of patients with clinical depression present to their doctors because of physical symptoms, such as pain.[2] Conversely, the prevalence of depression in patients with chronic pain varies depending on the site of care (e.g., community, primary care, pain clinics, sports medicine, and orthopedic clinics). According to a comprehensive literature review by Bair et al, the mean prevalence rates of concomitant major depression in pain patients was 52% in pain clinics; 38% in psychiatric clinics; 56% in orthopedic or rheumatology clinics; 85% in dental clinics addressing chronic facial pain; 13% in gynecologic clinics focusing on chronic pelvic pain; 18% in population-based settings, and 27% in primary care clinics.[3] The increased prevalence of depression in virtually all clinical settings suggests chronic pain can worsen depression symptoms and is a risk factor for suicide in people who are depressed. In a study conducted by Hitchcock et al, 50% of chronic pain patients surveyed reported that they had considered suicide as a result of the hopelessness associated with their pain.[4]

The interface between pain and depression is multifaceted and beyond the scope of this article. However, numerous double-blind, placebo-controlled studies evaluating the impact of anti-depressants on pain indicate a positive impact.[5] Interestingly, the positive impact on pain does not seem to be related to its impact on mood. It would make sense that by screening those patients with chronic pain for depression and anxiety at the onset, narcotics may not be needed, or at least lower doses can be prescribed. There are a number of validated screening tools to use in your office with minimal disruption to your workflow. The most widely used and best-validated instruments in the primary care setting are the PHQ-9 and its two-item

In this Section

Rule Highlight

4 Section 4(a)(4) of Medical Licensing Board's Emergency Rules requires the prescriber to "Assess both the patient's mental health status and risk for substance abuse using available validated screening tools".

"I requested several times not to be given pain medication. When I was sedated my post-op discharge nurse provided my husband a prescription for pain meds. ...Then, the first question my nurse had for me when checking on me was, 'Are you out of pain pills?' If I had taken all they sent me in three days, I could probably have overdosed. I was not in more pain than an OTC pain reliever would have prevented. Nurses and doctors need education that when patients say no, to listen more deeply, patients might have other reasons they don't want pills."

– Jamie N.

version, the PHQ-2.

The GAD-7, a 7-item anxiety scale, is a useful screening tool for generalized anxiety disorder (GAD).

Another issue to consider is risk for addiction. It is estimated that 32% of chronic pain patients may have addictive disorders.[6] However, assessing for potential addiction can be challenging. Formal screening tools that help predict those at risk are available and can be a valuable resource when used as a part of a thorough and comprehensive opioid prescription assessment treatment program. Screening tools alone cannot determine equivocally those patients with substance abuse or addiction problems. Regardless of what screening tool is used, misrepresenting and negative false responses by patients has been found to be as high as 50%. However, without the use of other resource variables, healthcare provider's clinical judgment can underestimate by three times those patients at high risk. The most common factor that is predictive of drug abuse, misuse and aberrant drug-related behavior is a personal or family history of drug or alcohol abuse. These predictive factors warrant close compliance monitoring, and may suggest that treatment choices exclude the use of chronic opiates.

There are an increasing number of tools that can be used to assess risk of addiction. Two that are currently popular include:

- The Screener and Opioid Assessment for Patients with Pain (SOAPP) ® Version 1.0 is a tool for clinicians to help determine how much monitoring a patient on long-term opioid therapy might require.

- The DAST-10 (Drug Abuse Screen Test) was designed to provide a brief instrument for clinical screening and treatment evaluation and can be used with adults and older youth.

Physical factors must also be considered as part of risk stratification. Opiates are generally taken in combination with other sedating medications. Respiratory depression is disproportionately affected when additional medications such as benzodiazepines, antidepressants, muscle relaxants (particularly SOMA) or anti-seizure medications (gabapentin, pregabalin) are used in conjunction with any opiates. The clinical presence of sleep apnea, COPD, or asthma mandates careful evaluation of the choice of chronic opiate therapy. If the patient is a smoker or is oxygen dependent then opiates must be more carefully considered. The use of opiates and other sedating

medications will also affect patients who have diagnoses of CHF or chronic liver disease. Choice of opiate and appropriate doses will have to be selected with care.

Consideration of other medications that a patient is taking is also a key factor in risk stratification. Interactions with amphetamine products can be exceptionally dangerous. Patients who are taking chronic opiates as well as weight loss medications (phentermine), narcolepsy medication (dextroamphetamine) or drugs for attention deficit disorder (Adderall®) may have adverse side effects of the central nervous system resulting in hypertensive crises, seizures and psychosis. This combination of amphetamine plus opiate is sometimes referred to as *prescription speed balling*. It is analogous to the exceptionally lethal combination of cocaine/morphine or heroin, which defines the original formula for speed balling.

Risk stratification is an ongoing process; as it has been said, "The real risk of addiction begins after starting opioids." Aberrant behaviors can be clues to the potential of addiction or to indications that controlled substances are being diverted for recreational uses and abuse. Aberrant behaviors can include early requests for refill, instances of lost medications, frequent requests for more potent (or name brand) medications, and the existence of multiple providers. Patients who are repeatedly non-adherent and patients who participate in serious aberrant behavior (such as cocaine use, non-prescriptive opiate use, opiates from multiple providers, etc.) should be considered for alternative therapies. Chronic opiate therapy may not be an optimal choice for patients who cannot exercise control in the routine management of their lives.

Physicians should be aware of the criteria that define substance abuse disorder. If the use of controlled substances results in maladaptive behavior whereby the individual is unable to fulfill major role obligations (school, home, work, etc.), and if substances continue to be used despite persistent or recurrent social and interpersonal problems, then a different choice needs to be made for treatment of the chronic pain problem.

The key to successful risk stratification is to know what you will do with the information when you find it. Identify mental health counselors and addiction specialist in your area that you feel comfortable working with and that have expertise in chronic pain patients. There are many therapies that can be used today to address both issues without the use of narcotics.

It is also helpful to have a risk stratification process in mind not only when initially evaluating a patient, but also when monitoring patients on long term narcotics over time. Will you simply use the risk stratification determined by your addiction screening tools or will you consider other variables when risk stratifying your patient? Risk stratification will be addressed again in the section on Monitoring. However, it is important to consider these questions when developing your own risk stratification scheme.

In summary, risk stratification must be assessed before the decision to institute or maintain chronic opioid therapy.

Risk evaluation must include specific assessment of:

- Mental illness (particularly depression, anxiety, PTSD and schizophrenia)
- Evidence of addiction (particularly personal or family history of drug or alcohol abuse)
- Evaluation of aberrant behaviors (actions that demonstrate irresponsibility)
- Presence of co-morbid diseases (particularly any type of cardio-pulmonary illness, chronic liver disease, or condition requiring the use of amphetamines)

Recommendations

1. Proper patient selection using benefit-to-risk assessment is crucial.
2. All initial patients should undergo mental health screening with treatment and/or counseling as needed. Consider ongoing mental health screening for those that are demonstrating unusual or suspicious behaviors or who are undergoing major changes in their life. 4 **Required by Section 4(a)(4) of Emergency Medical Rules**
3. All patients while on narcotics should be screened initially and periodically for addiction or addiction potential.
4. Clearly understand the impact of comorbid health conditions and medications when developing a treatment plan.
5. Risk stratify – ideally through a written standard operating procedure for your practice – all patients for whom you prescribe narcotics. 4 **Required by Section 4 of Emergency Medical Rules**

Talking Points

- *"Mr. Smith, I understand you are having a lot of pain. Current science tells us that there is quite a biologic overlap between pain and depression, so I would like to assess your mental health before we start any potential long-term medicines. The good news is that most depression responds very well to treatment."*
- *"I understand you are experiencing pain. I probably can't make all of your pain disappear so let's talk about some coping strategies."*

Resources

PainEDU.org; Course-in-a-Box: Opioid Risk Stratification and Patient Selection in Clinical Practice and PainEDU.org; Course-in-a-Box: Opioid Risk Management: The Screener and Opioid Assessment for Patients with Pain (SOAPP®) in Clinical Practice

Downloadable and print-ready PowerPoint™ presentations that comes complete with speaker notes. These tools are designed to be a resource for clinicians and educators to use in classrooms, grand rounds, conferences, and for in-service education.

Treatment of Nonmalignant Chronic Pain

Rational Use of Opioids for Management of Chronic Nonterminal Pain

[1] http://www.nami.org/Template.cfm?Section=press_release_archive&template=/contentmanagement/contentdisplay.cfm&ContentID=5601&title=Nearly%2040%20Percent%20Of%20Older%20Suicide%20Victims%20See%20Doctor%20During%20Week%20Before%20Killing%20Themselves

[2] http://www.integration.samhsa.gov/about-us/Pain_Management_Webinar_Slides.pdf

[3] Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity: a literature review. Arch Intern Med. 2003 Nov 10;163(20):2433-45.

[4] Hitchcock LS, Ferrell BR, McCaffery M. The experience of chronic nonmalignant pain. J Pain Symptom Manage. 1994 Jul;9(5):312-8.

[5] http://www.medscape.com/viewarticle/565763_3

[6] http://store.samhsa.gov/shin/content/SMA12-4671/SMA12-4671.pdf

Section 4: Setting Functional Goals

Among those experiencing chronic pain, about two-thirds report poor or un-refreshing sleep.[1]

In this Section

Overview

Pain is one of the most common afflictions we see in primary care. Estimates are that 100 million Americans suffer with pain and the vast majority seeks relief through their primary care provider.[2] Most healthcare providers are quite comfortable with having patients describe the character, quality, location and intensity of pain, but may be a bit less comfortable in describing the impact that pain has on the quality of their life and their overall productivity. Pain interferes with many daily activities, and one of the goals is to identify the areas most negatively impacted by pain. Understanding the specifics of how pain impacts patients' functionality is important because the truth is complete pain relief may not be an option. If we begin to look at chronic pain through a biopsychosocial lens and utilize a multidisciplinary approach, we should be able to improve the quality of life for most of our patients. Remember to query patients on the impact of pain on their hobbies and relationships – identifying a goal such a playing golf again or fishing with the grandkids can make the challenge to increase physical fitness more feasible.

One of the most widely used instruments for broadly measuring pain and the impact on everyday life is the Brief Pain Inventory. It captures the characteristics of a patient's pain as well as the impact on psychosocial functioning and ability to work. It was initially used for cancer patients, but studies have also determined that it is a valid instrument in evaluating chronic pain conditions such as low back pain and arthritis.[3]

There are a number of instruments that you and your patient may use to not only establish a baseline but also identify more functional outcomes for which to strive.

- The Brief Pain Inventory
- The Roland Morris Disability Questionnaire is a useful tool for patients with low back pain.
- The Physical Functional Ability Questionnaire (FAQ5) has not been validated, but is believed to be a useful assessment tool.
- The Global Pain Scale

Please keep in mind that chronic pain is not an emergency; therefore allow yourself sufficient time to develop a working relationship and negotiate a comprehensive treatment plan over a series of visits. You may want to adopt a rehabilitative approach that emphasizes restoration of normal movement and function and less emphasis on simple pain relief. Assessing patients for deconditioning is useful as many patients may be surprised how much their pain has also decreased their energy levels to the point of interfering with even the simple activities of daily living. This is a great opportunity to involve physical therapists or other musculoskeletal experts in objectively identifying true physical status and developing an individualized treatment plan to optimize improvement in physical function.

According to the International Association for the Study of Pain, activity goals should be set in three separate domains. The **physical domain** is the exercise program the patient follows and includes the number of exercises to be performed, the duration of exercise, and the level of difficulty. The **functional domain** involves tasks of everyday living such as housework or hobbies. The **social domain** relates to pleasurable social activities (e.g., visiting friends, going to church or the movies, going for a walk). Goals must be personally relevant, interesting, measurable and achievable.[4] Do not hesitate to consult others for serious sleep hygiene issues, physical deconditioning, mental health concerns or stress/relationship management.

You will want to document goals and strategies to achieve these in the patient's record. Provide a copy for your patient to review periodically between visits. The Opioid Manager is a useful tool that captures

In this Section

established goals and other pertinent information for your chronic pain patient.

Recommendations

1. Use a functional assessment screening tool to establish a baseline of your patient's status; then set realistic goals for functional improvement. [4] **Required by Section 4(a)(3) of Emergency Medical Rules**
2. Remember that pain management may be the safest most reasonable goal and that it is always worth reinforcing that a goal of complete resolution of pain is unrealistic.
3. Achievement of other important functional goals is equally important.
4. Require patient participation in all facets of the treatment plan, including generating a list of concrete goals/outcomes they believe they can achieve.
5. Periodically reassess patients with the same instrument to evaluate progress and to adjust your mutually defined treatment goals.
6. Consider chronic pain as a multidisciplinary problem that is best served by various skill sets in addition to your own.

Talking Points

- *"To truly understand your pain, I need to better understand the impact it has had on your sleep, your activities and your daily life so that we can develop a plan together that will improve your quality of life."*
- *"What were you hoping to get done today that your pain prevents you from doing?"*
- *"Chronic pain often interferes with your ability to remain physically active, sustain interpersonal relationships, and be involved in the community. From this list of possible long-range treatment goals, select a few areas that you think are important to improve, and describe what that improvement might look like."*

Resources

PainEDU.org; Course-in-a-Box: Setting Realistic Goals and Expectations for Patients with Chronic Pain
A downloadable and print-ready PowerPoint™ presentation that comes complete with speaker notes. This tool is designed to be a resource for clinicians and educators to use in classrooms, grand rounds, conferences, and for in-service education.

Pain Care Fast Facts: 5-Minute Clinical In-service; Establishing Pain Relief Goals

Treatment of Nonmalignant Chronic Pain

Rational Use of Opioids for Management of Chronic Non-terminal Pain

[1] http://www.sleepfoundation.org/article/ask-the-expert/pain-and-sleep
[2] http://www.uptodate.com/contents/definition-and-pathogenesis-of-chronic-pain
[3] http://www.ncbi.nlm.nih.gov/pubmed/15322437
[4] http://www.iasp pain.org/AM/AMTemplate.cfm?Section=HOME&SECTION=HOME&TEMPLATE=/CM/ContentDisplay.cfm&CONTENTID=7616

Section 5a: Non-Pharmacologic Options for Pain Management

Massage therapy may effectively reduce or relieve chronic back pain for 6 months or more.[1]

In this Section

Rule Highlight

5 Section 5 (1) of Medical Licensing Board Emergency Rules states that "the physician shall, where alternative modalities to opioids for managing pain exist for a patient, discuss them with the patient."

Overview

With more than 100 million people in the United States suffering from chronic pain from one source or another, the 21st century physician must have a variety of options for minimizing both acute and chronic pain. Couple that with the fact that at least 50% of those patients with chronic pain also have depression, and you have a complex medical issue that requires a multifaceted approach.[2] In this day and age, the well-rounded physician can choose to incorporate psychosocial and complementary medicine recommendations into a comprehensive treatment approach.

While you do not have to be equipped to provide the service directly, understanding the benefits of practices such as cognitive behavioral therapy and identifying a few key providers you feel comfortable referring to in your area will broaden the range of services you can recommend for your patients. Many of these interventions have little risk and can increase the sense of self-control as well as increase the quality of life for your patients. In addition, many patients would likely benefit from discussion and incorporation of these strategies, but may be afraid to discuss with their physician.

There have been a number of studies evaluating the effectiveness of various types of adjunctive therapy for the chronic pain patient, although much more work needs to be done. It is beyond the scope of this section to review all of the non-pharmacological options to manage chronic pain.

However, the American Cancer Society and UptoDate® website explains many of these options and can be a resource for you to become familiar with some of the terminology.

Recommendations

The following therapies are recommended:

• **Cognitive Behavioral Therapy (CBT):** focuses on assisting the patient to cope with pain and improve overall functional status. A meta-analysis by Morley et al compared the effectiveness of CBT and concluded that active psychological treatments based on the principle of cognitive behavioral therapy are effective.[3] According to Dr. Joseph Hullett, CBT works because it changes the way people view their pain writing, "CBT can change the thoughts, emotions, and behaviors related to pain, improve coping strategies, and put the discomfort in a better context." CBT can also change the physical response in the brain that makes pain worse. Dr. Hullet suggests this may make the body's natural pain relief response more powerful.[4] On average, a patient requires only 16 sessions to experience improvement/relief.

• **Physical Therapy (PT)** is an important component to establishing the right pace and goals for functional improvement. Physical therapists are healthcare professionals who maintain, restore, and improve movement, activity, and health, enabling individuals of all ages to have optimal functioning and quality of life, while ensuring patient safety and applying evidence to provide efficient and effective care.[5] PT treatments may include passive therapy such as TENS or Ultrasound treatment or active therapy, including exercises or even aerobic therapy.

• **Massage therapy** is the manual manipulation of soft body tissues (muscle, connective tissue, tendons and ligaments) to enhance health and wellbeing. There are different types of massage, including Swedish massage, deep tissue massage and trigger point massage, which focus on myofascial trigger points. Myofascial trigger points are muscle "knots" that are painful when pressed and can cause symptoms elsewhere in the body. A literature review of the overall effectiveness of massage therapy on various Non-Terminalous chronic pain conditions indicated that massage works well on certain types of chronic pain, such as low back pain, but works moderately well for other conditions such as fibromyalgia.[6] You can find a qualified massage therapist in your community via the American Massage Therapy Association website.

• **Mindfulness meditation training** is awareness of present moment experience, such as body and breath sensations. Studies show it can be very helpful in reducing stress associated with chronic pain, as well as preventing depression. Ongoing studies at Brown University are mapping how the sensory cortical alpha rhythms that help regulate how the brain processes and filters sensations, including pain, and memories such as depressive cognitions, respond to mindful mediation.[7]

• Other non-pharmacologic options for chronic pain include:

- Abbreviated Progressive Relaxation technique (APRT)
- Biofeedback
- Chiropractic care, spinal manipulation for chronic low back pain
- Acupuncture

- Weight management
- Hypnosis
- Prayer or visits by clergy, ministers, priests and rabbis
- Pet therapy
- Sleep hygiene
- Guided imagery

Talking Points

- *"I can see that you have a lot of responsibilities and would like to feel better and more productive as soon as possible. To achieve that, I believe we should take advantage of the expertise of other folks who have different skills and treatments that will enhance your improvement."*
- *"Becoming more productive in your daily life is hard work, therefore we want to optimize mind, body and spirit to enhance your ability to do the work of healing."*

Resources

Non-pharmacological treatment of chronic widespread musculoskeletal pain.
Hassett AL, Williams DA. Best Pract Res Clin Rheumatol. 2011 Apr;25(2):299-309. doi: 10.1016/j.berh.2011.01.005.

Non-pharmacologic Management of Pain
Scott F. Nadler, DO. University of Medicine and Dentistry of New Jersey, Newark, NJ
J.Am Osteopath Assoc. November 1, 2004 vol. 14 no. 11 suppl 6S-12S

Chronic Pain Management: Non-pharmacologic Therapies
Steven A. King, MD, MS. New York University. Consultant. 2013;53(4):275

Pain Clinical Updates; Physical Therapy for Chronic Pain

Chronic Pain Syndrome Treatment & Management

PainEDU.org; Pain Herbal Therapies for Pain

[1] http://www.medscape.com/viewarticle/745953
[2] http://psychcentral.com/lib/living-with-chronic-pain-and-depression/00016150
[3] Pain 80 (1999) 1–13
[4] http://www.webmd.com/pain-management/features/cognitive-behavioral
[5] http://www.apta.org/uploadedFiles/APTAorg/Practice_and_Patient_Care/PR_and_Marketing/Market_to_Professionals/TodaysPhysicalTherapist.pdf
[6] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1876616/
[7] http://www.samhsa.gov/data/2k12/DAWN096/SR096EDHighlights2010.htm

Section 5b: Initiating Opioid Therapy

In 2010, Emergency Department visits resulting from the misuse or abuse of pharmaceuticals occurred at a rate of 434.9 visits per 100,000 population compared with a rate of 378.5 visits per 100,000 population for illicit drugs.

Overview

"Chronic Pain" means a state in which pain persists beyond three to six months. In chronic pain the usual healing and recovery has not occurred and may or may not be associated with an acute or chronic pathologic process that causes continuous or intermittent pain over months or years. It affects approximately one-third of U.S. adults and strong opioids are prescribed in up to 9% of all office visits.[1] The decision to begin opioid therapy should be the result of a careful patient assessment, including potential mental health issues and risk of addiction, determination of the type of pain and if it is typically responsive to chronic opioid therapy, and identification of achievable functional goals. There is very little data to support use of long-term opioid therapy for common causes of chronic pain, such as fibromyalgia, low back pain and headache. Before beginning treatment with opioid therapy, you will want to exhaust non-pharmacologic interventions.

The American Academy of Family Practice has identified a number of interventions that can and should be considered prior to beginning a trial of opioid therapy including:[1]

- Cutaneous stimulators (e.g., transcutaneous electrical nerve stimulation)
- Local treatment (e.g., physical therapy, manipulation, massage, heat)
- Minor interventions (e.g., anesthetic or steroid joint injection)
- Topical anesthetics (e.g., lidocaine ointment or patches)

In this Section

Abuse of prescription painkillers by pregnant women can put an infant at risk. Cases of neonatal abstinence syndrome (NAS)—which is a group of problems that can occur in newborns exposed to prescription painkillers or other drugs while in the womb—grew by almost 300% in the US between 2000 and 2009.[3]

Of course, first-line pharmaco-therapy for chronic pain should be over-the-counter medicine such as NSAIDs, both traditional nonselective NSAIDs and the selective cyclooxygenase (COX)-2 inhibitors. NSAIDs have analgesic, anti-inflammatory and antipyretic activities that impact the generation of inflammation and the biochemical recognition of pain. Acetaminophen can also be a useful treatment option. While NSAIDs may be more effective in reducing pain, acetaminophen has a safer profile, which can be important for older patients.[2]

Neuropathic pain, which is a very common cause of chronic pain, is responsive to a number of non-opioid medications. Tricyclic anti-depressants and serotonin-norepinephrine reuptake inhibitors are indicated for neuropathic pain and may add additional benefit for co-existing mental health disorders. Certain antiepileptic drugs (pregabalin and gabapentin) are useful for both neuropathic pain and fibromyalgia.

If after careful evaluation, you believe that a trial of opioid therapy might be a useful and efficacious treatment, then you will want to follow a few key recommendations listed below. Most importantly, remember that you are the expert and your treatment plan should reflect your clinical judgment. Do not start a medication that you are not prepared to stop.

Recommendations

1. Patients with chronic non-terminal pain should receive a comprehensive evaluation, including assessment for potential opioid responsiveness and opioid risk as described elsewhere in this toolkit.

2. All non-pharmacologic interventions, including physical therapy and exercise, complementary and alternative medicines, and cognitive behavioral techniques should be explored before beginning chronic opioid therapy. **5 Required by Section 5(1) of Emergency Medical Rules**

3. Education is the key treatment modality. It is used to create understanding, set expectations and motivate patient participation.

4. Consider consultation with pain specialists or subspecialists and/or physical therapists at the point when a patient shifts from an acute pain situation to a chronic pain patient. Early non-

pharmacologic interventions may reduce the need for or dosing of opioid therapy. Expert outside opinion may also provide you the reassurance to go forth in either prescribing or not prescribing opioids.

5. Opioids should be introduced to your patient as a trial. It should only be continued if progress is documented toward functional goals, and if there is no evidence of adverse events, misuse or diversion. Do not start treatment if you are not prepared to stop if the above circumstances are identified.

6. A decision to treat with opioids is a commitment to periodic monitoring, with the potential to identify intentional and/or unintentional abuse/misuse – be prepared to have an uncomfortable conversation!

7. Opioids should be started at a low dose and titrated slowly to decrease risk of opioid-related adverse effects. You should initiate therapy with short acting opioids to minimize risk of adverse events.

8. At any point in treatment, but especially when the average daily dose of opioids increases to 30 mg/day, you will need to ask the question: Is the treatment helping? Is the patient better off and more functional today? If there is no clear benefit or there is evidence to suggest harm or significant risk, implement your exit strategy. A referral to a specialist may be appropriate and this could be a pain doctor, an addictionologist, a pain management or a mental health provider. If there seems to be benefit, document and continue tracking function and monitoring for safety. Please see the section on High-Dose Opioid Therapy for more information.

Talking Points

- *"Here's a list of things to watch out for. Just let me know if your pain is becoming uncontrolled—don't just take more of the drug."*
- *"I understand you are experiencing pain. We probably can't make all of your pain disappear so let's talk about some coping strategies."*
- *"Your type of pain does not respond well to opioid medications, so I would be starting you on a medication with much more risk than benefit. Let's try XYZ which has a really good track record for your type of pain."*

Resources

A review of medications can be found in the toolkit section on "Important Information about Commonly Prescribed Opioids."

Chronic Pain Initiative Tool Kit: Primary Care Provider©

Rational Use of Opioids for Management of Chronic Nonterminal Pain
Daniel Berland, MD, and Phillip Rogers, MD, University of Michigan Medical School, Ann Arbor, Michigan. Am Fam Physician. 2012 Aug 1;86(3):252-258.

PainEDU.org offers a number of short courses that are useful when starting therapy.

Practical Pain Management: Medications for Chronic Pain – Other Agents

Institute for Clinical System Improvement CSI Health Care Guideline: Assessment and Management of Chronic Pain.

Partners Against Pain®; Pain Management Tools

[1] http://www.aafp.org/afp/2012/0801/p252.html
[2] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1855338/
[3] http://www.cdc.gov/vitalsigns/PrescriptionPainkillerOverdoses/

Section 6: Informed Consent and Treatment Agreements

Seven million people abuse/misuse prescription drugs every month, of which 5.3 million abuse pain relievers.[1]

Overview

After you and your patient have jointly developed a treatment plan that includes controlled substances, you will want to discuss an Informed Consent and Treatment Agreement. The use of a Treatment Agreement, also called a Patient Contract, allows you to establish a standardized approach for management of your chronic pain patients who are on controlled substances. These agreements assist the provider in routinely monitoring all patients for their adherence to the treatment plan, their response to medication, the development of addiction, and cause for concern about potential diversion.

You will want to begin by discussing the Informed Consent and Treatment Agreement. You should discuss the risks and benefits of the use of controlled substances with the patient (or persons designated by the patient or the patient's surrogate or guardian if the patient is without medical decision-making capacity). It is important for patients to know that long-term opioid therapy for chronic pain carries the potential for addiction and/or withdrawal, but that you have designed a monitoring plan that will significantly reduce those risks. Of course you will want to prepare the patient for the likely side effects and how they should plan to manage them. If they have other important comorbid conditions that are being managed by specialty physicians, the patient should allow you to contact their provider as well as remind the specialty physician of their medications at follow-up visits.

In this Section

Rule Highlight

5 Section 5 (4) of Medical Licensing Board's Emergency Rules requires that "the physician shall, together with the patient, review and sign a 'Treatment Agreement' which shall include, goals, consent to drug monitoring, consent to conduct pill counts, requirement that patient takes meds as prescribed and prohibition from sharing."

Elements of the informed consent that you will want to include[2]: 5 **Required by Section 5 of Emergency Medical Rules**

- The potential risks and anticipated benefits of chronic opioid therapy.
- Potential side effects (both short- and long-term) of the medication, such as constipation and cognitive impairment.
- The likelihood that tolerance to and physical dependence on the medication will develop.
- The risk of drug interactions and over-sedation.
- Risk of Neonatal Abstinence Syndrome (NAS), also known as Neonatal Opioid Withdrawal Syndrome (NOWS).
- The risk of impaired motor skills (affecting driving and other tasks).
- Synergistic, or at the least additive, impact of benzodiazepines and opioids on breathing and the risk of overdose and overdose resulting in death.
- The risk of opioid misuse, dependence, addiction and overdose.
- The limited evidence as to the benefit of long-term opioid therapy.
- Some mention that opioids may increase pain over time.
- The physician's prescribing policies and expectations, including the number and frequency of prescription refills, as well as the physician's policy on early refills and replacement of lost or stolen medications.
- Specific reasons for which drug therapy may be changed or discontinued (including violation of the policies and agreements spelled out in the Treatment Agreement).

The Treatment Agreement outlines the joint responsibilities of physician and patient and usually includes[2]: 5 **Required by Section 5(4) of Emergency Medical Rules**

- The goals of treatment, in terms of pain management, restoration of function and safety.
- The patient's responsibility for safe medication use (e.g., not using more medication than prescribed or not using the opioid in combination with alcohol or other substances; storing medications in a secure location; and safe disposal of any unused medication).
- The patient's responsibility to obtain his or her prescribed opioids from only one physician or practice.
- The patient's agreement to periodic drug testing (blood, urine, hair or saliva).
- The physician's responsibility to be available or to have a covering physician available to care for unforeseen problems and to prescribe scheduled refills.

The Informed Consent and Treatment Agreement can be merged into one document for your convenience. There are many different templates that you and your staff can review to determine which is the best fit for your practice. You will find samples in the list of resources at the end of this section, as well as Appendix D and Appendix E.

Recommendations

1. All patients on long-term therapy that includes controlled substances should have an Informed Consent and Treatment Agreement completed before initiative therapy. This should be placed into the patient's medical record. 5 **Required by Section 5(4) of Emergency Medical Rules**
2. The Treatment Agreement should be reviewed at every follow-up appointment.

Talking Points

- *"Mrs. Jones before we actually start your treatment plan (do not just say narcotics) I would like to review some of the important side effects you may notice. I would also like to review some of the ongoing parameters that experts have recommended we use to minimize the risk of an undesirable outcome for you."*

If a patient responds that collecting a drug test is a form of spying on them:

- *"It may seem like that to you, but it's a standard part of care for all my patients. Any level of substance use can affect a patient's life and the management of the pain. Is there something we need to talk about?*

If a patient says you are treating me like a drug addict:

- *"I'm sorry if this gives you the impression that I am judging you. As your doctor, I have a job to identify and resolve any issues that may interfere with your pain treatment, sooner rather than later. The drug screen helps me do that."*

Resources

Informed Consent and Treatment Agreement Templates:

Washington State Department of Labor and Industries

American Academy of Family Practice: A Tool for Safely Treating Chronic Pain and the Medical Use Agreement

Pain.EDU: Agreement for Opioid Maintenance Therapy for Non-Terminal/Cancer Pain

University of Utah Hospitals and Clinics Pain Management Center: Sample Medication Management Agreement

Pain.EDU.org Low Literacy Medication Management Contract
* Low Literacy Patients

[1] http://www.acpm.org/?UseAbuseRxClinRef#Prevalence
[2] Federation of State Medical Boards | www.fsmb.org

Section 7: Monitoring Therapy

Fewer than 40% of physicians receive training in medical school to identify prescription drug abuse or recognize the warning signs of drug diversion.[1]

Overview

While the actual prevalence of opioid prescription misuse and abuse varies among clinical settings, the overall prevalence appears to be increasing. Physicians are charged with the difficult task of meeting patients expectations for pain treatment without allowing even unintentional misuse, abuse or diversion to develop. Studies show that one way to minimize this risk is increased monitoring of a patient's response to treatment (pain and function) and their use and management of their narcotics.

Patients should be seen more frequently at the onset of treatment and while opioids are being titrated. While the frequency of visits may decrease as the patient continues to improve or remains stable, you will still want to see patients on chronic opioid treatment periodically throughout the year. At each visit, your patient's response to treatment can be assessed by using the "5As" of chronic pain management:

- **Analgesia**: Has the patient experienced a reduction in pain?
- **Activity:** Has he/she demonstrated an improvement in level of function?
- **Adverse effects:** Experienced any significant side effects or adverse events?
- **Aberrant substance-related behaviors:** Are there any "red flags" in patient behavior, inconsistent urine drug monitoring results, or unexpected findings on the INSPECT report? (See section on Diversion)
- **Affect:** How is the patient's overall mood?

In this Section

You will also want to evaluate your patient's functional improvement and the impact your treatment has had on his or her pain. This can be done easily with a number of tools that can be incorporated into the medical record, two of which are noted here:

- **The Pain Assessment and Documentation Tool**
- **The Brief Pain Inventory**

Reviewing Indiana's Prescription Drug Monitoring Program, INSPECT, should be a part of every visit as well. For a brief review on INSPECT, see the User's Guide in the Resources section of this toolkit.

INSPECT will allow you to see if your patient is obtaining opioids from other providers, but also if they are receiving other controlled substances such as benzodiazepines and not sharing this information with you, either intentionally or unintentionally.

Another well-recognized monitoring tool is periodic drug monitoring. This provides an objective opportunity to ensure compliance with medications (albeit with limitations) and also to determine if your patient is using other illicit drugs. Immunoassay testing, also known as point of care (POC) testing, can be useful for more "on the spot" decision making, but for long-term patient care and decision making, you will want a test that utilizes gas chromatography or mass spectrometry. You should not hesitate to discuss any unexpected or confusing results with the laboratory toxicologist or a clinical pathologist.

Of course the difficult part is that any clinical record, INSPECT report or drug test result that suggests opioid misuse needs to be discussed with the patient. You will want to begin the discussion in a direct yet supportive fashion. It is important to remember that patients can unintentionally slide into a pattern of misuse, either deliberately or out of lack of education, increasing pain or sudden life stressors. However, you will need to determine if you are going to continue, modify, or terminate opioid treatment for this patient. The test results, discussion with the patient, and your final recommendations should all be documented in the medical record.

Recommendations

1. All non-terminal patients on chronic opioid therapy should receive regular, repeated visits with evaluation of progress against identified analgesic and functional goals, compliance with non-pharmacologic plans and activity, and development of adverse effects.
2. Collateral information about the patient's response to opioid therapy should be obtained from family members or other close contacts.
3. Patients will need to be seen more frequently until a stable medical regimen is achieved. Thereafter, follow-up visits for patients with a stable treatment plan and those receiving regular controlled substance prescriptions should probably occur at least once every 3-4 months. "High-risk" patients and patients receiving high doses of opioids require closer monitoring.
   6 **Required by Section 6 of Emergency Medical Rules**

4. Periodic drug testing should be utilized to monitor adherence to the treatment plan, as well as to detect the use of non-prescribed drugs. (Patients being treated for, or are at risk for addiction should be tested as frequently as necessary to ensure therapeutic adherence in accordance with your clinical judgment.) **7 Required by Section 7 of Emergency Medical Rules**
5. An INSPECT record should be reviewed at every visit. **7 11 See Section 7 & 11 of Emergency Medical Rules**
6. An opioid treatment trial should be discontinued if the goals are not met and opioid treatment should be discontinued at any point if adverse effects outweigh benefits or if aberrant behaviors are demonstrated.
7. Consider consultation if treatment goals are not met.
8. All information collected and decisions rendered should be documented in the medical record.

Talking Points

- *"During this check-up, I want you to fill out this brief questionnaire. It will help me with your treatment plan."*
- *"I know you have been suffering with your pain and I want to help, but I am concerned about your overuse of medication."*
- *"It is my choice to not prescribe at this time." (Be clear and have a referral plan to provider(s) who may accept this patient).*
- *"It is clinic policy to not prescribe these types of drugs for patients that may be developing or have a dependence problem. I can refer you to someone who can work with you both for pain and possible addiction."*

If a patient responds that collecting a drug test is a form of spying on them:

- *"It may seem like that to you, but it's a standard part of care for all my patients. Any level of substance use can affect a patient's life and the management of the pain. Is there something we need to talk about?"*

If a patient says you are treating me like a drug addict:

- *"I'm sorry if this gives you the impression that I am judging you. As your doctor, I have a job to identify and resolve any issues that may interfere with your pain treatment, sooner rather than later. The drug screen helps me do that."*

Resources

PainEDU Course-in-a-Box: Monitoring Patients on Chronic Opioid Therapy
A downloadable and print-ready PowerPoint™ presentation that comes complete with speaker notes. This tool is designed to be a resource for clinicians and educators to use in classrooms, grand rounds, conferences, and for in-service education.

Behavioral Monitoring and Urine Toxicology Testing in Patients Receiving Long-Term Opioid Therapy

Guidelines for the Use of Opioid Therapy in Patients with Chronic Non-Terminal Pain

Opioid Abuse Potential Prompts Monitoring Role for Internists

[1] http://www.acpm.org/?UseAbuseRxClinRef#Conversations

Section 8: High-Dose Opioid Therapy

Patients receiving 100 mg/d of opioids or more had an 8.9-fold increase in overdose risk (CI, 4.0 to 19.7) and a 1.8% annual overdose rate.[1]

Overview

The use of high-dose or chronic opioid therapy is controversial and is not recommended without a demonstrated need and a plan for appropriate monitoring. The need for progressively higher opioid doses may be a result of progression of the underlying condition, the development of tolerance, or an indicator of a substance use disorder or diversion. Opioid-induced hyperalgesia (OIH) is another potential reason for escalating need for opioids and is characterized by a paradoxical response whereby a patient receiving opioids for the treatment of pain could actually become more sensitive to pain. The type of pain experienced might be the same as the underlying pain or might be different from the original underlying pain.[2] For a more information about this condition, read through the article, A Comprehensive Review of Opioid-Induced Hyperalgesia.

A study published in the *Annals of Internal Medicine* identified that patients receiving an average daily opioid dose of 50 to 99 mg/d had a 3.7-fold increase in overdose risk (95% CI, 1.5 to 9.5) and a 0.7% annual overdose rate.[1]

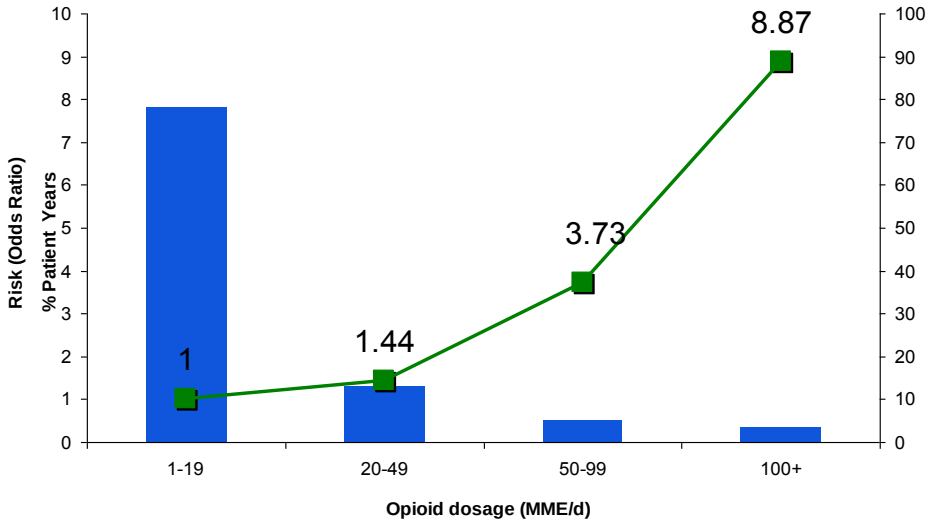
Therefore when patients are approaching daily opioid doses of 30 mg/day, you should take the opportunity to reassess the patient's condition, progress toward achieving functional and analgesic goals, occurrence of adverse side effects and/or tolerance and development of addiction or aberrant behaviors consistent with diversion. Depending on your assessment, you may find this is the appropriate time to consult other specialists, including pain specialists, physiatrists, rheumatologists, orthopedic or neurosurgeons or mental health providers to ensure that all non-narcotic avenues have been exhausted. Most specialists will tell you that the earlier in the course

In this Section

Rule Highlight

3 The requirements established by Medical Licensing Board's Emergency Rules concerning the use of opioids for chronic pain management "apply if a patient has been prescribed: more than 60 opioid containing pills a month for more than 3 consecutive months OR a morphine equivalent of more than 15 milligrams per day for more than 3 consecutive months." Section 3(a)

Figure 1: Opioid Prescriptions for Chronic Pain and Overdose Risk



Source: Dunn et al, Opioid prescriptions for chronic pain and overdose. Ann Int Med 2010;152:85-92.

of the illness the consult is obtained, the better. The two of you can then have a united course of action that promotes quality of life, minimizes pain, and most importantly maximizes patient function.

If after careful assessment and deliberation, your clinical judgment is to proceed with average daily doses higher than 60 mg/day, then you will want to ensure that you have discussed the risks and benefits of the treatment plan and documented the conversation in the medical record. You will also want to increase the frequency of follow-up appointments and begin more frequent and intense monitoring for development of adverse effects and aberrant behaviors.

Patients who are not making the expected progress toward achieving their goals, experience adverse effects, or engage in serious or repeated aberrant drug-related behaviors or diversion should be tapered or weaned off opioids. Optimal strategies for weaning vary, but consultation with a pharmacist can be instructive in this matter. When available, opioid detoxification in a rehabilitation setting (outpatient or inpatient) can be useful. Of course patients with addiction issues will need the expertise of an addiction specialist. You can find an addiction's specialist in your area through the Substance Abuse Treatment Facility Locator.

In summary, an average daily dose of 30 mg/day of opioid treatment provides an excellent opportunity to pause and reassess before the risks of treatment begin to substantially increase.

Recommendations

1. When patients are taking an average daily dose of 30 mg/day of opioids, clinicians should pause and reassess the patient's condition, progress toward achieving functional and

analgesic goals, occurrence of adverse side effects and/or tolerance and development of addiction or aberrant behaviors consistent with diversion.

2. Consider consulting other specialists including pain specialists, physiatrists, rheumatologists, orthopedic or neurosurgeons, or mental health providers to ensure that all non-narcotic avenues have been exhausted.

3. Physicians should taper or wean patients off of opioids who engage in repeated aberrant drug-related behaviors or drug abuse/diversion, experience no progress toward meeting therapeutic goals, or experience intolerable adverse effects.

Talking Points

- *"It is clinic policy to not prescribe these types of drugs for patients that may be developing or have a dependence problem. I can refer you to someone who can work with you both for pain and possible addiction."*
- *"I don't prescribe opiates for this type of pain, but I am happy to try to help in another way."*
- *"I understand you are experiencing pain. I probably can't make all of your pain disappear so let's talk about some coping strategies."*

Resources

CDC Prescription Painkiller Overdoses Policy Impact Brief

Opioid Prescriptions for Chronic Pain and Overdose: A Cohort Study
Kate M. Dunn, PhD; Kathleen W. Saunders, JD; Carolyn M. Rutter, PhD; et al
Ann Intern Med. 2010;152(2):85-92. doi:10.7326/0003-4819-152-2-201001190-00006

Opioid Dose and Drug-Related Mortality in Patients With Nonmalignant Pain
Tara Gomes, MHSc; Muhammad M. Mamdani, PharmD, MA, MPH; Irfan A. Dhalla, MD, MSc; et alArch Intern Med. 2011;171(7):686-691. doi:10.1001/archinternmed.2011.117

[1] http://annals.org/article.aspx?articleid=745518
[2] http://www.integration.samhsa.gov/pbhci-learning-community/Opioid-Induced_Hyperalgesia_Article.pdf

Section 9: Assessment and Management of Acute Pain in Primary Care

In this Section

Family physicians treat more patients with back pain than any other subspecialist and about as many as orthopedists and neurosurgeons combined.[1]

Overview

Pain costs Americans an estimated $160 billion each year. Patients, families, healthcare organizations and society as whole bear this financial burden. Medical complications associated with inadequately controlled acute pain can increase length of hospital stay, re-hospitalization rates and number of outpatient visits. Our goal is both effective and safe pain management.

Acute pain was once defined simply in terms of duration. It is now viewed as a complex, unpleasant experience with emotional and cognitive, as well as sensory features that occur in response to tissue trauma. In contrast to chronic pain, relatively high levels of pathology usually accompany acute pain. The pain resolves with healing of the underlying injury. Acute pain is usually nocioceptive, but may be neuropathic. Common sources of acute pain include trauma, surgery, labor, medical and dental procedure and acute disease states.

Acute pain serves an important biological function, as it warns of the potential for, or extent of, injury. A host of protective reflexes (e.g., withdrawal of a damaged limb, muscle spasm, autonomic responses) often accompany it. Acute pain might be mild and last just a moment, or it might be severe and more prolonged. Acute pain, by definition, does not last longer than six months and it resolves when the underlying cause of pain has been treated or has healed. An accurate assessment of acute pain should be performed when a patient presents with pain to the healthcare setting. A solid understanding of

the person and the etiology of the pain are essential for the development of an effective and appropriate short-term pain management plan. See Appendix G for the "Do's and Don'ts" for assessment and management of patients with acute pain.

Recommendations

For Primary Care

1. Develop an office policy for opioid prescribing and have this clearly posted and available for patients.
2. Perform a thorough history and physical at the onset.
3. Acute pain patients should be frequently evaluated for functional improvement, with adjustments to treatment as needed. Therefore, it is almost always contraindicated to include refills on opioid prescriptions for acute pain.
4. Educate about analgesia. Explain the condition, the natural history and how your patient can help the healing.
5. If medically possible, exhaust non-opioid medications and collaborate with other professionals, including physical therapists and pain specialists. Consider nontraditional therapies such as acupuncture and massage therapy.
6. Opioids are often not required for acute pain. If you feel a brief course of opioids are indicated and appropriate, be thoughtful and thorough in your discussions and practice.
7. Always prescribe a complete pain management program when an opioid is used to treat acute pain:
    a. Schedule NSAIDS
    b. Specific exercises
    c. Other modalities (e.g. heat, ice, massage and/or topicals)
8. Prescribe opioids intentionally. With the first opioid prescription, set patient responsibilities and the expectation that opioids will be discontinued when the pain problem has resolved or is not responding to current measures.

"As I arrived at the Emergency room where my son had been taken, there was a long line at the nurses' desk of people waiting to check in. I rushed past the line and emphatically said to the nurse "I'm Jarrod's mom and I want to see my son." The nurse replied and said, 'Ok come with me.' She hit the button so the ED doors would open. I barely stepped inside the doors and a physician was standing before me. He introduced himself and before anything else came out of his mouth I said, 'He's gone.' …He said we think your son accidentally overdosed on prescription drugs. We have an ability to make a difference as healthcare workers in the abundance of prescription drugs that are making their way to the streets."

– Marty C.

9. Write the taper on the prescription (e.g. 1 po each 6 hor for 3 days, 1 po each 8-12 hr for 3 days, 1 po each 24 hr for 3 days, stop).
10. Do not prescribe long-acting or controlled-release opioids (e.g., long-acting oxycodone and oxymorphone, fentanyl patches, long-acting hydromorphone and morphine or methadone) for acute pain.
11. Consider performing risk stratification, urine drug monitoring and or INSPECT monitoring at the onset of pain care.
12. Inform the patient of the risks of taking opioid analgesics and instruct the patient to take them only as prescribed, not more frequently or in greater quantities.
13. Educate patients about the risks of opioid analgesics, including, but not limited to: overdose that can slow or stop their breathing and even lead to death; fractures from falls, especially in patients aged 60 years and older; drowsiness leading to injury, especially when driving or operating heavy or dangerous equipment; tolerance and addiction. Educate the patient on acute pain – odds are it will diminish and resolve. Prolonged scheduled opioids may actually impair the person's ability to fully recover.
14. Patients should be advised to avoid medications that are not part of their treatment plan because they may worsen side effects and increase the risk of overdose.
15. Prepare patients that it may be difficult to taper off opioids, particularly from higher dose regimens, even when they are eager to do so.
16. Consider a referral/consult to a pain specialist if the patient is not responding to your treatment plan. You may want to do this early in the course of treatment if the patient does not respond to the standard first line medications and before you prescribe narcotics, as the specialist may have procedures or other interventions that resolve the issue.
17. Prolonged (many weeks) of scheduled opioids for acute pain may actually impair the person's ability to fully recover.
18. It is critical to assure that patients are provided with easy to follow graduated activity instructions that help them quickly improve functionality.

For Emergency Departments (ED)[2]

1. Emergency medical providers should not provide replacement prescriptions for controlled substances that were lost, destroyed or stolen.
2. Emergency medical providers should not provide replacement doses of methadone for patients in a methadone treatment program.
3. Long-acting or controlled-release opioids (such as OxyContin®, fentanyl patches and methadone) should not be prescribed from the ED.
4. EDs are encouraged to use INSPECT before prescribing opioids.
5. Physicians should send patient pain agreements to local EDs and work to include a plan for pain treatment in the ED.

6. Prescriptions for controlled substances from the ED should state the patient is required to provide a government issued picture identification (ID) to the pharmacy filling the prescription.
7. EDs should perform screening, brief interventions and treatment referrals for patients with suspected prescription opiate abuse problems.
8. For exacerbations of chronic pain, the emergency medical provider should contact the patient's primary opioid prescriber or pharmacy. The emergency medical provider should only prescribe enough pills to last until the office of the patient's primary opioid prescriber opens.
9. Prescriptions for opioid pain medication from the ED for acute injuries, such as fractured bones, in most cases should not exceed 30 pills.
10. ED patients should be screened for substance abuse prior to prescribing opioid medication for acute pain.

Talking Points

Compassionate and clear communications are essential for effective management of acute pain.

- *"My experience is that with this type of pain, Ibuprofen in conjunction with physical therapy is very effective."*

Resources

Institute for Clinical Systems Improvement; Health Care Guideline: Adult Acute and Subacute Low Back Pain

Meeting the Challenges of Acute Pain Management: Medication Choices for Acute Pain

[1] http://www.aafp.org/afp/2007/0415/p1181.html#afp20070415p1181-b3
[2]http://www.healthy.arkansas.gov/programsServices/injuryPreventionControl/injuryPrevention/Documents/PainMedication/ArkansasEmergencyDepartmentOpioidPrescribingGuidelines.PDF

Section 10: Tips to Identify Opioid Diversion

More than three out of four people who misuse prescription painkillers use drugs prescribed to someone else.[1]

Overview

Drug diversion is best defined as the diversion of licit drugs for illicit purposes. It involves the diversion of drugs from legal and medically necessary uses towards uses that are illegal and typically not medically authorized or necessary.[2] Best estimates are that 35-45% of patients on chronic opiate therapy are pursuing addiction or diverting. Legitimate patients come to us hurting, compromised, and functioning sub-optimally in their lives. We must be alert to not play into their perceived exclusive need for pain medication, and ultimately make their condition worse. Patients who are addicted cannot see the larger picture. Patients who divert do not care about the larger picture. Patients who are in pain are trying to cope and have lost perspective that a larger picture exists.

One of the most difficult duties that a physician has as it relates to the prescribing of opioids to patients with chronic pain is the issue of opioid diversion. Even in light of a failed urine drug screen (UDS) with confirmation, an inconsistent INSPECT, and/or noncompliance (not attending physical therapy, failure to obtain prescribed imaging, failure to attend appropriate interventional procedures, etc.), it is difficult to know when a patient is diverting his/her prescription opioids. However, the prescriber may feel the patient is diverting after ascertaining a history, or the medical office receives a phone call from an anonymous source stating that the patient is selling his/her opioid medication. Perhaps the most effective way to appropriately decide if the patient is diverting is the combination of a random pill count and a concomitant UDS with a confirmation.

In this Section

Rule Highlight

8 Section 8 (a) of the Medical Licensing Board's Emergency Rules require that "at the outset of an opioid treatment plan, and at least annually thereafter, a physician prescribing opioids for a patient shall perform or order a drug monitoring test, which must include a confirmatory test, on the patient."

If you believe a patient may be diverting his or her prescription, call them to come in to the office between scheduled appointments. It is of vital importance that a random pill count be part of the Prescriber-Patient Agreement and Informed Consent. Not only must this be part of the agreement, but it should be reviewed with the patient at the time he or she signs the agreement. If the patient is short on their pill count, it is vital to perform, at that exact point in time, a urine drug screen with confirmation. Here is the reason: if the confirmation comes back with the appropriate medication in the patient's system, it is likely that they are taking the prescribed opioid medication, but may be overtaking it.

If the patient's confirmation is negative for your prescribed opioid, then you can feel very comfortable that the patient is diverting. At this point, it would be very safe to stop prescribing and inform your local authorities. If the confirmation comes back with the appropriate medication and the pill count is short, it is highly likely the patient is either taking more than is prescribed, or the patient takes the medication but is diverting a portion of the prescription. At this point, it is good due diligence to have a conversation with the patient. If the patient is overtaking the medication, it may be a good idea to seek a pain management consultation to get a reassessment of the true pain generator(s). If you believe the patient is diverting and/or abusing, a referral to an addiction specialist is in order.

Patients who divert drugs come from all socioeconomic levels, races and ages. So it is important to be aware of certain "alert factors" to help identify red flag behaviors. You and your staff must become clinical detectives, while still being aware that sound clinical judgment must prevail in the end.

You will find an in depth article on recognizing and preventing medication diversion at Family Practice Management.

Recommendations

Be on the alert for:

Suspicious "history":

- Patient referred is already taking CS; especially combinations of narcotics, muscle relaxants, sedative/hypnotics
- Soft diagnosis – perhaps based solely on chief complaint
- Multiple doctors and pain physicians in the past
- Patient travelled out of the way to come to your clinic
- Solicitous behavior frequently heard: "You're the best. I always wanted to come to you."
- No past medical records; unable to obtain records from "referring doctor"
- Patient brings records that look old, tattered or suspicious in some other way
- Patient asks for a specific controlled substance (example: prefers Lortab® over Narco®)

Suspicious physical exam:

- No abnormal findings
- Abnormal findings in exam room inconsistent with witnessed behavior (patient has normal gait from car to office door, but limps once inside door)
- Exaggerative behaviors, pain descriptors – pain is always a 10 on a scale of 1 to 10.
- Unimpressive imaging
- Presence of needle "tracks"
- Patient smells like marijuana smoke

Equivocal compliance:

- INSPECT shows multiple providers, multiple pharmacies, prescriptions for multiple types and strengths of medications, out of the area doctors, etc.
- UDS is refused or abnormal; patient offers multiple excuses; presence of any illegal substances (marijuana)
- Inconsistent test results over time
- Patient seeks early refills
- Patient has excuses for lost pills (lost my prescription, my dog ate my pills, etc.)

Equivocal clinical improvement:

- Subjective improvement does not count
- Objective may include the following: is the patient going back to work, attending appointments with a spouse (who can confirm improvement), showing a need for less medication, visiting the ER less, etc.

What you should do when confronted by a suspected drug abuser[3]:

- Request picture I.D. or other I.D. and a Social Security number. Photocopy these documents and include in the patient's record.
- Call a previous practitioner, pharmacist or hospital to confirm the patient's story.
- Confirm a telephone number, if provided by the patient.
- Confirm the current address at each visit.
- Write prescriptions for limited quantities.

Talking Points

- *"It seems like you are running out of medication early. Let's talk about how much pain you are in."*
- *"I know you have been suffering with your pain and I want to help, but I am concerned about your overuse of medication."*
- *"It is clinic policy to not prescribe these types of drugs for patients that may be developing or have a dependence problem. I can refer you to someone who can work with you both for pain and possible addiction."*

Resources

To find your local law enforcement contact information in Indiana, visit this Police Department Locator site.

Recognizing and Preventing Medication Diversion

Drug Enforcement Administration: Recognizing the Drug Abuser

Partners in Integrity: What is the Prescriber's Role in Preventing the Diversion of Prescription Drugs?

U.S. Department of Health and Human Services & Centers for Medicare and Medicaid Services
Fishman SM, Papazian JS, Gonzalez S, Riches PS, Gilson A. Regulating opioid prescribing through prescription monitoring programs: balancing drug diversion and treatment of pain. *Pain Medicine*. 2004; 5(3); 309-324.

Hall W, Degenhardt L. Regulating opioid prescribing to provide access to effective treatment while minimizing diversion: an overdue topic for research. *Addiction*. 2007; 102(11); 1685-1688.

[1] http://www.cdc.gov/homeandrecreationalsafety/rxbrief/
[2] http://www.drugwarfacts.org/cms/Diversion#sthash.lYGrP8UE.dpbs
[3] http://www.deadiversion.usdoj.gov/pubs/brochures/pdfs/recognizing_drug_abuser_trifold.pdf

Section 11: What to Do if You Suspect Addiction

In this Section

- Overview of Addiction
- Recommendations
- Talking Points

In 2012, 23.1 million persons aged 12 or older needed treatment for an illicit drug or alcohol use problem (8.9 percent of persons aged 12 or older). Of these, 2.5 million (1.0 percent of persons aged 12 or older and 10.8 percent of those who needed treatment) received treatment at a specialty facility. Thus, 20.6 million persons (7.9 percent of the population aged 12 or older) needed treatment for an illicit drug or alcohol use problem but did not receive treatment at a specialty facility in the past year.

Overview

Opioid pain medications are addictive. Unfortunately, many doctors believe that patients who are simply taking opioids as prescribed will not become addicted. However a literature review conducted by Højsted and Sjøgren indicates that the prevalence of addiction varied from 0% up to 50% in chronic non-malignant pain patients, and from 0% to 7.7% in cancer patients depending of the subpopulation studied and the criteria used.[1]

Addiction is defined as a primary, chronic, neurobiologic disease with genetic, psychosocial and environmental factors influencing its development and manifestations. It is important to note that physical dependence and tolerance are normal physiological consequences of extended opioid therapy for pain and are not the same as addiction. In fact, most patients who take opioid medications daily for over 90 days will become physiologically dependent and will experience tolerance and withdrawal.[2]

Addiction is characterized by behaviors that include the following: **impaired control over drug use, craving, compulsive use, and continued use despite harm**.[3] A meta-analysis looking at the prevalence, efficacy, and risk for addiction for persons receiving

opioids for chronic back pain revealed aberrant medication-taking behaviors in up to 24% of cases.[4]

Some examples of these aberrant behaviors include[5]:

- Early refill requests
- Multiple reports of lost or stolen medications
- Taking more of the medication than prescribed
- Use of a relative or friend's opioids
- Buying medications off the Internet

If you suspect that a patient under your care has one or more addictions, address it. Address it even when the individual is not fully aware of the addiction or initially denies being addicted. Your impression of a possible addiction may be coming from one or several lines of evidence or mere clinical intuition.

Below you will find three key steps you will need to take in your approach to this patient.

Recommendations

1. Investigate further:

1.1. Clinical Interviewing: Ask more questions that are both direct (about use) and indirect (probing for consequences of use) about current or past mental illness. It is crucial that you avoid sounding judgmental, moralizing, or punitive when gathering accurate information. Do not underestimate the power of the addictive disease to minimize and falsify information.

There are tools that you can have your patient complete that can identify potential addiction issues, including:

- The DAST-10 Questionnaire regarding drug use
- The Addictions Behavior Checklist
- The Current Opioid Misuse Measure (COMM) is available with free subscription at

1.2. Diagnostic Testing: If you are not ordering urine drug screens for drugs of abuse, then start. If you are doing some already, do more. If you haven't done an INSPECT, do one now.

1.3. Collect collateral information from family members when possible.

2. Re-examine what you are prescribing:

2.1. Remember that opioids, psychostimulants and benzodiazepines are addictive in the long run, regardless of what beneficial medicinal effects are intended in the short term. Opioids are among the most addictive substances known, regardless of whether they are delivered by drug dealers or

physicians. Do not underestimate the power of the addict to manipulate physicians into continuing to supply addictive drugs under a pretense of "treatment."

2.2. Question the value of prescribing any addictive substance to a patient; whether or not it is the same type of drug that you are suspicious the patient may be addicted to. The concomitant use off two or more addictive medications by a patient who is not terminally ill is dangerous and often suggestive of underlying addiction and/or improperly-treated psychopathology.

2.3. Confirmation of addiction, or strong evidence suggesting that addiction is present, should initiate treatment planning and patient education with the goal of stopping the prescribing of any addictive substance to the patient and referral to formally trained addiction professionals for assessment and treatment.

3. Refer to professional addiction and/or dual diagnosis treatment:

3.1 Identify and become familiar with behavioral health resources and professionals in your geographic region for the treatment of addictions and dual diagnosis disorders (the comorbidity of mental illness and addiction). Understand that while peer-support groups such as Alcoholics Anonymous and Narcotics Anonymous are very beneficial to many seeking recovery from addictions, these groups do not offer professional medical treatments, cannot treat co-occurring mental illness, and should not be viewed as offering acceptable or adequate treatment standards for all patients with addictions. Do not attempt to treat addiction alone, with medications alone, or with psychotherapies alone and without professional collaborators formally trained in psychotherapeutic and pharmacological treatments for addictions.

The following is a link to a site to identify providers in your area visit the Substance Abuse Treatment Facility Locator.

3.3. Build working relationships and open lines of communication with centers and behavioral health professionals with expertise in treating addictions. If such centers and professionals are not adequately present in your community or healthcare system, then recognize this serious gap in healthcare provision and advocate for such resources with the appropriate stakeholders.

3.3 Refer your patient to the best place you can find, that the patient can get to regularly, that has the highest levels of professional expertise available. The best treatment centers are:

a.) Multidisciplinary, equipped with clinical therapists (e.g. social workers), psychologists, nurses and psychiatrists (preferably addiction psychiatrists);

b.) Dual Diagnosis-capable (e.g. don't just focus on one type of addiction or only addiction but not mental illness);

c.) Therapeutically multifaceted and integrative of individual, group, family and psychopharmacological treatments.

Talking Points

The following talking points introduce the opportunity to assess for and educate about addiction.

- *"Have you ever borrowed anyone's medication?"*

This question creates the opportunity to provide education about the most commonly abused medications. It also allows for education about the risk of addiction and dangerous consequences such as accidents, legal problems, poor job/work performance. The point could be made that while it may appear that what the patient is experiencing is similar to the lender's symptoms, the medication was prescribed for the individual, the individual's medication profile and medical conditions.

- "*Have you ever reached a point where you cannot stop using a medication/drug? Or you have to use more than you previously did to get the same effect?"*
- "*What do you think this medication/drug is doing to your body?"*
- *"Just because it's prescribed doesn't mean it's safe to take more than prescribed…or doesn't mean that you are 'safe' from becoming addicted."*
- *"Have you ever used more medication than prescribed?"*

Resources

Use, Abuse, Misuse, and Disposal of Prescription Pain Medication Time Tool Clinical Reference

Addiction: Part I. Benzodiazepines—Side Effects, Abuse Risk and Alternatives

Addiction: Part II. Identification and Management of the Drug-Seeking Patient

Opioids for Chronic Non-Terminal Pain: Prediction and Identification of Aberrant Drug-Related Behaviors: A Review of the Evidence for an American Pain Society and American Academy of Pain Medicine Clinical Practice Guideline

Confronting the Alcohol and Drug Abusing Patient

[1] Eur J Pain. 2007 Jul;11(5):490-518. Epub 2006 Oct 27. Addiction to opioids in chronic pain patients: a literature review. Højsted J, Sjøgren P.
[2] http://www.instituteforchronicpain.org/understanding-chronic-pain/complications/drug-dependance-addiction.
[3] http://www.fsmb.org/pdf/2013_model_policy_treatment_opioid_addiction.pdf

[4] Systematic Review: Opioid Treatment for Chronic Back Pain: Prevalence, Efficacy, and Association with Addiction Martell BA, O'Connor PG, Kerns RD, Becker WC, Morales KH, Kosten TR, Fiellin DA Annals of Internal Medicine January 16 2007; 146(2):116–27

Addiction & Pain Glossary

Aberrant drug-related behaviors: Actions that indicate addiction, including the following: rapidly escalating drug dosage, running out of prescriptions early, acquiring prescription drugs from outside sources, inconsistent UDS, multi-provider INSPECT, stolen medications chewing/snorting/injecting medications, and altering/stealing/selling prescriptions.

Abuse: A term with a wide array of definitions, depending on context. The American Psychiatric Association defines drug abuse as "a maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by one or more behaviors." DSM-V replaces the term "abuse" with "misuse".[1] In addition, **Substance abuse (SA)** can mean the use of any substance(s) for non-therapeutic purposes, or use of medication for purposes other than those for which it is prescribed. The medical diagnosis of SA is defined by any one of the following four criteria during a 12-month period: (1) failure to fulfill major obligations at work, school, or home; (2) recurrent use in situations in which it is physically hazardous; (3) recurrent substance-related legal problems; (4) continued use despite persistent social or interpersonal problems.[2] Substance abuse can lead to substance dependence.

Acupuncture: An ancient oriental medical technique where needles are placed at anatomic points along the 12 meridians of the body. Oriental medical theory, passed down for thousands of years, states that vital energy (chi) flows through the body along these 12 meridians. Although current medicine does not fully understand how acupuncture works, we do know from functional MRI studies that acupuncture activates/deactivates particular areas of the brain during needling. In addition, it is known that endorphin (endogenous opioid) levels rise during needling. Clinically, acupuncture has been successfully employed to treat a variety of disorders including opioid addiction.[3]

Acute pain: The normal, predicted physiological response to a noxious chemical, thermal, or mechanical stimulus and typically is associated with invasive procedures, trauma, and disease. Acute pain is generally time-limited. Duration of acute pain generally coincides with the time frame of normal healing, and serves to protect an injured body segment.

Addiction: A primary, chronic, neurobiologic disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. Addiction is characterized by behaviors that include the following: impaired control over drug use, craving, compulsive use, continued use despite harm. Physical dependence and tolerance are normal physiological consequences of extended opioid therapy for pain and are not the same as addiction.[1]

Adverse childhood events (ACE): This refers to childhood abuse (physical, emotional, or sexual), neglect, domestic violence, and household dysfunction. ACE is a significant risk factor for alcohol and drug abuse. There is a linear relationship between amount of ACEs and negative health outcomes.[4]

Biofeedback: This behavioral therapy method can teach a person to gain awareness and control over physiologic processes like blood pressure, skin temperature, heart rate, and etc. via real-time feedback of said parameters to the person. Biofeedback has been used to treat a wide variety of diseases, including psychiatric disorders such as anxiety, attention-deficit hyperactivity disorder (ADHD), and substance use disorders (SUD).[3]

Change: To make or become different. Major life changes, such as overcoming an addiction, often occur in five stages, as follow: (1) pre-contemplation stage is when a person has not yet considered making a change; (2) contemplation stage is when a person thinks of making a change, but doesn't know how, or even if the change is worth making; (3) preparation stage is when a person becomes ready to change and makes change plans; (4) action stage occurs when people carry out their change plans; (5) and finally, the maintenance stage occurs when a person tries to make the change stick over time. Relapses sometimes occur, and can be a normal part of change. A person may relapse several times before permanent change takes hold. Research shows that skipping any one of the change stages often results in failure of change to take hold.[5]

Childhood sexual abuse (CSA): This is a strong predictor of psychopathologies in adulthood, including a three-fold elevated risk for alcohol and drug dependence.[4]

Chronic pain: The state in which pain persists beyond the usual course of an acute disease or healing of an injury or that may or may not be associated with an acute or chronic pathologic process that causes continuous or intermittent pain over months or years.

Comorbidity: The presence and effect of two illnesses occurring in the same person simultaneously or sequentially. For example, there is significant psychiatric comorbidity in persons with substance dependence. That is, many individuals who abuse and depend on drugs or alcohol may have an underlying psychiatric condition such as depression, bipolar disorder, post-traumatic stress disorder (PTSD), anxiety disorder, obsessive-compulsive disorder (OCD), etc. Other non-psychiatric comorbidities such as respiratory, cardiac, renal, or hepatic disease, sleep apnea, or seizures are also important in the consideration of chronic opiate therapy.[4]

Conversion: A person is helped to see their addiction as a disorder which needs treatment. Unfortunately, so many people lose nearly everything in their lives and hit rock bottom before conversion is achieved.[6]

Counter-motivation: Is resistance against change. The term includes the complex biological, psychological, and social factors involved with resisting a change. When asked about a making a change, a person may display counter-motivation by interrupting, ignoring, arguing, denying, daydreaming, reminiscing, etc.[5]

Dependence or **Physical dependence:** A state of adaptation that is manifested by drug class-specific signs and symptoms that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of drug, and/or administration of an antagonist. Physical dependence, by itself, does not equate with addiction.[1] The medical diagnosis of **Substance dependence (SD)** is defined by any three of the following seven criteria during a 12-month period: (1) tolerance; (2) withdrawal; (3) substance often taken in larger amounts or over longer period than intended; (4) persistent desire or

unsuccessful efforts to cut down or control use; (5) great deal of time spent in activities necessary to obtain, use, or recover from the substance; (6) important social, occupational, or recreational activities given up or reduced; (7) continued use despite knowledge of having persistent or recurrent physical or psychological problem likely to have been caused or exacerbated by the substance.[2]

Detoxification (Detox) or **medically supervised withdrawal**: Gradual reduction, or tapering, of a medication dose over time, under the supervision of a physician, to achieve elimination of tolerance and physical dependence.[1] Detoxification may be aided by medical intervention, or occur naturally via the body's detoxification pathways. Detoxification is one of the first steps in the treatment of addiction.[7]

Discrepancy: This can refer to the difference between current situation and future goals. A counselor may help a client develop this in order to incite a desire to change.[5] For example, a person is currently unemployed, living on the streets, and using heroin which has caused poor health. This person has wanted children and their own home since childhood, but now sees the discrepancy between current situation and future dreams. Perhaps this person will gain new motivation to change.

Diversion: The use of prescription drugs for recreational consumption, i.e. diverting them from their original medical purpose.[8] The Federal Controlled Substances Act (CSA) establishes a closed system of distribution for drugs classified as controlled substances. Records must be kept from the time a drug is manufactured to the time it is dispensed. Any pharmaceutical which escapes the closed system is said to have been "diverted" and is illegal. Those people who "diverted" the drug are in violation of the law.[1] Conversely, drug diversion may also refer to legal programs which educate, rehabilitate, and "divert" first-time drug offenders from jail and their original destructive life course.[8]

Guided Imagery: This technique uses the imaginative capacity of one's own mind to create a relaxed state or, alternatively, to overcome some troubling aspect of life. This method of therapy has been used with success as one treatment for chronic pain.[3]

High: Abused drugs (e.g. alcohol, nicotine, some prescription medications, and opioids) raise dopamine levels in the limbic system faster, higher, and longer than any natural reward (e.g. food and sex), causing a euphoric sensation.[9]

Hypnosis: A procedure which alters one's state of consciousness to a mode that is more accepting of suggestion. This procedure is believed to create a way around the typical evaluative, critical, conscious mind and communicate directly with one's subconscious. Hypnosis has been used for smoking cessation, but with conflicting results.[3]

Lapse: A brief episode of drug use after a period of abstinence which is usually unexpected, of short duration, has relatively minor consequences, and is marked by a patient's desire to return to abstinence. A lapse can progress into a full-blown relapse with sustained loss of control.[1]

Maintenance treatment: Dispensing or administering an opioid medication (e.g. methadone or buprenorphine) at a stable dose over 21 days or more for the treatment of opioid addiction.[1]

Medication-assisted treatment (MAT): Any treatment of opioid addiction that includes a medication (i.e. methadone, buprenorphine, or naltrexone) and is approved by the FDA for opioid detoxification or maintenance treatment.[1]

Meditation: The self-regulation of attention. During mindfulness meditation one must focus their full attention on a designated object of meditation, like one's breath. This exercise trains the mind and provides a person with relaxation, metacognition, and the revelation of previously subconscious ideas. By focusing the mind, one can work to reduce pain and change the negative mental/emotional states involved with addiction.[3]

Misuse or **non-medical use**: Incorporates all uses of a prescription medication other than those that are directed by a physician and used by a patient within the law and requirements of good medical practice.[1]

Motivation: Complex mixture of biological, psychological, and social factors that together drive a person.[5]

Motivational interviewing: A directive, client-centered counseling style for eliciting behavior change by helping clients to explore and resolve ambivalence.[5] Ambivalence is the conflict of opposing ideas and attitudes which the client must articulate and resolve on his/her own, only guided by the counselor. For example, a client must first ask, "Am I ready to quit?" honestly and then decide within themselves which path to trod. It is the counselor's duty to lead them to this question, guide the process, and instill within them the confidence to pursue a change.

Neuroplasticity: The ability of the nervous system to adjust or compensate to an injury or disease.[10] Often neuroplasticity is a good thing, but with persistent pain or chronic drug/alcohol use, these changes can make matters worse, or cause new problems altogether (e.g. psychiatric disorders or opioid induced hyperalgesia).

Opioid abuse/dependence: Repeated use of a drug while producing problems in three or more areas over a 12-month period. Areas include tolerance, withdrawal, overdose, and use despite impending adverse consequences. The most commonly abused opioid is oxycodone from diverted prescriptions, followed by morphine, meperidine, fentanyl, methadone, buprenorphine, butorphanol, tramadol and pentazocine.[11]

Opioid Treatment Program (OTP), Methadone Clinic, or Narcotic Treatment Program: Any federally certified treatment program which provides supervised assessment and medication-assisted treatment of patients who are addicted to opioids.[1]

Pain: An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. Pain is a complex experience embracing physical, mental, social, and behavioral processes, compromising the life of many individuals.[10]

Pseudoaddiction: The iatrogenic syndrome resulting from the misinterpretation of relief seeking behaviors as though they are drug-seeking behaviors that are commonly seen with addiction. The relief seeking behaviors of pseudoaddiction resolve upon institution of effective analgesic therapy. Addiction and pseudoaddiction can both occur in the same person.[9]

Reciprocal risk factors: One primary condition puts you at risk for a second condition, but the second condition also can exacerbate symptoms of the first. For example, bipolar disorder puts a person at risk for developing substance abuse or addiction via cyclical mood changes. In return, substance abuse exacerbates a person's bipolar disorder – creating a destructive cycle.[12]

Recovery: A process of change through which individuals improve health and wellness, live a self-directed life, and strive to reach full potential. Recovery must arise from hope and is person-driven. Recovery occurs via many pathways; is holistic; and must be supported by peers, allies, relationships, and social networks. Recovery is culturally-based and influenced; is supported by addressing trauma; involves individual, family, and community strengths and responsibility. Finally, recovery must be based on respect.[1]

Rehabilitation (Rehab): Rebuilding a person's life as a whole after addiction or some other traumatic event. This process is complex and may involve a combination of changes in the biological, psychological, and social aspects of a person's life. This is often the most time intensive element of recovery and may take months to years.[6]

Relapse: A breakdown or setback in a person's attempt to change or modify any target behavior. Relapse may also be defined as an unfolding process in which resumption of substance misuse is the last event in a long series of maladaptive responses to internal or external stressors or stimuli. Relapse may be influenced by many aspects of life including physiologic and environmental factors.[1]

Self-efficacy: A person's belief that change is possible and that they can accomplish it.[5] In general, a person must first believe that they are fully capable before they undertake a change. For example, one must have confidence and know they are strong enough to leave drugs/alcohol. During this process it is important for both counselors and clients to remember that everyone has unused potential and that everyone is capable of change.

Self-medication: The use of un-prescribed drugs to treat a medical problem. Self-medication is sometimes used by individuals with mental disorders to ameliorate the discomfort of their disease. However, these patients often become addicted to their medications and thus comorbidity develops.[12]

Tolerance: A physiologic state resulting from regular use of a drug in which an increased dosage is needed to produce a specific effect. Or, a reduced effect is observed with a constant dose over time. Tolerance may, or may not, be evident during opioid treatment and does not equate with addiction. Tolerance can occur to an opioid's analgesic effects and to its unwanted side effects, i.e. sedation, and nausea.[1] Physiologically, when using a drug like alcohol, nicotine, some prescription medications, or opioids, changes take place in the brain. Over time, these changes down-regulate natural dopamine production and reduce the brain's ability to respond to dopamine. An addict will perceive this relative lack of dopamine in the brain as increased tolerance, and he/she will often counter it with increased drug use.[9]

Trial period: The period of time when medication or other treatment efficacy is tested to determine whether treatment goals can be met. If goals cannot be met, the trial is discontinued and an alternate treatment may be considered.[1]

Waiver: Documented authorization from Secretary of Health and Human Services that exempts a qualified physician from rules applied to Opioid Treatment Programs (OTPs) and allows him/her to use buprenorphine for treating addiction in an office-based practice.[1]

Withdrawal: If drug use is stopped abruptly, a withdrawal syndrome can occur where adaptive body responses, originally present to counter and detoxify the drug, become unopposed and often produce a painful experience for the drug user. Withdrawal is the cardinal sign of physical dependence on a drug.[7]

Drug Glossary

Adderall (dextroamphetamine and amphetamine mixed salts, or amphetamine salts): Are amphetamine stimulants used to treat attention-deficit/hyperactivity disorder and narcolepsy. Adderall has abuse potential and is a schedule II controlled substance in the U.S.[13]

Amphetamines: A class of drugs derived from phenylethylamine that can be administered via inhalation, injection, or "snorting" via nasal insufflation to produce stimulant and/or hallucinogenic effects. These drugs have their effects via changing catecholamine levels; catecholamine release may be enhanced, reuptake blocked, receptors stimulated directly by drug, or breakdown inhibited (i.e. monoamine oxidase blockage). In addition, some amphetamines stimulate release of serotonin and affect serotonin receptors directly, which causes the hallucinogenic effect of designer amphetamines. Amphetamines include methamphetamine as well as various medications for attention-deficit disorder, and various designer drugs developed by illegal labs to give hallucinogenic effect.[14] Amphetamine overdose or abuse is life-threatening and can cause hypertension, cardiac arrhythmia/failure, subarachnoid/intracerebral hemorrhage, stroke, convulsions, and/or coma.[15]

Bath salts: Refers to a new category of designer drugs whose exact chemical composition, short-term effects, and long-term effects are not well known. Often, these products contain amphetamine-like chemicals (e.g. methylenedioxypyrovaleron (MPDV), mephedrone, and pyrovalerone) as their active ingredients which cause stimulant and hallucinogenic effects. Mephedrone is known to trigger intense cravings on par with methamphetamine dependence, which makes bath salts incredibly addictive. Bath salts go by the following names: Ivory Wave, Purple Wave, Red Dove, Blue Silk, Zoom, Bloom, Cloud Nine, Ocean Snow, Lunar Wave, Vanilla Sky, White Lightning, Scarface, and Hurricane Charlie.[16]

Cocaine (Coke): A natural alkaloid extract of the Erythroxylon coca plant which is water soluble and absorbed across any mucosal surface (e.g. oral, nasal, GI, vaginal, etc.) or injected. This drug acts as a central nervous system stimulant and local anesthetic. Cocaine acts as a stimulant by blocking reuptake of norepinephrine, dopamine, and serotonin at nerve terminals leading to the buildup of neurotransmitters – causing euphoria among other effects. Anesthetic action of cocaine is via blockage of fast sodium channels, and thus nerve impulse conduction.[14]

Controlled Substance: A drug that is subject to special requirements under the federal Controlled Substances Act (CSA). Most opioids are Schedule II or III drugs under CSA, meaning they have high potential for abuse, are medically acceptable treatments in the U.S., and that their abuse may lead to psychological or physical dependence. All controlled substances have some potential for abuse.[1]

Crack cocaine (Crack): Sodium bicarbonate is used with cocaine to make a stable freebase "rock" form that is smoked with a characteristic "crackling" sound upon burning.[15]

Ecstasy (3, 4-methylenedioxymethamphetamine or MDMA): Derived from methamphetamine as a "designer drug," ecstasy has typical amphetamine stimulant activity with added vivid hallucinations. Typically MDMA is taken orally, but can be injected or "snorted." In addition to the risks of amphetamines, this drug can cause cognitive and memory problems even after ending use.[15]

Focalin (dexamethylphenidate): A d-threo enantiomer of racemic methylphenidate (Ritalin) and is used to treat attention-deficit/hyperactivity disorder. Like Ritalin, Focalin has abuse potential and is a schedule II controlled substance in the U.S.[13]

Heroin (diacetylmorphine): Semisynthetic crystalline white powder opioid that is smoked, injected, or "snorted" via nasal inhalation to produce an intense euphoria. Heroin may be referred to on the streets as big H, blacktar, boy, brown sugar, dope, horse, junk, mud, skag, or smack.[17]

Methamphetamine (Meth): A mixed-action monoamine with dopamine, serotonin, and norepinephrine system activity. Although this drug gives euphoria and decreased fatigue, it can also produce headache, diminished appetite, abdominal pain, vomiting/diarrhea, sleep disorder, paranoid/aggressive behavior, and/or psychosis. Additionally, chronic use of this drug can cause severe dental problems referred to at times as "meth mouth." On the streets, this drug may be referred to as speed, crank, chalk, ice, glass, or crystal.[15]

Narcotic (Gr. *narkotikos*: "stupor"): Legally, is any drug which is totally prohibited or under strict government regulation (e.g. heroin and morphine) having abuse or addictive potential. This is not a distinct drug class, and its use in medicine is discouraged.[18] In some settings, the term narcotic is specifically associated with opioids, but this is imprecise. Historically, this term was used to describe any drug that induced sleep or narcosis.[19]

Opiate (Gr. *opion:* "poppy-juice"): A compound structurally related to products found in opium (*Papaver somniferum*), including natural plant alkaloids like morphine, codeine, the baine, and other semisynthetic derivatives.[19]

Opioid: Any synthetic narcotic that has opiate-like activity but is not derived from opium (heroin, methadone, hydrocodone, oxycodone). Any agent, regardless of structure, that has the functional properties of an opiate.[19] These drugs are psychoactive via binding opioid receptors in the body, which can cause analgesia (unawareness of pain). Endorphins, which occur naturally in your body, are endogenous opioids. Opioids include naturally occurring, synthetic, or semi-synthetic opioid drugs and medications along with endogenous opioid peptides.[1]

Opioid agonist: Compounds that bind to the mu opioid receptors of the brain, producing a response similar to that of the natural ligand. Full mu opioid agonists (e.g. morphine, heroin, and methadone) produce increasingly intense opioid effects with higher dosage.[1]

Opioid antagonist: Bind to and block opioid receptors preventing activation by opioid agonists (e.g. naltrexone and naloxone).[1]

Opioid partial agonist: Occupy and activate opioid receptors, but their activation reaches a plateau beyond which more opioid does not increase effect (e.g. buprenorphine).[1]

Ritalin (methylphenidate): A piperidine derivative structurally related to amphetamine is a mild CNS stimulant with pharmacological properties similar to amphetamines. Ritalin has abuse potential and is a schedule II controlled substance in the U.S.[13]

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Appendix A

An Approach to Managing Chronic Non-Terminal Pain

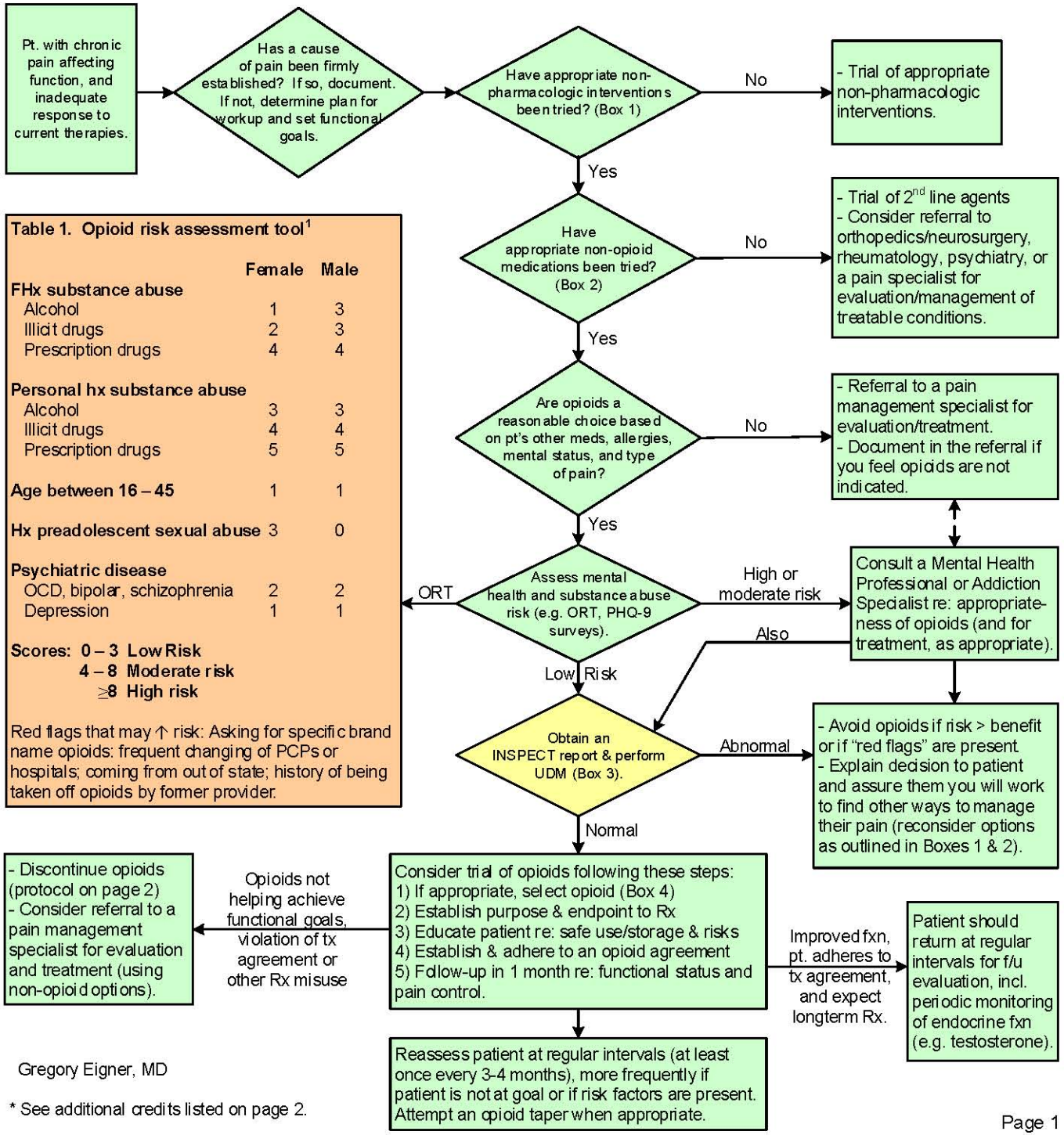


Table 1. Opioid risk assessment tool[1]

	Female	Male
FHx substance abuse		
Alcohol	1	3
Illicit drugs	2	3
Prescription drugs	4	4
Personal hx substance abuse		
Alcohol	3	3
Illicit drugs	4	4
Prescription drugs	5	5
Age between 16 – 45	1	1
Hx preadolescent sexual abuse	3	0
Psychiatric disease		
OCD, bipolar, schizophrenia	2	2
Depression	1	1

Scores: 0 – 3 Low Risk
4 – 8 Moderate risk
≥8 High risk

Red flags that may ↑ risk: Asking for specific brand name opioids: frequent changing of PCPs or hospitals; coming from out of state; history of being taken off opioids by former provider.

Box 1. Non-pharmacologic interventions[3]

MSK/inflammatory pain:
- Ice or heat packs
- Progressive exercise, stretching, yoga, relaxation, meditation
- Physical therapy, TENS therapy, hypnosis
- Manipulation (D.O., chiropractor)
- Occupational therapy, work conditioning
- Massage, acupuncture, biofeedback, Cognitive Behavior Therapy
- Surgical evaluation (e.g. joint replacement for OA)
- Interventional pain modalities
- Self-care; new mattress, new shoes
- Counseling (tobacco cessation, nutrition/weight loss)

Visceral pain:
- Dietary and other GI interventions

General:
- Review sleep hygiene

Box 2. Non-opioid medications for chronic pain[2]

MSK/inflammatory pain:
- Acetaminophen (max. 3-4 g/day)
- NSAIDs (in select nonelderly pts, monitoring GI/renal toxicity)
- Topical anesthetics (lidocaine – cream, ointment, patch)
- Anti-inflammatory creams (diclofenac cream, gel)
- Steroid injections
- Muscle relaxants (cyclobenzaprine)

Neuropathic pain:
- Tramadol (weak opioid)
- TCA's (SOR-A): nortriptyline, desipramine
- Topical anesthetics, Neuropathic creams
- SNRI's (SOR-A): duloxetine (Cymbalta®), milnacipran (Savella®)
- Anticonvulsants: gabapentin (Neurontin®), pregabalin (Lyrica®)

Visceral pain:
- NSAIDs and/or acetaminophen
- Antispasmodics (e.g. dicyclomine)

Restore sleep:
- Melatonin, TCA's, trazadone
- Avoid BZD's due to tolerance/abuse risk

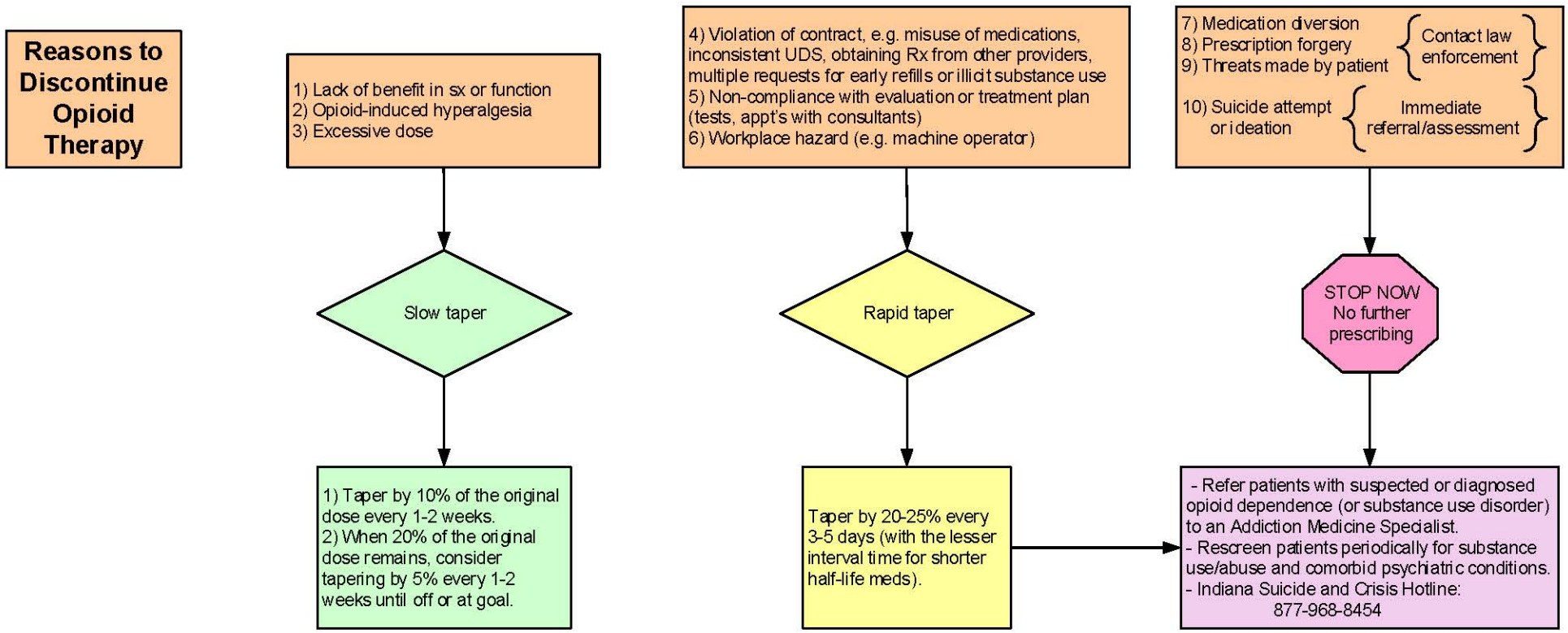
Box 3. Urine Drug Monitoring (UDM) – see Toxicology Section
- Obtain urine drug screen at start, then random testing ≥ once/yr
- List controlled substances that the patient is prescribed on lab requisition, including dose/frequency & time/date of last dose.
- "Opioids" reported on UDM are codeine and morphine only.
- Specific assay required for synthetic opioids (hydro/oxycodone).

Box 4. Opioid selection[2] **(augmenting other treatments)**
- Lack of evidence for long-term benefit in chronic non-cancer pain (e.g. low back pain). Avoid use in chronic H/A, fibromyalgia, IBS.
- Begin with a short-acting opioid (e.g. hydrocodone/oxycodone → morphine) while titrating up; transition to a single, long-acting form (e.g. MS Contin®) when a stable daily dose is established.
- When switching to a different opioid, calculate the Morphine Equivalent Dose (MED) and reduce by 25-50% initially for safety.
- Avoid MED > 50-100 mg/day dose to minimize overdose risk.
- Breakthrough dosing has not been shown to improve outcomes.
- Avoid concurrent use of multiple opioids or co-tx with BZD's.
- Brand name formulations (e.g. Percocet®, Oxycontin®, Opana®) have high street value and may pose increased diversion risk.
- Avoid methadone for safety (ADR's, long variable T-½, OD risk).

Gregory Eigner, MD

* See additional credits listed on page 2.

Discontinuing Opioids



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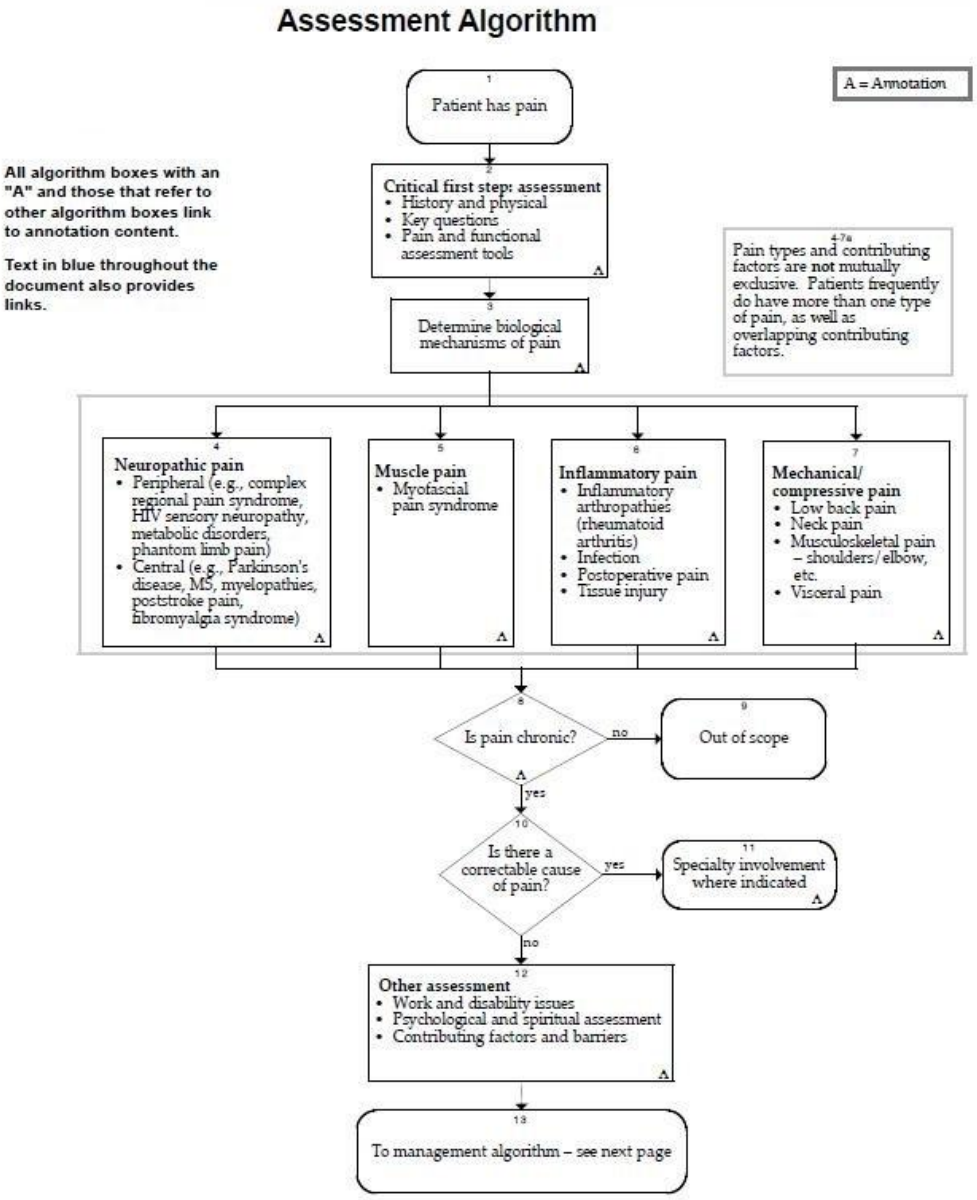
Medications that may be used to manage withdrawal symptoms (for patients that remain under your care):

1) Clonidine 0.1 – 0.2 mg q6h, or transdermal patch 0.1 mg/24h (monitor BP).
2) Promethazine 25 mg q6-8h, as needed for nausea.
3) Short term use of a non-BZD sleep aid for insomnia, if indicated.

Appendix B Assessment Algorithm

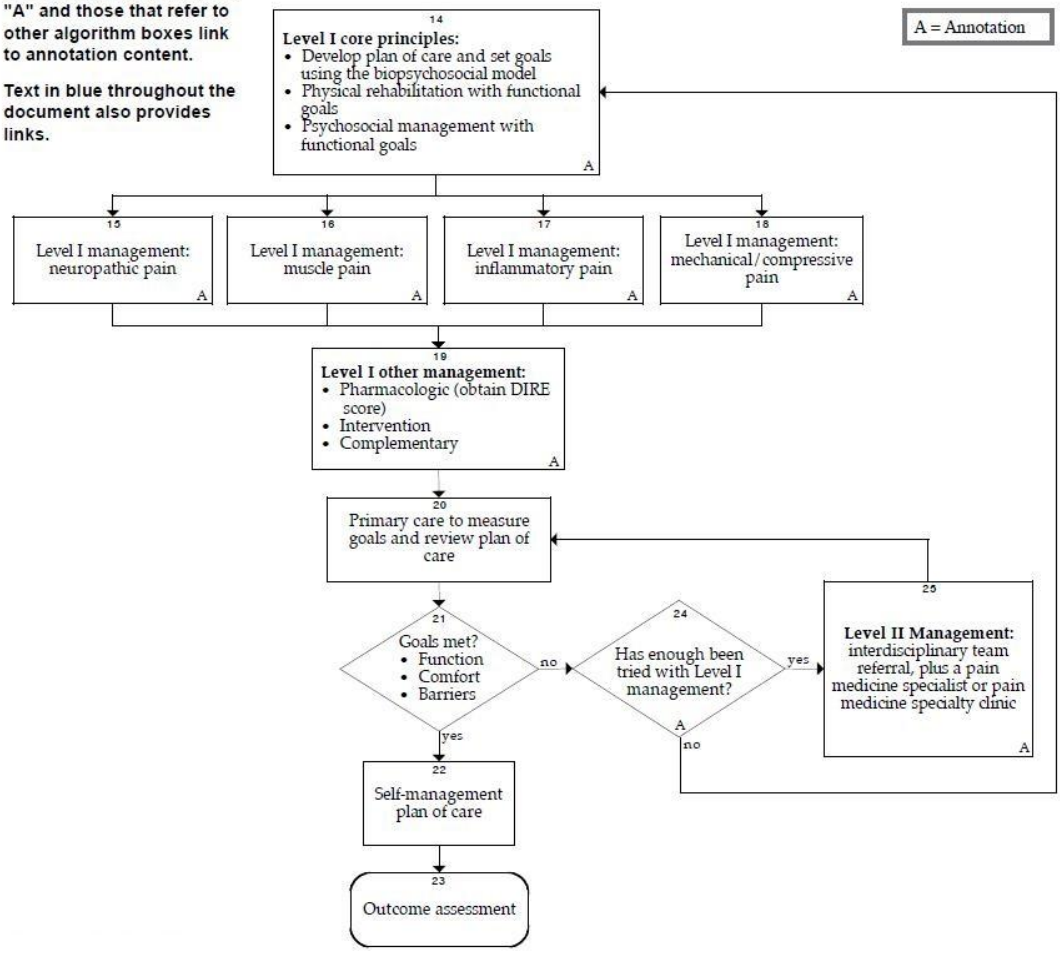


Appendix C
Management Algorithm

Management Algorithm

All algorithm boxes with an "A" and those that refer to other algorithm boxes link to annotation content.

Text in blue throughout the document also provides links.



Appendix D

Sample Chronic Pain Opioid Informed Consent

Please ask questions if there is anything that is hard to understand.

GOALS: There are two goals in the treatment of chronic pain: (1) lower pain; and (2) improved daily life functions. There are many possible treatments for chronic pain and I should use all of them I can before and during a chronic opioid trial (physical therapy, yoga, massage, home daily exercise, meditation, relaxation techniques, injections, chiropractic manipulations, surgery, cognitive therapy, hypnosis and many medications that are not addicting). Management of chronic pain can help but, it will not remove all of my pain and may not restore all my function.

NO GUARANTEES: Opioids are strong medicines and even opioids may not be good at lowering my pain. A good response will be a 20-40% decrease in pain. It is rare to receive more than that if opioids are used for over 4 months. The benefit I get from my opioid medicine should include increased activity and function. There is little scientific evidence that pain relief and benefit last more than 4 months after starting chronic opioids. Simply taking more may lead to more problems: addiction, sedation, falls, constipation or overdose.

SIDE EFFECTS: Opioids can be used safely but this requires honest communication and monitoring. Many bad things can happen when I take opioids and some will result in stopping the medication. Opioids can cause:

1. Constipation, nausea, vomiting and slows stomach emptying

2. Sleepiness, lightheadedness, slows thinking, falls, and increases clumsiness. These side-effects impair my ability to drive or use equipment. I must be careful and tell my doctor when I have these symptoms.

3. Problems breathing, sleep apnea, and reduced coughing. This is dangerous and very dangerous if I have lung disease.

4. Lowering of testosterone, loss of bone strength, loss of stamina and sex drive.

5. Unintentional overdose – increased 500% in Indiana during time of increased opioid use (~ 10 yrs).

6. Critical pregnancy concerns and neonatal abstinence syndrome – I should discuss with my doctor any plans to become pregnant and report any pregnancy ASAP. Very important to mothers and baby's health.

7. Increased risk of addiction and abuse – Addiction can happen even if started for valid pain use.

8. Many interactions with alcohol, Xanax/Valium/Klonopin-like medications. These interactions are especially dangerous if I have lung disease. They can cause me to "black-out" and even overdose. Taking opioids with these medications should be strongly avoided.

9. An increase in my pain called hyperalgesia. Opioids can change my brain and nerves in a way that causes me more pain and more trouble getting pain relief.

10. Dependence-withdrawal symptoms if I miss a dose or run out from over-taking. This is very uncomfortable and may include an uneasy feeling, increased pain, irritability, belly pain, diarrhea, sweats and goose-flesh.

AGREEMENT: I have read the above and have had all my questions answered. I know that chronic pain can be managed with many types of treatments. A chronic opioid trial may be part of my treatment but I must be an active participant in my care. Opioid medication is only one part of my pain management. There is limited scientific data to suggest that using opioids over 4 months will lower my pain and or improve my daily function. There is some scientific information that suggests using chronic opioids can increase my pain, make me feel less well, and increase my risk of unintentional death directly related to the opioid medication. I know that if my provider feels my risk from opioids is greater than my benefit, I will have my opioids compassionately lowered or removed altogether. I agree to a chronic opioid trial.

I further agree to allow this office to contact family or friends if there are concerns about my safety and use of the opioid medications.

Patient: _____

Date: _____

Witness: _____

Date: _____

Appendix E

Sample Prescriber-Patient Agreement
Opioid Treatment for Non-Terminal Pain[1]

This agreement is designed to share information about the medications you will be taking for pain. It will also help you and your healthcare provider comply with controlled substance regulations. Your prescriber's goal is to improve your quality of life while balancing the risks of medication. The success of your treatment depends on trust, honesty and understanding how opioids are used.

You have agreed to use opioids (morphine-like drugs) as part of your treatment for pain. These drugs can be useful, but have high potential for misuse and are therefore closely regulated. Violation of any part of this agreement may result in this medication being discontinued, as well as termination of your relationship with your provider.

I agree to the following conditions:

- I am responsible for my **pain medications**.
- I will not increase the dose of my medication unless my provider says it is OK. I understand that lowering the dose or stopping my medication without my provider's approval can cause withdrawal.
- I understand that this opioid medication is strictly for me. This medication should **never** be given or sold to others because it may endanger that person's health and is also **against the law.**
- I will not request or accept a controlled substance medication from any other prescriber or individual while I am a patient at [Name of doctor or clinic here]. (However, be sure to have a procedure in place for patients who go to emergency room for trauma or other acute pain needs).
- It is my responsibility to notify my healthcare provider of side effects that continue or are severe (i.e., sedation, confusion). I am also responsible for notifying my prescriber immediately if I need to visit another physician or need to visit an emergency room due to pain, or if I become pregnant.
- I will inform my healthcare provider of all medications I am taking, including herbal remedies. Medications like Valium or Ativan, sedatives such as Soma, antihistamines like Benadryl, and cough syrups can interact with opioid medications and be dangerous.
- I understand that opioid prescriptions will not be mailed.
- I will communicate fully with my prescriber about my pain level and my activities during my initial visits and during all follow-up visits.
- I will not use any illicit substances such as cocaine, marijuana, etc. while taking these medications.
- I understand that the use of alcohol together with opioid medications is dangerous and can lead to death.
- I am responsible for my opioid medications. I understand that:
    - Refill prescriptions can be written for a maximum of one month's supply and will be filled at the same pharmacy. Pharmacy: _____ Phone number: _____
    - It is my responsibility to schedule appointments for the next refill before I leave the clinic or within three days of my next clinic visit.
- I am responsible for keeping my pain medications in a safe and secure place, such as a locked cabinet or safe. I am expected to protect my medications. If my medication is stolen, I will report this to my local police

department and obtain a stolen item report. I will also report the stolen medication to my physician. If my medications are lost, misplaced or stolen, my physician may choose not to replace my medications.

- Refills will not be made as an "emergency." They will be made at planned clinic visits, during regular business hours. **No** refills of any medications will be done during the evening or on weekends.
- Refills can only be filled by a pharmacy in the [State], even if I am a resident of another state.
- I must bring back all medications prescribed by my healthcare provider in the original bottles at every visit.
- Prescriptions will not be written in advance due to vacations, meetings or other commitments.
- If an appointment for a prescription refill is *missed*, another appointment will be made as soon as possible. *Immediate* or *emergency* appointments will not be granted.
- If it appears to my healthcare provider that there is no improvement in my daily function or quality of life from the controlled substance, my medicine may be discontinued.
- I agree and understand that my physician has the right to perform random urine drug testing. If requested to provide a urine sample, I agree to cooperate. If I decide not to provide a urine sample, I understand that my doctor may change my treatment plan. This might include safe discontinuation of my opioid medications or complete termination of our patient-prescriber relationship. The presence of a non-prescribed drug (s) or illicit drug (s) in my urine may cause termination of our relationship.
- I agree to allow my healthcare provider to contact any healthcare professional, family member, pharmacy, legal authority, or regulatory agency to obtain or provide information about my care or actions *if the he or she feels it is necessary*.
- I understand that non-compliance with the above conditions may result in a re-evaluation of my treatment plan and discontinuation of my medication. I may be gradually taken off these medications, or even discharged from the clinic.

I _____ have read the above information or it has been read to me and all of my questions regarding the treatment of pain with opioids have been answered to my satisfaction. I hereby agree to participate in the opioid medication therapy and acknowledge that I have received this document.

Patient's Signature

_____Date_____

Prescriber's Signature

_____Date_____

[1]http://www.health.ri.gov/forms/agreements/SamplePrescriberPatientAgreementOpioidTreatmentForNonCancerPain.doc

Appendix F

Sample Combined Prescriber-Patient Agreement & Informed Consent

Franciscan St. Francis Health

Opioid (Narcotic) Consent Form and Management Agreement

This consent and agreement for treatment between the undersigned patient and prescribers at Franciscan St. Francis Pain Center is to establish clear conditions and consent for the prescription and safe use of pain controlling opioid medications or other controlled substances prescribed by the healthcare provider for the patient.

These medications are being prescribed only for the purpose of treating pain. Along with medications, other medical care may be prescribed to improve the ability to do daily activities. This may include exercise, use of non-opioid analgesics, physical therapy, psychological evaluation/ counseling, weight management, classes on managing pain, integrative therapies such as acupuncture and Healing Touch, or other beneficial therapies or treatment.

The Patient agrees to and accepts the following conditions for the management of pain medication prescribed by the Physician/Nurse Practitioner for the patient. Failure to comply with the conditions in this agreement may result in these medications being discontinued and possible termination of the prescriber/patient relationship.

I understand that a reduction in the intensity of my pain AND improvement in my daily life functions are the goals of this program. Should it become evident that these goals are not being met with the use of pain medications, I understand the medications may be weaned and/or discontinued.

1. I must comply with the following guidelines:
    a. I will only use this medication for purposes of pain control.
    b. I will take the prescribed medication only at the dose and frequency prescribed.
    c. I will not increase or change the dose or frequency without consulting my prescriber first.
    d. If I use my medication at a faster rate than prescribed I will be without medication for a period of time and this could result in dependence withdrawal that is uncomfortable and may include an uneasy feeling, increased pain, irritability, belly pain, diarrhea, sweats and goose-flesh and/or serious physical or psychological effects.
    e. EARLY refills may not be given.
    f. I will not attempt to get pain medication from any other healthcare provider.
    g. I will inform all other healthcare providers (ER, surgeon, dentist, etc.) that I am receiving pain medications from this prescriber. Should I receive any other prescriptions for pain medication I will inform this provider of the exact medication I received by the next business day.
    h. I am expected to keep scheduled office appointments.
    i. I will obtain all medications from one pharmacy.

        Pharmacy _____Location _____Phone_____

    j. I am required to keep my prescriber up to date on all medications that I am taking especially other sedating medications such as medications for anxiety (Xanax, Valium, Klonopin, Lorazepam, etc.), for depression or other mental health conditions, for allergies (antihistamines that cause drowsiness such as Benadryl), for sleep: prescription (Ambien, Restoril, Lunesta, etc.) and over-the-counter (Tylenol PM, etc.) for cough (Tussinex, etc.) and for muscle relaxation (Flexeril, Soma, Zanaflex, etc).
    k. I will consent to random drug screening at the provider's request. Unexpected results may result in changing or discontinuing my medications.
    l. I agree to bring my pain medication into the office to be counted if requested.

m. I will not use this medication with any alcohol containing beverages.
n. I will not use any illegal substances including marijuana, cocaine, amphetamines, etc.
o. I will not attempt to forge or call in a prescription for myself or any other individual. I will not attempt to alter the prescription in any way written by the prescriber. I understand that these are prosecutable offenses and may be reported to the authorities.
p. If I am arrested or incarcerated related to legal or illegal drugs my medications may be discontinued.
q. I will not share, trade or sell my medication for money, goods or services. I understand that these are prosecutable offenses and may be reported to the authorities.
r. I am responsible for the protection and security of my medications. I will keep them in my possession or in a secure place at all times not allowing anyone else, including family, friends, children and at-risk adults, access to these medications.
s. If my medications are lost or stolen a re-evaluation of my competence to continue on these medications may be performed.

2. I understand refills of my prescriptions should be addressed in person at scheduled office visits. I will not stop by the office without an appointment and I understand I will not be seen and refills will not be addressed without an appointment. Refills may not be made nights, weekends or holidays.
3. I agree to be evaluated by a psychiatric specialist, psychologist and/or addiction specialist at any time during my treatment at my doctor's request. I agree to the release of those records and reports to my prescriber. If, in their opinion I am not a candidate for further opioid treatment, I understand my medications may be weaned and discontinued.
4. I agree to waive any applicable privilege or right of privacy or confidentiality with respect to the prescribing of my pain medications. I authorize the Prescriber and pharmacy to cooperate fully with any city, state, or federal law enforcement agency in the investigation of any possible misuse, sale or other diversion of pain medication. I authorize the Prescriber to provide a copy of this agreement to my pharmacy and my other healthcare providers.
5. I understand that it is my responsibility to keep others and myself from harm, including the safety of my driving. If there is any question of impairment in my ability to safely perform any activity, I agree not to attempt to perform such activity until I have discussed this with my provider.
6. I further accept full responsibility for any sickness, injury or untoward event which may happen to anyone else as a result of my taking any of the medications prescribed by this provider.
7. I understand that the long-term effects of opioid therapy have yet to scientifically be determined and treatment may change throughout my time as a patient. I understand, accept and agree that there may be unknown risks associated with the long-term use of opioids and my doctor will advise me as knowledge and training advance and will make appropriate treatment changes.
8. I understand that all medications have potential side effects. For pain medications these include but are not limited to: addiction, physical dependence, pseudoNonaddiction, chemical dependence, constipation which may be severe enough to require medical treatment, difficulty with urination, drowsiness, cognitive impairment, nausea, itching, depressed respiration, reduced sexual function and adverse effects or injury to the organs. A distinct clinical syndrome, "hyperalgesia syndrome", has been described in the literature and can actually result in increased pain from continual and escalated does of opioid medication.
9. I understand if I take more medication than prescribed or combine opioids with other sedating medication or alcohol it could result in coma, organ damage, or even death. These interactions are especially dangerous if I have lung disease such as COPD or sleep apnea.
10. Women of child bearing age: I understand if I am planning to become pregnant, if I become pregnant or if I am suspicious that I am pregnant, I will notify my prescriber immediately. I further accept that any medication may cause harm to my embryo/fetus/baby and hold the prescriber and all staff harmless for injuries to the embryo/fetus/baby.

I have read the above and have had all my questions answered. I know that pain can be managed with many types of treatments. If I am receiving pain medications for a trial period, for an expected acute or subacute condition or for a specific timeframe such as a work related injury then this agreement applies to the timeframe that this provider prescribes pain medication.

Opioid medication is only one part of my pain management plan of care. There is limited scientific data to suggest that using opioids over 4-5 months will lower my pain and or improve my daily function. There is some scientific information that suggests using opioids can increase my pain, make me feel less well, and increase my risk of unintentional death directly related to the opioid medication. I know that if my provider feels my risk from opioids is greater than my benefit, I may have my opioids compassionately lowered or removed altogether.

I understand that no agreement can anticipate all events in medical treatment that may arise and that for myself and my heirs, I will hold harmless the prescriber, the practice, the clinic, its officers, owners and staff for all resultant problems. By my signature below, I agree to all the above terms both explicit and implicit.

Patient _____ Date_____

Prescriber_____Date_____

Witness (receipt of copy of agreement):_____

Staff Please Note: A copy of this agreement should be provided the patient upon signing.

Appendix G

Assessment and Management of Patients with Acute Pain

Table 1: Do's for Assessment and Treatment of Acute Pain

Perform a thorough medical evaluation, including detailed history.
Perform a comprehensive pain assessment including the following: ▪ Location of pain ▪ Description of pain such as aching, throbbing, shooting, stabbing, gnawing, sharp, tender, burning, exhausting, tiring, penetrating, nagging, numb miserable and/or unbearable ▪ Is it occasional or continuous? ▪ What time of day is pain the worse? ▪ Document pain intensity using the Numerical Pain Intensity Scale (NPI), Visual Analog Scale (VAS), Faces Pain Scale-Revised (FPS-R) or the Verbal Descriptor Scale (VDS) ▪ Identify aggravating and alleviating factors ▪ Determine if the pain interferes with activity, sleep, mood, normal work and ability to concentrate
Review the current treatments or medicines that the patient is currently using.
Review the effectiveness of any previous pain treatment.
Review what side effects or symptoms the patient is having from the medications they are using.
Consider anti-inflammatory drugs and non-opioid drugs as first line therapy.
Consider ancillary services such as massage, acupuncture or relaxation techniques such as deep breathing.
Prescribe physical and occupational therapy as soon as possible if indicated.
If no improvement consider referral/consult to pain specialist for additional non-pharmacological interventions.
Screen patients for depression, other mental health conditions and potential substance abuse prior to starting any opioid therapy.
Clarify that opioids are for time-limited use and explain that discontinuing opioids may be difficult.

Table 2: Don’ts for Assessment and Treatment of Acute Pain

Don’t use opioids when there are alternative safe, effective treatments.
Don’t prescribe more opioids than your patient is reasonably expected to need.
Don't start long-term use of opioids by accident.
Don't prescribe extended-release opioids for acute pain or to opioid-naive patients.
Don't assume patients know how to use opioids safely.
Don’t continue to prescribe opioids without verifying appropriate use by your patient.
Don’t assume patients are doing well with the opioids without careful evaluation.
Don't abandon patients with a prescription drug problem.
Don't start a treatment that you are not prepared to stop.
Don't initiate chronic opioid therapy before considering safer alternatives.

TITLE 844 MEDICAL LICENSING BOARD OF INDIANA

Emergency Rule
DIGEST

Temporarily adds provisions under P.L. 185-2013 (SEA 246) regarding physicians prescribing opioids for chronic pain. Effective December 15, 2013.

SECTION 1 This document establishes standards and protocols for physicians in the prescribing of controlled substances for pain management treatment. It is adopted under the authority of IC 25-22.5-13-2.

SECTION 2 (a) The definitions in this SECTION apply throughout this document.

(b) "Chronic Pain" means a state in which pain persists beyond the usual course of an acute disease or healing of an injury, or that may or may not be associated with an acute or chronic pathologic process that causes continuous or intermittent pain over months or years.

(c) "Controlled substances" has the meaning set forth in IC 35-48-1-9.

(d) "Morphine Equivalent Dose" means a conversion of various opioids to a standardized dose of morphine by the use of accepted conversion tables.

(e) "Opioid" means any of various narcotics containing opium or one or more of its natural or synthetic derivatives.

(f) "Outset of an opioid treatment plan" means that a patient has been prescribed opioids as described in SECTION 3(c) of this document and therefore the provisions stated in SECTION 3(a) of this document become applicable to that patient.

(g) "Terminal" means a condition caused by injury, disease, or illness from which, to a reasonable degree of medical certainty:

(1) there can be no recovery; and

(2) progression to death can be anticipated as an eventual consequence of that condition.

SECTION 3 (a) This SECTION and SECTIONS 4 through 11 of this document establish requirements concerning the use of opioids for chronic pain management for patients.

(b) Notwithstanding subsection (a), this SECTION and SECTIONS 4 through 11 of this document shall not apply to the use of opioids for chronic pain management for the following:

(1) Patients with a terminal condition.

(2) Residents of a health facility licensed under IC 16-28.

(3) Patients enrolled in a hospice program licensed under IC 16-25.

(4) Patients enrolled in an inpatient or outpatient palliative care program of a hospital licensed under IC 16-21 or a hospice licensed under IC 16-25.

However, a period of time that a patient who was, but is no longer, a resident or patient as described in subdivisions (2) through (4), shall be included in the calculations under subsection (c).

(c) The requirements in the SECTIONS identified in subsection (a) only apply if a patient has been prescribed:

(1) more than sixty (60) opioid-containing pills a month; or

(2) a morphine equivalent dose of more than fifteen (15) milligrams per day;

for more than three (3) consecutive months.

(d) Because the requirements in the SECTIONS identified in subsection (a) do not apply until the time stated in subsection (c), the initial evaluation of the patient for the purposes of SECTIONS 4, 7(a) and 8(a) shall not be required to take place until that time.

(e) Notwithstanding subsection (d), the physician may undertake those actions earlier than required if the physician deems it medically appropriate and if those actions meet the requirements a further initial evaluation is not required. If the physicians conducts actions earlier than required under this subsection, any subsequent requirements are determined by when the initial evaluation would have been required and not at the earlier date it actually was conducted.

SECTION 4 (a) The physician shall do the physician's own evaluation and risk stratification of the patient by doing the following in the initial evaluation of the patient:(1) Performing an appropriately focused history and physical exam and obtain or order appropriate tests, as indicated.

(2) Making a diligent effort to obtain and review records from previous health care providers to supplement the physicians understanding of the patient's chronic pain problem, including past treatments, and documenting this effort.

(3) Asking the patient to complete an objective pain assessment tool to document and better understand the patient's specific pain concerns.

(4) Assessing both the patient's mental health status and risk for substance abuse using available validated screening tools.

(5) After completing the initial evaluation, establishing a working diagnosis and tailoring a treatment plan to meaningful and functional goals with the patient reviewing them from time to time.

(b) Where medically appropriate, the physician shall utilize non-opioid options instead of or in addition to prescribing opioids.

SECTION 5 The physician shall discuss with the patient the potential risks and benefits of opioid treatment for chronic pain, as well as expectations related to prescription requests and proper medication use. In doing so, the physician shall:

(1) Where alternative modalities to opioids for managing pain exist for a patient, discuss them with the patient.

(2) Provide a simple and clear explanation to help patients understand the key elements of their treatment plan.

(3) Counsel women between the ages of 14 and 55 with child bearing potential about the risks to the fetus when the mother has been taking opioids while pregnant. Such described risks shall include fetal opioid dependency and neonatal abstinence syndrome (NAS).

(4) Together with the patient, review and sign a "Treatment Agreement", which shall include at least the following:

(A) The goals of the treatment.

(B) The patient's consent to drug monitoring testing.

(C) The physician's prescribing policies which must include at least:

(i) a requirement that the patient take the medication as prescribed; and

(ii) a prohibition of sharing medication with other individuals.

(D) A requirement that the patient inform the physician about any other controlled substances prescribed or taken.

(E) The granting of permission to the physician to conduct random pill counts.

(F) Reasons the opioid therapy may be changed or discontinued by the physician.

A copy of the treatment agreement shall be retained in the patient's chart.

SECTION 6 (a) Physicians shall not prescribe opioids for patients without periodic scheduled visits. Visits for patients with a stable medication regimen and treatment plan shall occur face to face at least once every four (4) months. More frequent visits may be appropriate for patients working with the physician to achieve optimal management. For patients requiring changes to the medication and treatment plan, if changes are prescribed by the physician, the visits required by this subsection shall be scheduled at least once every two (2) months until the medication and treatment has been stabilized.

(b) During the visits required by subsection (a) the physician shall evaluate patient progress and compliance with the patient's treatment plan regularly and set clear expectations along the way (such as, attending physical therapy, counseling or other treatment options).

SECTION 7 At the outset of an opioid treatment plan, and at least annually thereafter, a physician prescribing opioids for a patient shall run an INSPECT report on that patient under IC 35-48-7-11.1(d)(4) and document in the patient's chart whether the INSPECT report is consistent with the physician's knowledge of the patient's controlled substance use history.

SECTION 8 (a) At the outset of an opioid treatment plan, and at least annually thereafter, a physician prescribing opioids for a patient shall perform or order a drug monitoring test, which must include a confirmatory test, on the patient.

(b) If the test required under subsection (a) reveals inconsistent medication use patterns or the presence of illicit substances, a review of the current treatment plan shall be required. Documentation of the revised plan and discussion with the patient must be recorded in the patient's chart.

SECTION 9 When a patient's opioid dose reaches a morphine equivalent dose of more than sixty (60) milligrams per day, a face-to-face review of the treatment plan and patient evaluation must be scheduled, including consideration of referral to a specialist. If the physician elects to continue providing opioid therapy at a morphine equivalent dose of more than sixty (60) milligrams per day, the physician must develop a revised assessment and plan for ongoing treatment. The revised assessment and plan must be documented in the patient's chart, including an assessment of increased risk for adverse outcomes, including death, if the physician elects to provide ongoing opioid treatment.

SECTION 10 (a) IC 25-27.5-5 addresses the scope of practice of physician assistants in their dependent practice under supervising physicians including limiting the duties and responsibilities of physician assistants to those that are delegated by the supervising physician and that are within the supervising physician's scope of practice. IC 25-27.5-6 addresses supervisory responsibilities of the supervising physician, or when applicable, a physician designee. The prescribing of opioids for chronic pain management as regulated by this document falls within the requirements on supervising physicians, or when applicable, on physician designees, under IC

25-27.5-5 and IC 25-27.5-6 including appropriate delegating of duties and responsibilities to physician assistants and appropriate supervision of physician assistants.

(b) IC 25-23-1-19.4 through IC 25-23-1-19.8, and 848 IAC 5, address the practice of advanced practice nurses with prescriptive authority in collaboration with a physician. The prescribing of opioids for chronic pain management as regulated by this document falls within the requirements on collaborating physicians regarding the prescriptive authority for advanced practice nurses under IC 25-23-1-19.4 though IC 25-23-1-19.8 and 848 IAC 5.

SECTION 11 (a) Initial running of an INSPECT report as required under SECTION 7 of this document shall not be required for any patient who fell within the scope of SECTION 3(c) of this document before December 15, 2013. Initial conducting of a drug monitoring test as required under SECTION 8(a) of this document shall not be required for any patient who fell within the scope of SECTION 3(c) of this document before January 1, 2015. However, all other requirements of this document apply to these patients; that is, every requirement except for the initial running of the INSPECT report and the initial or annual conducting of a drug monitoring test.

(b) Notwithstanding subsection (a) and SECTION 7 of this document, the first running of an annual INSPECT report under SECTION 7 of this document shall not be required to be conducted before November 1, 2014. Nothing about this subsection shall be construed to prohibit a physician from running a report sooner than required by this subsection.

(c) Notwithstanding SECTION 8(a) of this document, the first conducting of an annual drug monitoring test under SECTION 8(a) of this document shall not be required to be conducted before January 1, 2015. Nothing about this subsection shall be construed to prohibit a physician from conducting a test sooner than required by this subsection.

SECTION 12. SECTIONS 1 through 11 of this document take effect December 15, 2013.

Tips for Implementing in Your Practice

The prevalence of lifetime substance use disorders ranges from 36% to 56% in patients treated with opioids for chronic back pain; forty-three percent of this population has current substance use disorder (SUD) and 5% to 24% have aberrant medication-taking behaviors.[1]

Overview

Physicians must be able to safely and effectively prescribe scheduled drugs and, at the same time, must identify and manage misuse and abuse in their practices – all in a relatively short office visit. You will likely find a team approach the most cost-effective strategy for screening, assessing, educating and monitoring your chronic pain patients receiving opioid therapy. Many of the screening tools can be self-administered while in the waiting room or exam room, scored by your nursing staff and ready for your review prior to seeing the patient.

Recommendations

1. Review the Medical Licensing Board Prescribing Rules with your office staff.
2. Review and determine which of the available mental health and addiction screening tools and pain assessment tools you will be using in your practice.
3. Have your office/nursing staff become familiar with the instruments and how to score.
4. Obtain an INSPECT provider number at the INSPECT Prescription Monitoring Program and train your office staff on how to download a report as part of the patient's chart preparation.
5. Determine which drug testing laboratory you would like to use and obtain protocol for specimen collection and submission.
6. Select and modify, if needed, a Treatment Agreement that is most compatible with your practice and ensure that nursing staff is comfortable discussing in more detail after you leave the room.
7. Encourage staff to review the talking points at the end of various toolkit sections to identify "conversation starters."
8. Identify mental health specialists and addiction specialists in your area that you can refer patients to for further treatment if necessary.

9. Consider discussing the process and criteria for referring patients to local pain specialists and other subspecialists. Develop a personal relationship with a pain physician so you may discuss how to deal with patients who are maintained on long-term opiate therapy. The pain specialist can act as your therapeutic shield.
10. Consider creating "educational packets" for patients you are starting on opioid therapy and ensure that nursing staff are comfortable with the materials.
11. Develop a protocol for which you will address patients in whom you find evidence of aberrant behaviors and discuss with staff.

Resources

Screening for Depression/Anxiety

The most widely used and best-validated instruments in the primary care setting are the Patient Health Questionnaire (PHQ)-9 and its two-item version, the PHQ-2.[2]

The PHQ-4 is a valid ultra-brief tool for detecting both anxiety and depressive disorders.[3]

The GAD-7, a 7-item anxiety scale, is a useful screening tool for generalized anxiety disorder (GAD) [4]

The Primary Care PTSD Screen is a four-item screen designed for use in primary care and other medical settings to screen for post-traumatic stress disorder.

Screening for Substance Abuse

The Screener and Opioid Assessment for Patients with Pain (SOAPP)® Version 1.0 is a tool for clinicians to help determine how much monitoring a patient on long-term opioid therapy might need.

The Alcohol Use Disorders Identification Test (AUDIT) is a 10-item questionnaire that screens for hazardous or harmful alcohol consumption. It is particularly suitable for use in primary care settings and has been used with a variety of populations and cultural groups. It should be administered by a health professional or paraprofessional.

The AUDIT-C is a simple 3-question screen for hazardous or harmful drinking that can stand alone or be incorporated into general health history questionnaires.

The DAST-10 (Drug Abuse Screen Test) was designed to provide a brief instrument for clinical screening and treatment evaluation and can be used with adults and older youth.

Informed Consent and Treatment Agreement Templates

Sample Opioid Treatment Agreement
Washington State Department of Labor and Industries

Medication Use Agreement
American Academy of Family Practice (2001)

Agreement for Opioid Maintenance Therapy for Non-Terminal/ Cancer Pain
PainEDU.org (2011)

Sample Medication Management Agreement
P. Fine, MD, University of Utah Hospitals and Clinics Pain Management Center

Pain Medicine Contract for Low Literacy Patients
L. S. Wallace, MD. 2013. Inflexxion, Inc.

General Patient Education

BitterPill.IN.gov
Educational website from Indiana Prescription Drug Abuse Task Force

opioids911.org/
An independent, noncommercial, Internet-based educational activity from *Pain Treatment Topics* for patients and their caregivers focusing on the proper and safe use of opioid pain relievers.

FamilyDoctor.org:
The Safe Use, Storage and Disposal of Opioid Drugs

painACTION.com
A Patient Guide to Pain Management

American Chronic Pain Association
Frequently Asked Questions

Safe Storage/Disposal

StopOxy.com
How to Safely Dispose of Prescription Medication

painACTION.com
How to Take, Store and Dispose of Opioid Medicine

FDA.gov
Disposal of Unused Medicines- What You Should Know

Driving and Work Safety

PainEDU.org
Chronic Opioid Therapy- Driving and Work Safety

opioids911.org/
Frequently Asked Questions about Opioid Safety

Medication Misuse

America's Medicine Cabinet: Use Medicines Safely
Institute for Safe Medication Practices (ISMP)

[1] http://www.acpm.org/?UseAbuseRxClinRef
[2] http://www.aafp.org/afp/2008/0715/p244.html
[3] http://www.ncbi.nlm.nih.gov/pubmed/19996233
[4] http://www.medscape.org/viewarticle/533407

User's Guide to INSPECT

A 2010 study found that when prescription drug monitoring program (PDMP) data were used in an emergency room, 41% of cases had altered prescribing after the clinician reviewed PDMP data –with 61% of the patients receiving fewer or no opioid pain medications than had been originally planned by the physician prior to reviewing the PDMP data, and 39% receiving more opioid medication than previously planned because the physician was able to confirm the patient did not have a recent history of controlled substance use.[1]

What is INSPECT?

INSPECT is Indiana's prescription drug monitoring program (PDMP). INSPECT collects and tracks controlled substance prescriptions that are dispensed to Indiana residents. This data is then made available to medical practitioners and law enforcement to access under certain conditions.

Each time a controlled substance is dispensed by a pharmacy to an Indiana resident, the pharmacy is required to report that data to INSPECT within seven days of the dispensation. That information is stored in a database and is available to query for registered users of the program. Users of INSPECT can request patient Rx History Reports, which show an individual's controlled substance history for a given period of time, including what products were obtained, dates the prescription was written and filled, and information on the prescribing practitioners and dispensing pharmacies listed within the report.

INSPECT does not collect information on any drug that is not a controlled substance or any drugs that are administered to an individual in an inpatient or hospice setting. INSPECT also does not collect any information on a substance dispensed that is less than a 72-hour supply. (Meaning practitioners can dispense samples out of the office and it does not need to be reported to INSPECT as long as it is less than a 72-hour supply.)

INSPECT is free to access and is available for registered users to query at any time, requiring only an internet connection. INSPECT can be accessed by going to www.in.gov/inspect. For locations that are part of the Indiana Health Information Exchange, INSPECT can be immediately accessed by clicking the "INSPECT" tab in your EMR system dashboard viewer.

INSPECT is administered by the Indiana Board of Pharmacy and offices are located in the Indiana Professional Licensing Agency.

Eligibility

Healthcare practitioners that hold a CSR (controlled substance registration) license and an individual DEA number are eligible to apply for access to INSPECT. Sworn law enforcement members are also eligible for an INSPECT account, but may only request reports on individuals involved in an active, ongoing investigation.

To complete an application for access, please follow the registration instructions enclosed, or go to www.in.gov/inspect and click on "Registration Information."

"INSPECT is an invaluable tool for physicians to help complete the prescribing picture."

–John T. Finnell II, MD ER Physician with Wishard Emergency Medicine, Indianapolis

Why Use INSPECT?

A healthcare practitioner accessing INSPECT and obtaining Rx History Reports will be informed of the complete controlled substance history of their patients. Rx History Reports are usually immediately available moments after the request is submitted. The report assists practitioners with patient evaluation and in determining the best treatment and care for a patient. A report may give a practitioner confidence in prescribing a controlled substance to a patient or may deter the practitioner from writing a prescription for a controlled substance altogether.

Reviewing an Rx History Report will also identify if a patient is obtaining controlled substances from multiple practitioners and/or multiple pharmacies, which is known as "doctor-shopping."

Doctor-shopping occurs when a patient seeks to obtain controlled substances from multiple healthcare practitioners, often simultaneously, by either withholding material facts regarding their past and/or present controlled substance treatment or by engaging in deceptive practices meant to stymie attempts by their healthcare practitioners to better coordinate the provision of care.

Although Indiana statute (IC 16-42-19) does not use the term "doctor shopping," it does clearly state that a person may not do any of the following:

1. Obtain or attempt to obtain a legend drug or procure or attempt to procure the administration of a legend drug by any of the following:

A. Fraud, deceit, misrepresentation, or subterfuge.

B. The concealment of a material fact.

2. Communicate information to a physician in an effort to unlawfully to procure a legend drug or unlawfully to procure the administration of a legend drug. Such a communication is not considered a privileged communication.

You can have an employee/agent run the report. However, it is important to note that if you elect to utilize such an agent you are responsible for that agent's access (i.e. any data breaches, unauthorized access, etc. will fall back on you and your license). Also, any administrative issues that require INSPECT staff support need to be addressed by the registered user, not an agent.

Sharing Information with Law Enforcement

Legislation passed during the 2010 General Assembly adds a provision to IC-35-48-7-11.1 stating:

> *(n) A practitioner who in good faith discloses information based on a report from the INSPECT program to a law enforcement agency is immune from criminal or civil liability. A practitioner that discloses information to a law enforcement agency under this subsection is presumed to have acted in good faith.*

Concerns Regarding INSPECT

Monitoring of Prescribing - INSPECT does not monitor physician or practitioner prescribing, or create red flags or "alerts" based on a practitioner's prescribing history.

Practitioner Liability for using INSPECT – It is not currently mandatory to register with or to use INSPECT. A practitioner will not be held liable for anything that occurs because of using or not using INSPECT.

Interstate Data Sharing

INSPECT now shares data with all states surrounding Indiana, in addition to several other states. This means a practitioner with access to INSPECT can make a request for a report on an individual and select any or all of the surrounding states to include data in that report. For example, a practitioner in Jeffersonville, IN may choose to include data from Kentucky or Ohio, or both, when making a request for a patient's Rx History Report. The report returned to the practitioner would

"I have found INSPECT to be a highly valuable tool. This web site, along with my practice of drug screening each new patient, has been very effective in keeping my office free of drug seekers and doctor shoppers."

–Mark K. Stine, M.D., Family Physician, Indianapolis

include patient data not only from Indiana but also from Kentucky and Ohio, if any activity occurred there.

INSPECT currently shares data with the following states: Kentucky, Ohio, Michigan, Illinois, Virginia, Connecticut, North Dakota, Arizona and Kansas.

NOTE: If a user is accessing INSPECT via his or her hospital EMR system or by other integrated data methods, obtaining interstate data may not be included as an option.

Person of Interest Notifications

INSPECT is required by statute (IC 35-48-7-11.5) to inform prescribers and dispensers of patients that meet a predetermined threshold of controlled substance dispensations. That threshold is: patients who have received controlled substances from at least 10 unique DEA numbers in a 60-day period.

Patients who have exceeded that threshold become the subject of a Person of Interest (POI) alert which is then sent by INSPECT to every prescriber and dispenser of that patient. Recipients of a POI alert should request an Rx History Report on that patient via the INSPECT WebCenter. POI alerts contain NO private health information, but do contain enough information for the recipient to perform a request for an Rx History Report.

Practitioner Self-Lookup

Registered users of INSPECT can perform a Practitioner Self-Lookup request if they are a prescriber. Similar to a credit report, this report allows practitioners access to their full controlled substance prescribing history for the requested period of time. This can be a helpful tool if a practitioner has been the victim of Rx pad theft or fraud.

"I have come to love INSPECT and all that it offers. We have a real problem in this area with drug abuse and patients using the healthcare system to sustain their habits. This program gives us one more tool with which to make an educated decision regarding prescription use by patient."

–Anthony Hornaday, D.D.S., Oral and Maxillofacial Surgeon Muncie

Contact Information

Questions regarding INSPECT, patient history reports or other functions of the INSPECT Web application should be directed to the INSPECT office at:

402 W. Washington Street, Room W072, Indianapolis, IN 46204.
Phone (317) 234-4458
Fax (317) 233-4236

inspect@pla.in.gov
www.in.gov/inspect

[1] https://www.ncjrs.gov/pdffiles1/ondcp/pdmp.pdf

Legal Questions Regarding Prescribing Controlled Substances

Disclaimer: These FAQ's are for informational purposes only. They do not constitute legal advice. If you have a specific fact situation about which you need legal guidance, contact a licensed attorney.

Q: What law or rule governs the prescribing of controlled substances?
A: 856 Indiana Administrative Code 2-6-3 Purpose of prescription; prohibitions applies. It states in part: *A prescription for a controlled substance to be effective must be issued for a legitimate medical purpose in a reasonable quantity by an individual practitioner acting in the usual course of his professional practice. The responsibility for the proper prescribing and dispensing of controlled substances is upon the prescribing practitioner, but a corresponding responsibility rests with the pharmacist who fills the prescription. An order purporting to be a prescription issued not in the usual course of professional treatment or in legitimate and authorized research is not a prescription, within the meaning and intent of IC 1971, 35-24.1-3-8 [Repealed by Acts 1976, P.L.148, SECTION 24; Acts 1977, P.L.26, SECTION 25.See IC 35-48] as amended, and the person knowingly filling such a purported prescription, as well as the person issuing it, shall be subject to the penalties provided for violations of the provisions of law relating to controlled substances.*

Q: What do you do if you suspect someone is prescribing illegally?
A: You should contact one of the following agencies:

- The Indiana Medicaid Fraud Control Unit at (317) 915-5300 or online at www.in.gov/attorneygeneral/2789.htm
- The Indiana State Police at 1-800-453-4756
- The Drug Enforcement Administration:
    - Northern Indiana – (219) 681-7000
    - Central and Southern Indiana – (317) 226-7977

Q: Can I simply refuse to write any opioid prescriptions?
A: As noted above, the responsibility for proper prescribing is upon the prescribing practitioner. If you believe that it is in your patient's best interest not to prescribe them opioids then you are well within your rights to refuse to prescribe that class of drugs. Generally, opioids should not be a first choice treatment option. A treatment plan might include use of opiates, but should always be individualized. Multidisciplinary (non-opiate) options almost always exist.

Q: Do I have to continue opioid prescriptions started by another MD?
A: Absolutely not. In fact, you should perform your own history and physical and determine a treatment plan independent of any other treating physician, including whether opioids are appropriate for your patients.

Q: Is it appropriate to simply stop prescribing opioids to someone whom I think is abusing them? Am I permitted to wean an addict off of controlled substances?
A: It is not necessarily negligence if you stop prescribing opioids to a patient you believe is abusing the drugs. Some physicians cut patients off cold turkey and others prescribe a few pills to allow the patient time to seek treatment. It is always a good idea to refer these patients to a treatment facility so that a formal substance use disorder evaluation can be obtained. Unless you have been certified to treat addicts, you may be at more risk for weaning an addict than you are for refusing to wean that person. Remember, if you are not treating a legitimate medical condition with an individualized treatment plan, than exercise your obligation to activate the opiate exit strategy.

Q: Can I get in trouble if I notify the authorities about someone possibly selling narcotics?
A: No. There are no repercussions for a practitioner who, in good faith, reports a person suspected of selling dangerous drugs. Do not hesitate to notify your physician colleagues if you see their names on your patient's INSPECT report, thus indicating unwitting participation in a doctor shopping scheme.

Q: Could the urine drug monitoring results from my office ever be used to prosecute my patient for illicit drug use/trafficking?
A: It is highly unlikely. One of the burdens a prosecutor has is proving that such a person possessed a controlled substance within the prosecutor's jurisdiction. The drug screen merely establishes that the person has ingested a controlled substance, but does not establish where.

Q: If someone steals a prescription pad from me and forges controlled substance prescriptions on my pads, can I be criminally prosecuted?
A: There is not a criminal statute under which you could be prosecuted for being the victim of a theft. However, there remains the possibility that you could be sued civilly if you negligently left your prescription pad out where someone could easily access it.

Q: How much verbal abuse should my office personnel tolerate before contacting authorities?
A: You or one of your employees should contact law enforcement any time you feel someone may inflict physical harm. It is a good idea to have your patient sign an opiate agreement to define behavior expectations. Misbehavior generally connotes lack of patient responsibility, and may impact the decision to continue with opioid treatment. Aggressive behavior, whether physical and or verbal, is a form of aberrancy and should be considered a factor impacting the decision to continue opioid treatment.

Q: What type of patient threats/aggressions should be reported to authorities?
A: All threats to commit violence should be taken seriously and reported to the proper authorities.

Q: Am I at risk for prescribing controlled substances to someone who has a history of substance abuse and he/she overdoses?
A: In general, it is not recommended to prescribe a controlled substance to a person who has a

history of abuse. You should employ non-opioid modalities prior to considering opioids. If you feel you must prescribe a controlled medication, you should keep in mind that it must be for a legitimate medical purpose and the quantity prescribed should be reasonable. If you practice good medicine and adhere to the standard of care, you should not be at risk if your patient overdoses. However, every situation is fact sensitive and it is possible your judgment could be questioned. That is why documentation of your justification for prescribing a controlled substance is so important.

Q: If I am monitoring a patient's urine and detect THC, am I at risk if I continue to provide opioids and the person overdoses or is found to be a diverter?
A: Patient compliance is a key component to successful opioid therapy. The best practice is to ensure the patient understands that it is illegal and dangerous to mix opioids and mind-altering drugs. It may also be a violation of the Treatment Agreement. It is usually best to offer the patient a Substance Use Disorder evaluation. If the patient seems to understand the importance of cessation and is otherwise not at risk, continuing the therapy may be a reasonable approach if monitored closely. If this is a repeated occurrence or the individual is otherwise a high risk patient, terminating the opioid agreement would be the better course of action.

Q: If I am monitoring a patient's urine and detect no opioid usage, am I at risk if I continue to provide opioids and the person overdoses or is found to be a diverter?
A: Yes. If you are prescribing opioids for a patient who is not using the drugs, it is readily apparent that he or she has no legitimate medical need for them. If you check the patient's INSPECT report and find that he or she is still filling the prescription, then it can be inferred that the patient is diverting the drugs. If you continue to prescribe opioids, you are aiding the diversion and can be prosecuted criminally, civilly and administratively.

Q: If a patient, who is known to be an alcohol abuser and is on opioids that I prescribed, is in an accident and appears impaired with an illegal but relatively low alcohol level, am I at risk?
A: The best practice is to withhold controlled substances from known substance abusers. If a law enforcement officer suspects that a driver is under the influence of a controlled substance and alcohol, he can demand a blood test in a hospital setting. If the person tests positive for alcohol and an opioid that you prescribed, you may have to justify the prescribing of that drug. Keep in mind the opioid must be prescribed for a legitimate medical reason and in the course of professional practice. This must be documented in the medical chart.

Q: I have a patient who almost always tests negative for her opioids and is found to be diverting to teenagers and one of the teens overdosed. Am I at risk for that?
A. Once you have objective and clear evidence, such as a urine screen that reveals your patient is not in compliance, the best practice would be to terminate the opioid agreement. If the behaviors have been clearly egregious, releasing him/her from your care may be reasonable. Alternatively, keep treating the patient, but stop all controlled substances. If she is not taking the drugs you are prescribing, then she obviously does not need them. If you continue to prescribe for her and a tragedy happens, you may be held accountable for prescribing opioids without a legitimate medical purpose.

Q: Is it legal for me to write for methadone once daily to treat pain in someone no longer in a narcotic treatment program for addiction?
A: A legitimate pain diagnosis must be documented. Unless licensed accordingly, doctors cannot prescribe opioids for maintenance or treatment of addiction. Although opioid prescription in this scenario is not illegal, it may not be the wisest thing to do. It is much better to find alternative forms of treatment.

Q: Is it legal for me to provide morphine to treat pain for someone who is in a narcotic treatment program and receiving methadone/Suboxone?
A: It is not necessarily illegal if you are prescribing the morphine for a legitimate medical purpose, other than addiction treatment. For example, if you diagnose a patient with kidney stones and the patient is in severe pain, the prescribing of morphine would likely be justified. If you undertake such a measure, you should ensure that the patient's methadone/Suboxone prescriber is aware of the situation.

Q: Does a provider have an obligation to notify the police if the provider has evidence that a patient diverted (shared or sold) his or her controlled substance prescriptions?
A: There is no legal obligation to report drug diversion like there is to report child abuse. It is simply the right thing to do. Under Indiana Code 16-42-19-16(2) information communicated to a physician in an effort to unlawfully to procure a legend drug is not considered a privileged communication.

Q: Does a provider have an obligation to continue care (for 30 days) if a patient violated his or her Treatment Agreement? For example, the patient tests positive for cocaine.
A: You have no obligation to continue care for any time frame as long as it is not explicitly stated in the Treatment Agreement. Some practitioners believe that violators should be cut off immediately; other providers believe it is more appropriate to continue prescribing a modest amount of the drug until the patient can find another provider or get treatment.

Q: Can the INSPECT report be put in the medical record?
A: Yes, the INSPECT report can and should be made part of the patient's medical record.

Q: Who does the provider notify if a patient has falsified/forged a controlled substance prescription?
A: The local police or sheriff's department having jurisdiction over the provider's practice. The Indiana State Police or the Drug Enforcement Administration may also be notified at the phone numbers referenced in the FAQs above.

Q: Can a provider be liable for choosing not to treat a high-risk patient (such as alcohol use disorder) with a controlled substance?
A: No one can force you to treat a person with a controlled substance if you choose not to. It is known that personal or family abuse of alcohol is a legitimate high-risk opioid use factor. It is highly unlikely you could be held liable for choosing an alternative form of treatment if you do so in good faith.

Q: If a provider identifies active substance abuse in a patient during the course of routine treatment, is that information subject to a higher level of confidentiality? (For the purpose of transfer of records or HIPAA)
A: No. Higher levels of confidentiality can apply to mental health treatment, which includes addiction treatment. The substance abuser likely has been violating the law and is subject to being reported to law enforcement.

Q: Can a provider prescribe controlled substances to a patient who uses marijuana?
A: A provider can prescribe controlled substances to a marijuana user, but should do so cautiously and only for a legitimate medical reason. Marijuana contains hundreds of chemicals that have yet to be identified. It is not known how controlled substances will interact with those chemicals. Many Treatment Agreements explicitly forbid THC use while using other controlled substances. If your Treatment Agreement stipulates that THC is not allowed, you should terminate the opioid agreement if the individual will not or cannot stop using THC. In that case, a referral to a Substance Use Disorder evaluation is appropriate.

Q: Should DEA numbers of providers directly be written on physician's prescription pads?
A: Yes. This is recommended by the DEA.

Q: Should providers review INSPECT data with their patients?
A: There is no requirement that a provider review an INSPECT report with his or her patient. That is left up to the discretion of the provider. A provider who is dismissing a doctor-shopping patient may want to show the patient the report to support his or her position.

Q: Should providers document in the patient's medical records the INSPECT score?
A: Yes. This is an objective piece of evidence regarding the patient's use of prescription controlled substances.

Q: Should providers contact local or state police for suspected diversion of controlled substances?
A: It is perfectly acceptable to contact your local or state police.

Q: What reports must be filed if a practitioner experiences a theft or significant loss of controlled substances?
A: The practitioner shall notify the local DEA office, in writing, of the theft or significant loss of any controlled substances within one business day of discovery of such loss or theft. The practitioner shall also complete and submit DEA Form 106 which may be found at www.DEAdiversion.usdoj.gov.

Q: Does DEA have any publications that provide information to practitioners on controlled substance prescribing?
A: Yes, common prescribing and registration information for practitioners can be found within the Practitioner's Manual. For additional information on controlled substances, practitioners should review Policy Statement: Dispensing Controlled Substances for the Treatment of Pain.

Q: Do the local or state police accept anonymous complaints?
A: Yes, however, the more information you can provide the police, the greater the chance they will be able to act on the information.

Q: What is the process the local or state police conduct once a complaint is provided?
A: If you file a complaint with the police, they may want to speak with you in person to get as many details as possible. The police will initiate an investigation and if they find sufficient evidence of a crime will seek to charge the suspect(s). It is possible they may need to follow up with you at some point to confirm or gather more information. It is also possible, given the nature of the complaint, that you may have to testify in court or give a deposition about the criminal conduct.

Important Information about Commonly Prescribed Opioids

Overview

A key component in the treatment of chronic non-malignant pain includes drug therapy. There is a wide range of non-narcotic drug choices indicated for treatment of pain including topical analgesics, NSAIDs, acetaminophen, corticosteroids, antidepressants, and anticonvulsants (Table 1). When alternative classes of medications are deemed inappropriate or ineffective at meeting treatment goals, opioids may be considered for treatment of moderate to severe pain. This particular class of drug exhibits potent analgesic properties, primarily through activity at mu- or kappa- receptors located within the central nervous system (CNS). When used appropriately, integrating opioids into the treatment plan can result in favorable outcomes.

Table 1: Medications Commonly Used for Treatment of Pain

NON-OPIOID ANALGESICS	Aspirin Acetaminophen **NSAIDs** (e.g.- ibuprofen, naproxen, meloxicam, etodolac, diclofenac, ketorolac) **Cox-II inhibitors** (e.g.- celecoxib)
ANTIDEPRESSANTS	**Tricyclic antidepressants** (e.g.- amitriptyline, nortriptyline) **SNRIs** (e.g.- venlafaxine, duloxetine)
ANTICONVULSANTS	Gabapentin Pregabalin
STEROIDS	Methylprednisolone Prednisone Triamcinolone
TOPICAL ANALGESICS	Capsaicin Menthol/Methyl-salicylate Diclofenac Lidocaine
NON-OPIOID/OPIOID COMBINATIONS	Hydrocodone/APAP Oxycodone/APAP Tramadol/APAP
OPIOID ANALGESICS	**Phenanthrenes** (e.g.- codeine, hydrocodone, hydromorphone, morphine, oxycodone, oxymorphone) **Diphenylheptanes** (e.g.- methadone) **Phenylpiperidines** (e.g.- fentanyl) **Other** (e.g.- tramadol, tapentadol)

In this section the following topics will be reviewed:

A. Opioid Treatment Initiation
B. Opioid Treatment Titration
C. Long-acting Versus Short-Acting Opioids
D. Managing Breakthrough Pain
E. Methadone
F. Opioid Conversion
G. Preventing and Managing Opioid-Related Side Effects
H. Monitoring (including adherence)
I. Weaning Opioids
J. Opioids in Pregnancy
K. Safe Use, Storage and Disposal

Opioid Treatment Initiation

The first step of opioid therapy is to select an appropriate agent. The effect of an opioid in terms of safety, efficacy and tolerability vary from individual to individual, thus it is not possible to determine if one opioid is superior to another.[1] Some factors to consider when choosing an opioid include:

1. Dose ceiling based on non-opioid analgesic component on combination products
    a. If substantial dose increases are anticipated, you may want to select a non-combination agent
2. Pregnant and breastfeeding patients
    a. Most opioids carry pregnancy category C rating
    b. Some opioids, such as oxycodone, are rated pregnancy category B[6]
3. Use of methadone in patients with QTc prolongation >500ms should be avoided
    a. Caution in patients with QTc prolongation >450ms
    b. All patients who begin methadone treatment should obtain electrocardiogram (ECG) prior to therapy and at regular intervals throughout course of treatment

To begin opioid therapy, remember the saying "start low and go slow."

1. Initiate one opioid at a time
    a. In most circumstances, start with short-acting agent
    b. For unremitting chronic pain, you may consider initiating opioid therapy with long-acting agent
        i. One exception is transdermal fentanyl, which is only indicated for opioid tolerant patients
2. Always use the lowest effective dose of the opioid

A. Opioid Treatment Titration

Pharmacologically, in most instances, there is no maximum dose for non-combination opioids, although QT prolongation with some opioids has been reported. Dose ceilings for combination products are typically based on the non-opioid analgesic component. For example, hydrocodone/APAP products will have a maximum dose based on acetaminophen content (4000mg APAP/day for acute users, 2500-3000mg APAP/day for chronic users).

1. Titrate up by 25-100% of daily dose[1]
    a. For elderly patients increase dose on lower end of spectrum
2. Frequency of each dose increase is no sooner than every **five half-lives** or longer[1]
    a. Methadone and fentanyl doses should not be increased more frequently than every seven days or longer due to risk of rapid accumulation leading to toxicity[1]
3. Continue titration until one or more of the following:
    a. Therapeutic goals have been met
    b. Patient experiences intolerable side effects
    c. Treatment has shown to be ineffective
4. Re-evaluate patient if opioid dose increases are unsuccessful in reducing pain
    a. Ensure patient is being compliant with medications
    b. Determine if there is a cause that is contributing to higher level of pain
        i. Increased activity level
        ii. Disease state progression
        iii. Other factors
    c. Consider switching to alternative opioid if appropriate
    d. Consult Interventional Pain Management in more complex cases

C. Long-Acting Versus Short-Acting Opioids

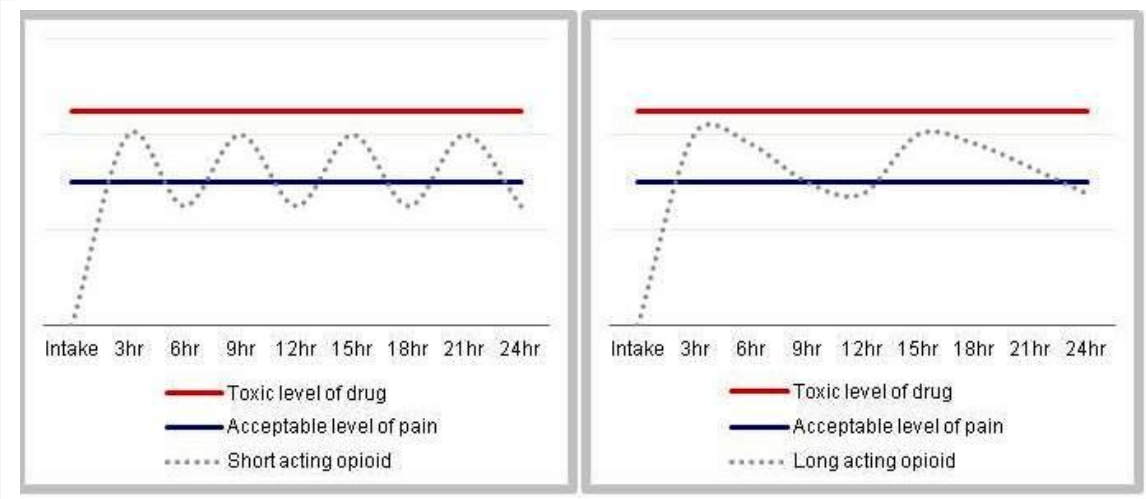
Several points should be considered when selecting a long-acting agent. In certain patient populations, when dosed appropriately, long-acting opioids can provide superior pain control than immediate acting alone. Please note long-acting opioids are **NOT** indicated for PRN use, thus, patients in need of opioid analgesics only on a PRN basis should receive short-acting opioids.

1. After the total daily dose has been determined from trialing short-acting opioid, consider converting to long-acting agent for management of chronic pain
2. Long acting formulations may be utilized for pain that is not managed with short-acting agents alone
3. Benefits for switching to long-acting pain medication include:
    a. Better pain control due to controlled release of drug and other factors
    b. More convenient dosing schedule
    c. Less abuse potential with most formulations

Table 2: Opioid Starting Doses for Opioid-Naïve Patients [3-20]

OPIOID		STARTING DOSE	DOSE TITRATION	IMPORTANT CONSIDERATIONS
Codeine $t_{1/2}$=2.5 to 4hr		30mg PO Q4-6H	Increase as needed and as tolerated	Maximum daily dose based on APAP content for combination products.
Fentanyl transdermal $t_{1/2}$=17hr		Opioid-**tolerant**: 25mcg/hour transdermally Q72H	Increase no more frequently than every 6 days and as tolerated	**Contraindicated in opioid-naïve patients.** Fever or high body temperature may cause elevated levels of drug to be released from patch.
Hydrocodone $t_{1/2}$=3.8 to 4.5hr		5 to 10mg PO Q4-6H	Increase as needed and as tolerated	Maximum daily dose based on APAP, ASA or IBU content.
Hydromorphone	**IR** $t_{1/2}$=2.5hr	2mg PO Q4-6H	Increase as needed and as tolerated	**Extended-release** formulation is **contraindicated in opioid-naïve patients.**
	ER $t_{1/2}$=11hr	Opioid-**tolerant**: Initiate at 25% dose reduction from equianalgesic dose. Dosing interval once daily (Q24H)	Increase no more frequently than every 3 to 4 days and as tolerated	
Methadone $t_{1/2}$=7 to 59hr		2.5mg PO Q8H	Increase by 2.5mg Q8H, no more frequently than every 7 days and as tolerated	Once stable and adequate pain control has been achieved may try extending dose interval to Q12H, keeping same total daily dose.
Morphine $t_{1/2}$=2 to 4hr	**IR**	15mg PO Q4H	Increase as needed and as tolerated	Initiate with immediate release product. **Do not begin therapy with controlled release product.** Once total daily dose determined, may convert to CR, keeping same total daily dose.
	CR	Opioid-**tolerant**: Determine total daily dose then divide to dosing interval Q12H or Q8H		
Oxycodone	**IR** $t_{1/2}$=3.5 to 4hr	5mg PO Q6H	Increase as needed and as tolerated. Do not extend **controlled release** dosing interval	Maximum daily dose based on APAP or ASA content for combination products.
	CR $t_{1/2}$=4.5 to 8hr	10mg PO Q12H		
Oxymorphone $t_{1/2}$=7.3 to 11.3hr	**IR**	5 to 10mg PO Q6H	Increase as needed and as tolerated	**Contraindicated** for use in patients with moderate to severe hepatic impairment. Take on empty stomach (1 hour before or 2 hours after a meal).
	ER	5mg PO Q12H	Increase by 5 to 10mg every 12 hours no more frequently than every 3 to 7 days	
Tapentadol	**IR** $t_{1/2}$=4hr	50mg, 75mg or 100mg PO Q4-6H PRN. Choose dose according to pain intensity	Increase to 75-100mg Q4-6H. Maximum total daily dose 600mg/day	Nucynta® ER is the only FDA approved opioid to date with an indication for management of diabetic peripheral neuropathy induced neuropathic pain.
	ER $t_{1/2}$=5hr	50mg PO BID	Increase by 50mg BID no more frequently than every 3 days. Maximum 500mg/day	
Tramadol	**IR** $t_{1/2}$=5.6 to 6.7hr	25mg PO QAM	Increase 25mg in separate doses every 3 days up to 100mg/day (25mg QID). Then may increase 50mg/day every 3 days as tolerated up to maximum 400mg/day	Dose limit due to lowering of seizure threshold.
	CR $t_{1/2}$=6.5 to 10hr	100mg once daily	Increase 100mg per day every 3 to 5 days. Maximum 300mg/day	

Figure 2: Short-acting Versus Long-acting Area Under the Curve



4. A major concern regarding long-acting opioids is risk of CNS toxicity associated with improper use or abuse.
    a. Modes of abuse include, but are not limited to:
        i. Crushing or chewing tablet to circumvent long-acting mode of delivery
        ii. Dissolving long-acting medication in solution for injection
    b. Manufacturers have made strides in their efforts to create abuse-deterrent formulations
        i. Changed physical properties of drug
            1. Oxycodone controlled release (OxyContin CR®)[17]
            2. Oxymorphone extended release (Opana ER®)[18]
        ii. Changed mode of delivery
            1. Fentanyl matrix patches (e.g.- Fentanyl patches by Mylan®)
            2. Buprenorphine/Naloxone sublingual film (Suboxone®)[14]
        iii. Combined with opioid antagonist
            1. Buprenorphine/Naloxone (Suboxone®)[14]
            2. Morphine/Naltrexone (Embeda®)[15]
        iv. Combined with aversion ingredient
            1. Oxycodone immediate release (Oxecta®)[16]

C. Management of Breakthrough Pain

A breakthrough pain episode, or an increase in pain at some point during a patient's therapy, is not indicative of opioid tolerance. During these pain flares it is appropriate to use a short-acting opioid to treat breakthrough pain. If the acute pain is recurring, you may consider resuming long-acting opioid titration.

D. Methadone

Methadone is an effective long-acting opioid that is often used when other pain medications fail to provide adequate analgesia, or cause a patient to experience intolerable side effects. Use of methadone for treatment of chronic pain is sometimes controversial due to the disproportionately high incidence of overdoses in comparison to other opioids. Risks associated with methadone use are greatly attributed to its complex pharmacokinetic and pharmacodynamic properties. Understanding the unique characteristics of this drug is fundamental to its safe use.

Methadone is a synthetic opioid that is structurally different from morphine, but has similar affinity as morphine for the mu-opioid receptor.[22] This drug exerts agonistic effects at the mu-opioid receptor, but also exhibits analgesic activity through N-methyl-D-aspartate (NMDA) receptor inhibition.[21] Antagonistic effects at the NMDA receptor are also thought to prevent the development of tolerance.[22] Methadone is highly lipophilic and tissue binding occurs. The drug accumulates in the liver and other organs, and gradually releases from tissue reservoir into the plasma, resulting in a very long duration of action.

Two main risks associated with methadone include respiratory depression and QT prolongation. Respiratory depression is directly associated with dose, so it is extremely important to dose conservatively, titrate slowly and take into consideration lipophilicity of the drug. Prior to initiating methadone therapy, due to risk of QT prolongation, it is important to get a baseline EKG and monitor 30 days after start of therapy then annually thereafter. Caution is advised in patients with QT interval between 450ms and 500ms and should be avoided or discontinued when greater than 500ms.

E. Opioid Conversion

There are four main reasons to change opioids:

1. Pain is controlled but patient experiences intolerable adverse effects[1]
2. Pain is not adequately controlled, but dose may not be increased due to adverse effects[1]
3. Change in patient status requires change in route of administration[2]
4. Other (availability of drug, cost, formulary issues, etc.)

Equianalgesic ratio guidelines may serve as a useful reference for opioid dose conversions, however, there are important considerations to keep in mind. Several studies have demonstrated a large variability in calculated morphine equivalent of commonly-used opioids, such as transdermal fentanyl, oral methadone and long-acting oxycodone, dependent upon the equianalgesic ratio selected. [2,3] Equianalgesic ratio guidelines are derived largely from single-dose studies with small sample sizes. Data collected by such trials are used by pharmaceutical manufacturers for marketing purposes— not as a tool to convert between opioids. Cross-over trials have shown that data contained in the equianalgesic opioid dosing table are unidirectional and therefore not reciprocal. The guidelines are designed to convert from oral morphine to another opioid, but **not** in the reverse direction.

Opioid conversion is not only a mathematical calculation— it is one piece of a comprehensive patient assessment which requires evaluation of the underlying clinical situation. Clinically, the use of such guidelines should be used with great attention and caution.

Guidelines for switching and rotating opioids:

1. Use a consistent dose conversion table for guideline purposes
2. Be conservative in calculations when switching between opioids
    a. Start with doses 30-50% lower than the equivalent dose of the second opioid
    b. If switching to transdermal fentanyl, do not reduce equianalgesic dose
3. Consider further changes in the calculated equianalgesic dose based on medical condition and pain
    a. If patient is elderly or has significant cardiopulmonary, hepatic, or renal disease consider further dose reduction
    b. Reduce more if the patient experiences significant opioid adverse effects or is medically frail
4. Calculate a rescue dose as 5-15% of the total daily (24 hours) opioid dose and administer at an appropriate interval (usually dosed every 4 to 6 hours as needed)
5. Monitor patient closely for analgesia, function and side effects
6. Adjust scheduled dose after 24 hours based on total opioid intake (scheduled and unscheduled rescue doses) over previous day

F. Preventing and Managing Opioid-Related Side Effects

Although opioids have shown to be effective in diverse populations, side effects are common. Opioid side effects in patients with chronic pain may impair quality of life, increase morbidity, and reduce compliance.[6] Co-morbidities and concurrent medications that contribute to the incidence and severity of opioid side effects should be assessed and treated, or discontinued if possible.

Common side effects of opioid administration include sedation, dizziness, nausea, vomiting, constipation, physical dependence, tolerance, and respiratory depression. Concerns of physical dependence and addiction may lead to improper prescribing and inadequate pain management. Long-term opioid use may cause hypogonadism in males and females, osteoporosis, immune suppression, paradoxical hyperalgesia, and myoclonus.

The most concerning opioid-induced adverse effect is respiratory depression. In healthy individuals, carbon dioxide is the primary driving force of respiration. Opioids produce a dose-dependent reduction in the responsiveness of brain stem respiratory centers to increases in arterial partial pressure of carbon dioxide. Clinically, opioid-induced respiratory depression manifests as a reduction in rate of breathing and is often accompanied by a compensatory increase in tidal volume, however, this compensation is incomplete. Opioids can lead to prolonged pauses between breaths, delayed exhalation and periodic breathing. Tolerance to respiratory depression develops over a period of days to weeks.

Table 3: Equianalgesic Opioid Dosing (Oral)

DRUG	ESTIMATED EQUIANALGESIC DOSE (mg)	COMMENTS
Buprenorphine	0.4 (sl)	
Codeine	180 to 200	
Fentanyl	N/A	Transdermal fentanyl (TDF) patch (used for chronic pain) dosed in mcg, is roughly equivalent to 50% of the total daily dose of oral morphine in mg (e.g., TDF 25 mcg/hour patch is roughly equal to 50 mg oral morphine per day).
Hydrocodone	30	Equivalence to oral morphine not clearly defined; generally thought to be equal to or less potent than oxycodone.
Hydromorphone	7.5	Oral bioavailability may be as high as 60%, particularly with chronic dosing; ranges from 29-95%. Research has shown a lower dose ratio and a directional influence seen when converting between morphine and hydromorphone. It is suggested that when switching from morphine (M) to hydromorphone (HM) (using the same route of administration; e.g., SQ to SQ or oral to oral), a conversion ratio of 5:1 (M:HM) when switching from morphine to hydromorphone and a dose ratio of 3.7:1 (M:HM) when switching from hydromorphone to morphine (again, using the same route of administration). Oral: rectal bioavailability approximately equal; the FDA-approved dosing interval for rectal hydromorphone is every 6 hours.
Methadone	20 acute 2 to 4 chronic	Methadone dosing is highly variable and conversion to/from other opioids is NOT linear.
Morphine	30	
Oxycodone	15 to 20	Because of the variations in bioavailability between morphine (15-64%) and oxycodone (60% or more), the equianalgesic ratio to oral morphine:oxycodone ranges from 1:1 to 2:1, partially dependent on the patient's ability to absorb the opioid. A ratio of 1.5:1 is used clinically as a compromise.
Oxymorphone	10	Conversion from oral morphine or oral oxycodone to oxymorphone is shown as 30:10 and 20:10, respectively per package labeling. Some data suggests the conversion ratio when switching to oxymorphone is closer to 18:10 for morphine and 12:10 for oxycodone, especially once at steady state.
Tapentadol	N/A	No data established
Tramadol	120	With chronic dosing, oral tramadol achieves between 90 and 100% bioavailability. Despite bioavailability date, equipotent use of oral morphine and oral tramadol ranges from 1:4 to 1:10 (morphine:tramadol). Therefore, using an equivalence of 120 mg oral tramadol may be very conservative.

Equianalgesic data presented in this table is that which is most commonly used by healthcare practitioners, but it is approximate. The clinician is urged to read the following caveats, along with the text, and use good clinical judgment at all times.[2]

Table 4: Adverse effects of opioids

ADVERSE EFFECT	MANAGEMENT/PEARLS
Constipation	Most common opioid induced adverse effect—Prophylactic treatments are essential • Initiate bowel regimen at start of opioid therapy • Monotherapy with stool softeners alone is ineffective • Tolerance to constipating effects never develops and is dose related • Prescribe a stool softener w/stimulant laxative (e.g.- docusate w/sennosides) initially • Other choices: MOM, bisacodyl, lactulose, or sorbitol • Do not use bulk forming laxatives (e.g.- psyllium, methylcellulose, or polycarbophil)
Nausea and/or vomiting	Prophylaxis generally not required at start of therapy—Nausea from opioids usually transient • There is no proven benefit of one antiemetic over another • Add or increase non-opioid or adjuvant analgesic so opioid dose can be reduced • Available options: antipsychotics, metoclopramide, serotonin antagonists (typically more effective preventing nausea/vomiting rather than treating it), antihistamines, and corticosteroids
CNS adverse effects sedation decreased cognition confusion delirium	Most CNS effects are transient, although some patients may require additional therapy to help cope with unwanted side effects • Eliminate unnecessary medications that may worsen underlying CNS effects • Consider lowering opioid dose, as sedation commonly presents at initiation of opioid therapy or with dose increases • Consider adding psychostimulant (e.g.- modafanil, methylphenidate), or increase caffeine intake • Change to a different opioid
Pruritus	Most likely an adverse effect due to histamine release rather than an allergic reaction • Sometimes pruritus will spontaneously resolve even without changing opioid therapy • Treatment options: antihistamines, opioid rotation, dose reduction, or moisturizers
Physical dependence and tolerance	Physical Dependence is a physiologic process and is a predictable event with opioid use • Characterized by withdrawal symptoms if drug is abruptly stopped • Physical dependence ≠ addiction • Tolerance is when the body adapts to effects of the opioid, so increased doses are needed to achieve same level of pain relief
Myoclonus	All opioid analgesics can produce myoclonus, particularly with high-dose administration • Tends to occur when patients are drowsy or entering light sleep, ranging from infrequent and mild to distressing. • Treatment options: low-dose benzodiazepines (clonazepam or lorazepam) or skeletal muscle relaxants
Urinary Retention	Opioids increase smooth muscle tone in the bladder and ureters, causing bladder spasm and urgency; they also increase sphincter tone, making urination difficult • Urinary retention is most common in elderly males • Decreasing opioid dose is the most effective treatment of urinary retention • Foley catheter is recommended for chronic issues
Hypogonadism in both genders	Symptoms: fatigue, mood changes, decreased libido, loss of muscle mass, and osteoporosis - Recommend monitoring total and free testosterone in both male and female patients

The longer a patient receives opioids, the wider the margin of safety. Clinically significant opioid-induced respiratory depression is extremely rare when patients receive optimal doses of an opioid. When carefully titrated, opioids can be used safely, even in patients at risk for respiratory depression.

G. **Monitoring**

During titration phase

1. All patients should be seen every 2 to 4 weeks at minimum until dosing requirements have stabilized
    a. More frequent visits are advised for high risk patients
        i. Addiction problems
        ii. Suspected drug abuse behaviors
        iii. Co-existing psychiatric problems
        iv. Co-existing medical problems
2. Until patient is clinically stable and judged to be compliant with therapy, it is recommended that clinician check INSPECT at least quarterly

During maintenance phase

1. Monitor at least every 1 to 4 months for patients on stable doses and at low risk for adverse outcomes
    a. More frequent visits are recommended for high risk or complex patients
2. INSPECT should be checked at least annually
    a. Check more frequently for patients with high abuse potential
3. Address the five A's at each visit
    a. Affect
    b. Activity
    c. Analgesia
    d. Adverse effects
    e. Aberrant behavior

Consultation and management of complex patients

Prescribers may wish to consider referring patients to pain management specialist if any of the following conditions or situations is present or if other concerns arise during treatment:

- Patient has a complex pain condition and clinician wishes verification of diagnosis
- Patient has significant co-morbidities, including psychiatric illness
- Patient is at high-risk for aberrant behavior or addiction
- Patient has developed tolerance to opioid, particularly at high doses

H. Weaning Opioids

Table 5: Opioid tapering indications and method

CLINICAL INDICATIONS FOR TAPERING OPIOID THERAPY	TAPER METHOD
• Medication adverse effects indicate risks are greater than benefit, or • Comorbidities increase risk of complication • Pain problem resolves	10% every 7 days
• Function and pain are not improved • Patient expresses a desire to discontinue therapy	10% every 2 to 4 weeks
• Rapid taper is desired (cases that involve dangerous or illegal behaviors)	15-33% every 3 to 7 days — While opioid withdrawal is unpleasant, it is not dangerous to the patient

- Symptoms of abstinence syndrome, such as nausea, diarrhea, muscle pain and myoclonus can be managed with clonidine 0.1 – 0.2 mg orally every 6 hours or clonidine transdermal patch 0.1mg/24hrs (Catapres TTS-1™) weekly during the taper while monitoring for often significant hypotension and anticholinergic side effects. In some patients it may be necessary to slow the taper timeline to monthly, rather than weekly dosage adjustments
- Symptoms of mild opioid withdrawal may persist for up to six months after opioids have been discontinued
- Consider using adjuvant agents, such as antidepressants to manage irritability, sleep disturbance or antiepileptics for neuropathic pain
- Do not treat withdrawal symptoms with opioids or benzodiazepines after discontinuing opioids
- Referral for counseling or other support during this period is recommended if there are significant behavioral issues
- Refer to pain specialist or chemical dependency center for complicated withdrawal symptoms

I. Opioids in Pregnancy

Managing chronic pain in pregnant women is challenging. Chronic opioid therapy in this setting affects at least two patients, one of whom (the fetus) is unable to consent to treatment. Ethical issues have resulted in a lack of research, thus, it is difficult to evaluate benefits and risks of chronic opioid therapy in pregnancy. Most literature on pregnancy and opioids have focused on women in methadone maintenance treatment, or women who use opioids for analgesia during labor, rather than chronic opioid therapy for chronic pain. Although there are survey data that associate use of chronic opioid therapy during pregnancy with adverse newborn outcomes, including low birth weight, premature birth, hypoxic-ischemic brain injury, and neonatal death, it is difficult to separate effects of opioid use from other maternal factors that may contribute to these adverse newborn outcomes. Other neonatal complications associated with maternal opioid use include prolonged QT syndrome and opioid withdrawal syndrome. The risks of adverse neonatal outcomes may be lower when women

are on methadone for chronic pain management rather than for opioid dependence treatment. Higher doses of antenatal methadone in tolerant mothers do not seem to increase complication rates.

Considering potential risks of opioids during pregnancy, clinicians should counsel women of childbearing age about risks and benefits of chronic opioid therapy during pregnancy and after delivery. Minimal or no use of opioids during pregnancy should be encouraged unless potential benefits outweigh risks (e.g. severe disabling pain only controlled with opioids). If chronic opioid therapy is used during pregnancy, providers should be prepared to anticipate and address the additional risks to the patient and newborn. While antenatal harms may be difficult to predict and prevent, opioid withdrawal can be expected in up to half of newborns of opioid-dependent mothers. If the mother is receiving chronic opioid therapy at or near time of delivery, a professional who is experienced in the management of neonatal withdrawal should be available.

A PubMed search was conducted to obtain relevant articles using search terms such as "pregnancy" and "pain". Additional searches were performed using the Internet and references from any relevant articles. Finally, Drugs in Pregnancy and Lactation was also consulted for further information. Findings from these searches are summarized below.

Table 6: FDA Pregnancy Categories

FDA PREGNANCY CATEGORY	DESCRIPTION
A	Adequate and well-controlled studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters).
B	Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.
C	Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
D	There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
X	Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh benefits.

Acetaminophen

Acetaminophen is considered the treatment of choice for mild pain in pregnancy.[1] Acetaminophen is listed as a Pregnancy Category B medication and is not known to have a teratogenic effect.[1,2] Studies have shown acetaminophen does not increase the risk of miscarriage or stillbirth regardless of the duration of exposure.[1] Recommendations provided by Drugs in Pregnancy and Lactation state acetaminophen is compatible in pregnancy and there does not appear to be any risk to the embryo or fetus from maternal use of therapeutic doses.[3]

Aspirin and NSAIDs

Aspirin is considered a Pregnancy Category D medication due to several risks associated with its use.[4] A recommendation provided by Drugs in Pregnancy and Lactation states the use of aspirin during pregnancy, especially chronic or intermittent high doses, should be avoided.[3] High doses of aspirin may be associated with increased perinatal mortality, intrauterine growth restriction, teratogenic

effects, and an increased risk of hemorrhage in both mother and fetus.[3] Although data is limited, findings surrounded the use low-dose aspirin (40-150 mg/day) during pregnancy have not demonstrated increased fetal risk.[3] Low-dose aspirin may actually be beneficial in the prevention of gestational hypertension, pre-eclampsia, and eclampsia, but further research is needed to confirm these initial findings.[3]

In the first two trimesters, NSAIDS are considered Pregnancy Category C medications.[5-16] Studies evaluating NSAID use in the first trimester have reported varied results with some studies indicating an increased risk of cardiac defects, oral clefts, gastroschisis, and spontaneous abortion.[1-3] While less teratogenic effects have been reported during the second trimester, caution is still advised.[1] During the third trimester, NSAIDS are contraindicated and considered Pregnancy Category D.[1,5-16] This is due to an increased risk of neonatal pulmonary hypertension secondary to premature closure of the ductus arteriosus.[1-3] An additional risk associated with the use of NSAIDs during pregnancy is the prolongation of gestation due to decreased prostaglandin synthesis and the inhibition of labor initiation.[2,3] Overall, the use of aspirin and NSAIDS should be minimized in pregnancy and avoided during the third trimester. Alternative agents such as acetaminophen should be considered.[1,2]

Table 7: FDA pregnancy category and lactation recommendations of aspirin and NSAIDs

Drug	FDA Pregnancy Category[4-16]	Drugs in Pregnancy and Lactation Recommendation[3]
Aspirin	D	Compatible (Low Dose) Human data suggest risk in 1st and 3rd trimesters (High Dose)
Diclofenac	C (1st and 2nd Trimester) D (3rd Trimester)	Human data suggest risk in 1st and 3rd trimesters
Etodolac	C	Human data suggest risk in 1st and 3rd trimesters
Fenoprofen	C	Human data suggest risk in 1st and 3rd trimesters
Flurbiprofen	C	Human data suggest risk in 1st and 3rd trimesters
Ibuprofen	C (1st and 2nd Trimester) D (3rd Trimester)	Human data suggest risk in 1st and 3rd trimesters
Indomethacin	C	Human data suggest risk in 1st and 3rd trimesters
Ketoprofen	C	Human data suggest risk in 1st and 3rd trimesters
Ketorolac	C	Human data suggest risk in 1st and 3rd trimesters
Meloxicam	C (1st and 2nd Trimester) D (3rd Trimester)	Human data suggest risk in 1st and 3rd trimesters
Nabumetone	C	Human data suggest risk in 1st and 3rd trimesters
Naproxen	C	Human data suggest risk in 1st and 3rd trimesters
Oxaprozin	C	Human data suggest risk in 1st and 3rd trimesters
Sulindac	C	Human data suggest risk in 1st and 3rd trimesters

*Category for Hydrocodone/Acetaminophen

Opioids

Most opioids are Pregnancy Category C with the exception of oxycodone and nalbuphine, which are considered Pregnancy Category B.[1] These agents are considered safe for the short-term management of acute pain. The pregnancy category of opioids changes to D if used for prolonged periods of time or in high doses near the end of pregnancy, as opioids may decrease the respiratory drive of the neonate.[1-3] Data surrounding the use of opioids in pregnancy is limited with the majority of information coming from the use of methadone in opioid dependence.[1] Due to its history of use, methadone may be considered for the management of chronic pain in pregnancy despite known risks such as neonatal withdrawal, decreased fetal activity, altered fetal heart rate, neonatal thrombocytopenia, preterm birth and low birth weight. Methadone should not be used in the inpatient setting for acute pain.[1] Pregnant patients receiving chronic opioid therapy should be

tapered to the lowest effective dose and discontinued if possible.[30] Tapering should be slow to avoid the risk of maternal opioid withdrawal as this has been associated with uterine smooth muscle irritability, premature labor and spontaneous abortion.[30]

Regular opioid use during pregnancy is associated with neonatal abstinence syndrome (NAS). NAS can begin 1-3 days following birth and may take 5-10 days to resolve.[30] NAS can be treated with comfort measures and small doses of morphine to relieve withdrawal symptoms.[30] Adverse effects associated with neonatal withdrawal include hypertonia, neonatal tremor, neonatal agitation, and myoclonus with additional reports of convulsions, apnea, respiratory depression and bradycardia;[1,30] however, NAS is not associated with any long-term sequelae.[30]

A case-control study compared 17,449 congenital defect pregnancies to 6,701 control pregnancies to determine if use of opioids in early pregnancy is associated with congenital heart defects (CHDs) or other birth defects.[31] Opioid use was defined as the reported use of 1 or more opioids taken at any dose, frequency or duration. Products of interest included those with any of the following components: codeine, hydrocodone, meperidine, oxycodone, propoxyphene, morphine, tramadol, methadone, hydromorphone, fentanyl or pentazocine. The exposure window of interest was from 1 month before to 3 months following conception. Primary birth defects of interest included CHDs, cleft palate and neural tube defects. Investigators found 2.6% of birth defect mothers had used opioids during this time compared to 2.0% of the control group. The four most common opioids reported were codeine (34.5%), hydrocodone (34.5%), oxycodone (14.4%) and meperidine (12.9%). Investigators found maternal opioid use resulted in a significantly increased risk for CHDs (OR 1.4; 95% CI, 1.1-1.7) and a significantly increased risk of spina bifida (OR 2.0; 95%CI, 1.3-3.2). However, a sub-analysis of individual opioids found the four most common opioids were not significantly associated with CHDs.[31] Limitations of this trial include the maternal reporting of opioid use, as the questionnaire was given an average of 9-11 months following birth. Additionally, no doses, frequencies, or durations of opioid use were recorded. Authors concluded that while opioid use was associated with an increased risk of CHDs and spina bifida, this increased risk translates into a modest absolute increase in risk above the baseline birth defect risk.[31]

Table 8: FDA Pregnancy Category and Lactation Recommendations of Opioids

DRUG	FDA PREGNANCY CATEGORY[17-29]	DRUGS IN PREGNANCY AND LACTATION RECOMMENDATION[3]
Buprenorphine	C	Limited human data (Animal data suggest low risk)
Buprenorphine/ Naloxone	C	N/A
Codeine	C	Human data suggest risk
Fentanyl	C	Human data suggest risk in 3rd trimester
Hydrocodone	C*	Human data suggest risk in 3rd trimester
Hydromorphone	C	Human data suggest risk in 3rd trimester
Meperidine	C	Human data suggest risk in 3rd trimester
Methadone	C	Human data suggest risk in 3rd trimester
Morphine	C	Human data suggest risk in 3rd trimester
Nalbuphine	B	Human data suggest risk in 3rd trimester
Naloxone	C	Compatible
Oxycodone	B	Human data suggest risk in 3rd trimester
Oxymorphone	C	Human data suggest risk in 3rd trimester
Tapentadol	C	No human data; Animal data suggest fetal harm
Tramadol	C	Human data suggest risk in 3rd trimester

*Category for Hydrocodone/Acetaminophen

Summary

- Acetaminophen is listed as Pregnancy Category B and is considered the drug of choice in pregnancy for mild pain.[1]
- NSAIDS should be used with caution and avoided in the third trimester.[1-3]
- Opioids are considered Pregnancy Category B or C, but are considered Category D if used in high doses towards the end of pregnancy or for extended periods of time.[1-3]
- Oxycodone or nalbuphine may be considered for the management of acute pain in pregnancy while methadone may be considered for the management of chronic pain in pregnancy.[1]
- A case-control study found opioid use in early pregnancy was associated with an increased risk of CHDs and spina bifida, but the true clinical significance of this finding unknown.[31]

Recommendations

- For mild pain in pregnancy acetaminophen is considered the treatment of choice.[1-3]
- Aspirin and NSAIDs should be used with caution and avoided in the third trimester.[1-3]
- For moderate-to-severe acute pain oxycodone or nalbuphine may be considered.[1]
- For moderate-to-severe chronic pain methadone may be considered.[1]

J. Safe Use, Storage and Disposal

Safe Use

Key ideas to convey to patients about proper use of opioids:

- Read the prescription container label each time to check dosage. Take opioids ONLY as directed.
- It is illegal to give away, trade, share, or sell prescription opioids
- The responsibility of the patient to report stolen medications to the police and the clinician
- The potential effect of regulatory issues on occupation, lifestyle, and use (e.g., pilots, commercial drivers, etc.)
- Do not drive or engage in potentially dangerous activities when initiating therapy, increasing doses, or when opioids are taken with other drugs or substances that affect the central nervous system.[8]

Safe Storage

Controlled substances should be thought of like other valuables in the home, such as jewelry or cash. Patients should be advised to take prescription opioids or other controlled substances out of the medicine cabinet and put them in a secure, but still handy, location, such as:

- An existing safe
- A cut-proof bag designed for travel
- Portable lock boxes
- Lacking medicine box

Remind patients not to store medications in their car, to keep them in their original containers, and to avoid storing them in the refrigerator or freezer (unless specifically directed). Patients, family members, or caregivers should monitor pill containers so they will know if any pills are missing. Charting on a daily basis can be very helpful, because innocent errors do occur.

Safe Disposal

FDA is aware of recent reports that have noted trace amounts of medicines in the water system. Disposal of these select few medicines by flushing contributes only a small fraction of the total amount of medicine found in the water. The majority of medicines found in the water system are a result of the body's natural routes of drug elimination (in urine or feces).

Scientists to date have found no evidence of harmful effects to human health from medicines in the environment. Based on the available data, FDA believes that the known risk of harm to humans from accidental exposure to these medicines far outweighs any potential risk to humans or the environment from flushing them.

There is a small number of medicines that may be especially harmful and, in some cases, fatal with just one dose if they are used by someone other than the person for whom the medicine was prescribed. The following list from FDA tells you what expired, unwanted, or unused medicines you should flush down the sink or toilet to help prevent danger to people and pets in the home.

Table 9: FDA List of Recommended Medication to be Disposed by Flushing

MEDICINE	ACTIVE INGREDIENT
Abstral, tablets (sublingual)	Fentanyl
Actiq, oral transmucosal lozenge *	Fentanyl Citrate
Avinza, capsules (extended release)	Morphine Sulfate
Daytrana, transdermal patch system	Methylphenidate
Demerol, tablets *	Meperidine Hydrochloride
Demerol, oral solution *	Meperidine Hydrochloride
Dilaudid, tablets *	Hydromorphone Hydrochloride
Dilaudid, oral liquid *	Hydromorphone Hydrochloride
Dolophine Hydrochloride, tablets *	Methadone Hydrochloride
Duragesic, patch (extended release) *	Fentanyl
Embeda, capsules (extended release)	Morphine Sulfate; Naltrexone Hydrochloride
Exalgo, tablets (extended release)	Hydromorphone Hydrochloride
Fentora, tablets (buccal)	Fentanyl Citrate
Kadian, capsules (extended release)	Morphine Sulfate
Methadone Hydrochloride, oral solution *	Methadone Hydrochloride
Methadose, tablets *	Methadone Hydrochloride
Morphine Sulfate, tablets (immediate release) *	Morphine Sulfate
Morphine Sulfate, oral solution *	Morphine Sulfate
MS Contin, tablets (extended release) *	Morphine Sulfate
Nucynta ER, tablets (extended release)	Tapentadol
Onsolis, soluble film (buccal)	Fentanyl Citrate
Opana, tablets (immediate release)	Oxymorphone Hydrochloride
Opana ER, tablets (extended release)	Oxymorphone Hydrochloride
Oxecta, tablets (immediate release)	Oxycodone Hydrochloride
Oxycodone Hydrochloride, capsules	Oxycodone Hydrochloride
Oxycodone Hydrochloride, oral solution	Oxycodone Hydrochloride
Oxycontin, tablets (extended release) *	Oxycodone Hydrochloride
Percocet, tablets *	Acetaminophen; Oxycodone Hydrochloride
Percodan, tablets *	Aspirin; Oxycodone Hydrochloride
Xyrem, oral solution	Sodium Oxybate
Acetaminophen; Oxycodone Hydrochloride	Percocet, tablets *
Aspirin; Oxycodone Hydrochloride	Percodan, tablets *
Fentanyl	Abstral, tablets (sublingual)
	Duragesic, patch (extended release) *
Fentanyl Citrate	Actiq, oral transmucosal lozenge *
	Fentora, tablets (buccal)
	Onsolis, soluble film (buccal)
Hydromorphone Hydrochloride	Dilaudid, tablets *
	Dilaudid, oral liquid *
	Exalgo, tablets (extended release)
Meperidine Hydrochloride	Demerol, tablets *
	Demerol, oral solution *
Methadone Hydrochloride	Dolophine Hydrochloride, tablets *
	Methadone Hydrochloride, oral solution *
	Methadose, tablets *
Methylphenidate	Daytrana, transdermal patch system
Morphine Sulfate	Avinza, capsules (extended release)
	Kadian, capsules (extended release)
	Morphine Sulfate, tablets (immediate release) *
	Morphine Sulfate, oral solution *
	MS Contin, tablets (extended release) *
Morphine Sulfate; Naltrexone Hydrochloride	Embeda, capsules (extended release)
Oxycodone Hydrochloride	eOxecta, tablets (immediate release)
	Oxycodone Hydrochloride, capsules
	Oxycodone Hydrochloride, oral solution
	Oxycontin, tablets (extended release) *
Oxymorphone Hydrochloride	Opana, tablets (immediate release)
	Opana ER, tablets (extended release)
Tapentadol	Nucynta ER, tablets (extended release)

http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm186187.htm

Resources

Opioids911
Safety Resources Toolkit for Healthcare Providers

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Clinical Drug Testing in Chronic Non-Terminal Pain Management (A Primer)

This guide provides information for clinical practitioners – physicians, nurse practitioners, and physician assistants – who provide primary care in office settings and community health centers for deciding whether to introduce drug testing in their practices for the management of chronic Non-Terminal pain and gives guidance on implementing drug testing for such.

This information has been summarized from *Clinical Drug Testing in Primary Care* Technical Assistance Publication Series 32 HHS Publication No. (SMA) 12-4668. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2012. It is available from: http://kap.samhsa.gov.

Section 1—Introduction

Reasons to Use Clinical Drug Testing in Chronic Non-Terminal Pain Management

When used appropriately, drug testing can be an important clinical tool for chronic Non-Terminal pain management with opioid medications. While a useful tool for making clinical decisions, it should not be the only tool. When combined with a patient's history, collateral information from a spouse or other family member (obtained with permission of the patient), questionnaires, biological markers, and a practitioner's clinical judgment, drug testing provides information that helps clinicians assess patient use of opioids for chronic pain management. Practitioners can use drug testing to help monitor patients' use of prescribed scheduled medications, as part of pharmacovigilance, and to help identify patients who may need an intervention for substance use disorders (SUDs) including substance dependence and substance abuse. *Substances* in this context refers to alcohol and drugs that can be abused. As the front line in health care, medical practitioners are ideally situated to identify substance use problems in patients with chronic Non-Terminal pain. Despite the potential benefits of drug testing in monitoring chronic Non-Terminal pain medication, few primary care practitioners use it.

Drug Testing in Healthcare Settings

Drug testing is useful in healthcare settings:

- For determining or refuting perinatal maternal drug use;
- As an adjunct to psychiatric care and counseling;
- For monitoring medication compliance during pain treatment with opioids;
- For monitoring other medications that could be abused or diverted; and
- To detect drug use or abuse where it may have a negative impact on patient care in other medical specialties.

Cautions

Important distinctions exist between drug testing in the workplace and in clinical settings (Table 1). For example, many laboratories and point-of-care-test (POCT) devices test either for the federally mandated workplace drugs or for the same drugs, but using modified cutoff concentrations as the default drug-testing panel. These panels are not suitable for clinical drug testing because these panels do not detect some of the most commonly prescribed pain medications, such as synthetic opioids (e.g., hydrocodone) and anxiolytics (e.g., benzodiazepines, such as alprazolam), or other drugs of abuse. Initial screening test cutoffs may not be low enough for clinical practice in some instances (e.g., cannabinoids, opiates, amphetamines).

Trends in drug use and abuse change over time and can necessitate a change in drug testing panels. The technology for drug testing evolves quickly, new drug-testing devices become available, and old tests are refined. Although this guide presents current information, readers are encouraged to continue to consult recent sources. Wherever possible, the guide refers readers to resources that provide up-to-date information.

Table 1: Characteristics of Clinical Drug Testing

Specimen	• Primarily urine, some oral fluid tests
Collection Procedures	• Practitioners and clinical staff (hospital or clinical laboratory) follow procedures for properly identifying and tracking specimens. • In general, rigorous protocols are not used. Chain of custody usually is not required; however, laboratories under College of American Pathologists accreditation and/or State licensure should have specimen collection, handling, and storage protocols in place.
Specimen Validity Testing	• In general, laboratories do not conduct the same validity testing for substitution or adulteration as is required for Federal workplace testing. • Validation often is not required with clinical use of POCT. • Some laboratories record the temperature of the specimen and test for creatinine and specific gravity of urine specimens. • Pain management laboratories may have specimen validity testing protocols that involve creatinine with reflexive specific gravity, pH, and/or oxidants in place.
Confirmatory Methods	• GC/MS, liquid chromatography/mass spectrometry (LC/MS), liquid chromatography/ mass spectrometry/mass spectrometry LC/MS/ MS.
Testing for Predetermined Substances	• No set drug testing panel. • Drugs tested vary by laboratory and within laboratories. • Clinicians may specify which drugs are tested for and usually select panels (menus) that test for more than the federally mandated drugs. Various panels exist (e.g., pain).
Cutoff Concentrations	• Cutoff concentrations vary. • In some circumstances, test results below the cutoff concentration may be clinically significant. • Urine and oral fluid drug concentrations are usually not well correlated with impairment or intoxication, but may be consistent with observed effects.
Laboratory Certification	• Laboratories do not need HHS certification. However, clinical laboratories in the United States and its territories must be registered with Clinical Laboratory Improvement Amendments (CLIA) and comply with all State and local regulations concerning specimen collection, clinical laboratory testing, and reporting. • POCT using kits calibrated and validated by manufacturers does not require CLIA certification.
Medical Review	• MRO review is not required.

Section 2—Terminology and Essential Concepts in Drug Testing

Drug Screening and Confirmatory Testing

The term *drug testing* can be confusing because it implies that the test will detect the presence of all drugs. However, drug tests target only specific drugs or drug classes and can detect substances only when they are present above predetermined thresholds (cutoff levels).

Traditionally, drug testing usually, but not always, involves a two-step process: an initial drug screen that identifies potentially or presumptively positive and negative specimens, followed by a confirmatory test of any screened positive assays.

Screening tests (the initial tests) indicate the presence or absence of a substance or its metabolite, but also can indicate the presence of a cross-reacting, chemically similar substance. These are qualitative analyses – the drug or metabolite is either present or absent. Screening tests can be done in a laboratory or onsite (point-of-care test [POCT]) and usually use an immunoassay technique. Laboratory immunoassay screening tests are inexpensive, easily automated, and produce results quickly. Screening POCT immunoassay testing devices are available for urine and oral fluids (saliva) and produce results immediately.

Confirmatory tests verify or refute the result of the screening assay. It is usually a second different analytical procedure performed on a different aliquot, or on part, of the original specimen. Confirmatory tests usually:

- Provide quantitative concentrations (e.g., ng/mL) of specific substances or their metabolites in the specimen.
- Have high specificity and sensitivity.
- Require a trained technician to perform the test and interpret the results.
- Can identify specific drugs within drug classes.

In clinical situations, confirmation is not always necessary as clinical correlation is appropriate. Laboratories do not automatically perform confirmatory tests. When a patient's screening test (either a POCT or laboratory test) yields unexpected results (e.g., negative in pain management treatment), the practitioner decides whether to request a confirmatory test. A confirmatory test may not be needed if patients or family members admit to drug use or not taking scheduled medications when told of the drug test results. However, if the patient disputes the unexpected findings, a confirmatory test should be done. Section 4 provides information that can be helpful in deciding whether to request a confirmatory test.

Testing Methods

Conventional scientific techniques are used to test specimens for drugs or drug metabolites. Most commonly, immunoassay testing technology is used to perform the initial screening test (Meeker, Mount, & Ross, 2003). Appendix B, Laboratory Initial Drug-Testing Methods in the *Clinical Drug Testing in Primary Care* TAP Series 32 briefly describes these methods.

The most common technologies used to perform the confirmatory test are gas chromatography/mass spectrometry, liquid chromatography/mass spectrometry, and various forms of tandem mass spectrometry. Information about these methods and other confirmatory testing methods are in Appendix C, Laboratory Confirmatory Drug-Testing Methods of *Clinical Drug Testing in Primary Care* TAP Series 32. Other testing methods are used to detect adulteration or substitution. Appendix D, Laboratory Specimen Validity-Testing Methods, *Clinical Drug Testing in Primary Care* TAP Series 32, provides a short explanation of methods for specimen validity testing.

Test Reliability

Both POCTs and laboratory tests are evaluated for reliability. The *sensitivity* indicates the test's ability to reliably detect the presence of a drug or metabolite at or above the designated cutoff concentration (the true-positive rate). *Specificity* is the test's ability to exclude substances other than the analyte of interest or its ability not to detect the analyte of interest when it is below the cutoff concentration (the true-negative rate).

Tests are designed to detect whether a specimen is positive or negative for the substance. Four results are possible:

- True positive: The test correctly detects the presence of the drug or metabolites.
- False positive: The test incorrectly detects the presence of the drug when none is present.
- True negative: The test correctly confirms the absence of the drug or metabolites.
- False negative: The test fails to detect the presence of the drug or metabolites.

Confirmatory tests must have high specificity. Screening tests are manufactured to be as sensitive as possible, while minimizing the possibility of a false-positive result (Dolan, Rouen, & Kimber, 2004). They cannot reliably exclude substances other than the substance of interest (the analyte), and they cannot reliably discriminate among drugs of the same class. For example, a low- specificity test may reliably detect morphine, but be unable to determine whether the drug used was heroin, codeine, or morphine. Notable exceptions are cannabinoids, cocaine metabolite, oxycodone/oxymorphone, methadone, and methadone metabolite (EDDP, or 2-ethylidine-1,5-dimethyl-3,3- diphenylpyrrolidine) which are very specific for those compounds.

Generally, the cutoff level for initial screening tests is set to identify 95–98 percent of true-negative results, and 100 percent of true-positive results. Confirmatory test cutoff concentrations are set to ensure that more than 95 percent of all specimens with screened positive results are confirmed as true positives (Reynolds, 2005). However, confirmation rates are highly dependent upon the analyte. For cannabinoids and cocaine metabolite, the confirmatory rate usually exceeds 99 percent. The clinically important point is that false positives are rare for cocaine metabolite or cannabinoids.

Window of Detection

The *window of detection*, also called the detection time, is the length of time the substances or their metabolites can be detected in a biological matrix. It part, it depends on:

- Chemical properties of the substances for which the test is being performed
- Individual metabolism rates and excretion routes
- Route of administration, frequency of use, and amount of the substance ingested
- Sensitivity and specificity of the test
- Selected cutoff concentration
- The individual's health, diet, weight, gender, fluid intake, and pharmacogenomic profile
- The biological specimen tested.

All biological matrices may show the presence of both parent drugs and their metabolites (Warner, 2003). Drug metabolites usually remain in the body longer than do the parent drugs. Blood and oral fluid are better suited for detecting the parent drug; urine is most likely to contain the drug's metabolites. Table 2 provides a comparison of detection periods used for various matrices.

Cutoff Concentrations

The administrative *cutoff* (or *threshold*) of a drug test is the point of measurement at or above which a result is considered positive and below which a result is considered negative.

Because the majority of drug testing is done for workplace purposes, most laboratories and many POCTs use the Federal mandatory guidelines for workplace testing cutoff concentrations. However, Federal cutoff concentrations are **not** appropriate for clinical use. Practitioners need to know the cutoff concentrations used in the POCTs, or by the laboratory testing their patients' specimens, and should understand which analyte and at what cutoff the test is designed to detect. Detection thresholds for Federal, employer, and forensic drug testing panels are set high enough to detect concentrations suggesting drug abuse, but they do not always detect therapeutic concentrations of medications. For example, the threshold for opiates in federally mandated workplace urine drug screening is 2000 ng/mL. The usual screening threshold for opiates in clinical monitoring is much lower, at 300 ng/mL for morphine, hydrocodone, and codeine to detect appropriate use of opioid pain medication (Christo et al., 2011).

Table 2: Window of Detection for Various Matrices

Matrix	Time*
Breath	
Blood	
Oral Fluid	
Urine	
Sweat†	
Hair‡	
Meconium	
	Minutes Hours Days Weeks Months Years

*Very broad estimates that also depend on the substance, the amount and frequency of the substance taken, and other factors previously listed.

†As long as the patch is worn, usually 7 days.

‡7–10 days after use to the time passed to grow the length of hair, but may be limited to 6 months hair growth. However, most laboratories analyze the amount of hair equivalent to 3 months of growth.

Sources: Adapted from Cone (1997); Dasgupta (2008).

Detection thresholds for Federal, employer, and forensic drug testing panels are set high enough to detect concentrations suggesting drug abuse, but they do not always detect therapeutic concentrations of medications. For example, the threshold for opiates in federally mandated workplace urine drug screening is 2000 ng/mL. The usual screening threshold for opiates in clinical monitoring is much lower, at 300 ng/mL for morphine, hydrocodone, and codeine to detect appropriate use of opioid pain medication (Christo et al., 2011).

For laboratory tests, practitioners can request lower cutoff concentrations than are commonly used in workplace testing. However, in some cases, the error rate increases as the cutoff concentration decreases.

Cross-Reactivity

Cross-reactivity occurs when a test cannot distinguish between the substances being tested for and substances that are chemically similar.

Drug class-specific immunoassay tests compare the structural similarity of a drug or its metabolites with specially engineered antibodies. The ability to detect the presence of a specific drug varies with different immunoassay tests, depending on the cross-reactivity of the drug with an antibody. For example, a test for opioids may be very sensitive to natural opioids, such as morphine, but may not cross-react with synthetic or semisynthetic opioids, such as oxycodone.

Substances other than the drug to be detected may also cross-react with the antibody and produce a false-positive result. Some over-the-counter (OTC) decongestants (e.g., pseudoephedrine) register a positive drug test result for amphetamine. Phentermine, an anorectic agent, commonly yields a false-positive initial amphetamines test. Dextromethorphan can produce false-positive results for phencyclidine (PCP) in some assays.

However, cross-reactivity can be beneficial in clinical testing. As an example, a urine test that is specific for morphine will detect only morphine in a patient's urine. The morphine- specific test will miss opioids, such as hydrocodone and hydromorphone. A urine drug test or panel that is reactive to a wide variety of opioids would be a better choice for a clinician when looking for opioid use by a patient. Conversely, the lack of sensitivity to the common semisynthetic opioid, oxycodone, is detrimental to patient care when a clinician is reviewing the results of a "urine drug screen" and sees "opiates negative" when oxycodone abuse is suspected. Thus, cross-reactivity can be a double-edged sword in clinical practice.

To avoid false-positive results caused by cross-reactivity, practitioners should be familiar with the potential for cross-reactivity and ask patients about prescription and OTC medication use.

Drug-testing accuracy continues to improve. For example, newer drug tests may correct for interactions that have been formerly associated with false-positive results.

Practitioners can find some of this information in the instructions in the POCT packaging material, or they can talk with laboratory personnel to know exactly what a laboratory's tests will and will not detect.

Drug Test Panels

A *drug test panel* is a list (or menu) of drugs or drug classes that can be tested for in a specimen. No single drug panel is suitable for all clinical uses; many testing options exist that can be adapted to clinical needs. These panels are designed to monitor adherence to pain treatment plans, to detect use of non-prescribed pain medications, and to screen for use of illicit drugs. Clinical practitioners can order more comprehensive drug test panels to identify drugs or classes of drugs that go beyond the federally mandated drugs for testing. Which drugs are included in the testing menu vary greatly between and within laboratories; laboratories differ in the drugs or metabolites included in their comprehensive panel and have more than one type of panel. Therefore, you should contact the laboratory to determine the capabilities and usual practices of the laboratory. It is just as important for you to know what a "urine drug screen" will not detect as it is to know what it will detect. Some laboratories have a comprehensive pain management panel for people prescribed opioids for pain (Cone, Caplan, Black, Robert, & Moser, 2008). Panels can be customized for individual practices or patients, but using existing test panels from the laboratory is generally less expensive for patients and less time- consuming for practitioners than ordering tests for many individual substances. However, these panels vary by laboratory and are not standardized. It should be noted that laboratories may default to the federally mandated drug tests if you do not order a different test panel.

Panels are available in various configurations. The more drugs on a panel, the more expensive the test. Substances typically on these panels include, but are not limited to:

- Amphetamine, methamphetamine.
- Barbiturates (amobarbital, butabarbital, butalbital, pentobarbital, phenobarbital, secobarbital).
- Benzodiazepines (alprazolam, chlordiazepoxide, clonazepam, clorazepate, diazepam, flurazepam, lorazepam, oxazepam, temazepam).
- Illicit drugs (cocaine, methylenedioxyamphetamine [MDA], methylenedioxymethamphetamine [MDMA], methylenedioxyethylamphetamine [MDEA], marijuana).
- Opiates/opioids (codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, meperidine, methadone, morphine, oxycodone, oxymorphone, propoxyphene).

Consult with the laboratory when determining the preferred test panels.

The test menu for POCTs differs per the manufacturer and the device. Most POCTs screen for drugs included in the federally mandated test panel and other drugs or metabolites. Different devices and manufacturers offer various configurations of drugs tested for in devices.

Test Matrix

A *test matrix* is the biological specimen used for testing for the presence of drugs or drug metabolites. Almost any biological specimen can be tested for drugs or metabolites, but the more common matrices include breath (alcohol), blood (plasma, serum), urine, sweat, oral fluid, hair, and meconium. Depending on its biological properties, each matrix can provide different information about a patient's drug use. Urine is the most widely used test matrix (Watson et al., 2006). Detailed information about test matrices is in Section 3.

Point-of-Care Tests

A *POCT* is conducted where the specimen is collected, such as in the practitioner's office. POCTs use well-established immunoassay technologies for drug detection (Watson et al. 2006).

POCTs:

- Reveal results quickly;
- Are relatively inexpensive ($5–$20, depending on the POCT, the drugs or drug metabolites tested for, and the number of tests purchased);
- Are relatively simple to perform; and
- Are usually limited to indicating only positive or negative results (qualitative, not quantitative).

When reading the test results, it is important to know that how quickly the test becomes positive or the depth of the color do not indicate quantitative results.

A comparison of POCTs and laboratory tests is in Section 3.

Adulterants

An *adulterant* is a substance patients can add to a specimen to mask the presence of a drug or drug metabolite in the specimen, creating an incorrect result to hide their drug use. Methods to detect adulterants exist, and most laboratories and some POCTs can detect common adulterants. No one adulterant (with the exception of strong acids, bases, oxidizers, and reducing agents) can mask the presence of all drugs. The effectiveness of an adulterant depends on the amount of the adulterant and the concentration of the drug in the specimen. A specimen validity test can detect many adulterants. Numerous adulterants are available, especially for urine (see Section 5).

Specimen Validity Tests

Specimen validity tests determine whether a urine specimen has been diluted, adulterated, or substituted to obtain a negative result. A specimen validity test can compare urine specimen characteristics with acceptable density and composition ranges for human urine, detect many adulterants (e.g., oxidizing compounds), or test for a specific compound (e.g., nitrite, chromium VI) at concentrations indicative of adulteration. Many laboratories perform creatinine and pH analyses of all specimens submitted for drug testing. An adulteration panel can be ordered that determines the characteristics of the urine sample and checks for the presence of common adulterants. POCT devices are available that test for specimen validity, as well. Although validity testing is not required in clinical settings, it is sometimes advisable if the patient denies drug use. Point-of-care validity tests are available, and some POCT devices also test for validity at the same time they test for the drug analyte.

Additional information on validity follows:

- Specimen adulteration should be suspected if the pH level is less than 3.0 or greater than 11.0.
- If the creatinine is less than 20 mg/dL, the specimen is tested for specific gravity.
- *Specific gravity* of urine is a measure of the concentration of particles in the urine. Specific gravity may be an integral part of a POCT device's specific validity testing panel. Specimens with a low creatinine and an abnormal specific gravity may be reported as dilute, invalid, or substituted, depending on the laboratory's reporting policies (SAMHSA, 2008).

If the laboratory finds the specimen is dilute, it will report the specimen as dilute. However, the laboratory will also report the positive or negative test results. Depending on the degree of dilution, an analyte may still be detected.

Appendix D, Laboratory Specimen Validity-Testing Methods, *Clinical Drug Testing in Primary Care* TAP Series 32, provides a more information on laboratory specimen validity testing.

Section 3—Preparing for Drug Testing

Deciding Which Drugs to Screen and Test for

Decisions about which substances to screen for can be based on:

- The patient, including history, physical examination, and laboratory findings;
- The substance suspected of being used;
- The substances used locally;
- The substances commonly abused in the practitioners' patient population; and
- Substances that may present high risk for additive or synergistic interactions with prescribed medication (e.g., benzodiazepines, alcohol).

Choosing a Matrix

Practitioners can choose among several matrices for drug and alcohol testing for adults: urine, oral fluid, sweat, blood, hair, and breath (alcohol only). Neonates can be tested using meconium. Urine is the most commonly used matrix for drug testing and has been the most rigorously evaluated (Watson et al., 2006); it is discussed at length in Section 5. Table 3 provides a brief comparison of the advantages and disadvantages of the seven matrices. As most drug testing in the management of chronic Non-Terminal pain uses urine, our comments will center on that matrix. Additional information on matrices can be found in Section 3, Preparing for Drug Testing in C*linical Drug Testing in Primary Care* TAP Series 32.

Once ingested, drugs of abuse are rapidly distributed via the blood to all parts of the body. Abused drugs are generally lipid soluble and are mainly metabolized by the liver to more water-soluble metabolites. These metabolites are removed from blood by the kidneys and excreted in urine. Because many drugs are cleared from the blood rapidly, testing of blood or its components (serum) has short periods of detection, as does breath for testing for alcohol consumption and oral fluids because the drug passes quickly into, and is eliminated from, breath and oral fluids. Depending on the drug itself and previously listed factors that affect metabolism, urine usually has a window of detection that is slightly longer than oral fluid. Urine detection times vary from less than 1 day after ingestion to several weeks. Hair has a longer window of detection, but is best suited for detection of heavy drug use. The cells that generate hair absorb the metabolites that are circulating in the blood at the time the hair is produced; therefore, hair has the longest window of detection, depending on the length of the hair. It is notable that drugs may be incorporated into hair from external sources, such as mechanical contact between the hair and the drug. In utero drug exposure also can be monitored with maternal and neonatal urine and/or hair testing.

Table 3: Advantages and Disadvantages of Different Matrices for Drug Testing

Matrix	Advantages	Disadvantages
Urine	• Available in sufficient quantities • Higher concentrations of parent drugs and/or metabolites than in blood • Availability of point-of-care tests (POCTs) • Well-researched testing techniques	• Short to intermediate window of detection • Easy to adulterate or substitute • May require observed collection • Some individuals experience “shy bladder” syndrome and cannot produce a specimen
Oral Fluid	• Noninvasive specimen collection • Easy to collect • Reduced risk of adulteration • Directly observed specimen collection • Parent drug rather than metabolite can be the target of the assay • Able to detect same-day use, in some cases • Availability of POCTs • Detect residual drug in the mouth	• Limited specimen volume • Possibility of contamination from residual drug in mouth that cannot be correlated with blood concentrations • Short window of detection (24-48 hours) • Requires supervision of patient for 10–30 minutes before sampling • Salivation reduced by stimulant use • Need for elution solvent to efficiently remove drugs adsorbed to collection device • Cannabinoids in oral fluid have been shown to arise from contamination of the oral cavity rather than excretion in saliva from blood

Table 3: Advantages and Disadvantages of Different Matrices for Drug Testing

Matrix	Advantages	Disadvantages
Sweat	• Detects recent use (fewer than 24 hours with a sweat swipe) or allows for cumulative testing with the sweat patch (worn for up to 7–14 days) • Noninvasive specimen collection • Difficult to adulterate • Requires little training to collect specimen • May be an economical alternative to urine	• Few facilities and limited expertise for testing • Risk of accidental or deliberate removal of the sweat patch collection device • Unknown effects of variable sweat excretion among individuals • Only a single sweat collection patch available so multiple analyses cannot be done if needed (i.e., more than one positive initial test) • May be affected by external contaminants • Requires two visits, one for patch placement and one for patch removal
Blood	• Generally detects recent use • Established laboratory test method	• Expensive, except to detect ethanol • Limited window of detection • Invasive specimen collection (venipuncture) • Risk of infection • Requires training to collect specimen • May not be an option for individual with poor venous access
Hair	• Longest window of detection • May be able to detect changes in drug use over time (from 7–10 days after drug use to 3 months, depending on length of hair tested) • Directly observed specimen collection • Noninvasive specimen collection • Four tests will cover 1 year • Easy storage and transport • Difficult to adulterate or substitute • Readily available sample, depending on length of hair tested	• Cannot detect use within the previous 7–10 days • Difficult to interpret results • Costly and time consuming to prepare specimen for testing • Few laboratories available to perform testing • No POCTs currently available • Difficult to detect low-level use (e.g., single-use episode) • May be biased with hair color (dark hair contains more of some basic drugs [cocaine, methamphetamine, opioids] due to enhanced binding to melanin in hair) • Possibility of environmental contamination • Specimen can be removed by shaving
Breath	• Well-established method for alcohol testing • Readily available	• Used only for alcohol and other volatiles • Short window of detection • May be difficult to obtain adequate sample, especially with patients who are very intoxicated or uncooperative • Uncommon in clinical setting

Sources: Center for Substance Abuse Treatment (2006a); Dolan, Rouen, & Kimber (2004); Kwong & Ryan (1997); Warner (2003).

Oral Fluid

The parent drug is usually found in higher concentrations in oral fluids, although metabolite(s) may be present. Compared with urine specimens, oral fluid specimens present fewer opportunities for adulteration or substitution as the use of commercial adulterants or mouthwashes were not found to interfere with the immunoassay or did not affect test results if the products were used more than 30 minutes before specimen collection (Dams, Choo, Lambert, Jones, & Huestis, 2007, Bosker & Huestis, 2009; Drummer, 2006; Niedbala, Kardos, & Fries, et al., 2001; Niedbala, Kardos, Fritch, Cannon & Davis, 2001). The most common collection vehicle is a swab or absorbent pad on a stick that is placed between the lower cheek and gum to collect fluid and is left in place for a few minutes. It is then inserted into a vial containing a buffer solution for shipment to the laboratory. POCTs are also available for oral fluid testing.

On occasion, dry mouth syndrome can slow oral fluid collection, often requiring several minutes to collect an adequate sample (Drummer, 2006). Some medications and illegal drugs cause a dry mouth, and some oral fluid collection devices assist collection by stimulating oral fluid flow. Patients should not eat immediately before testing because some food tends to inhibit oral fluid production. If blood is present in the patient's oral fluid, collection of an alternative specimen, such as blood or urine, would be needed. Oral fluid limits the number of repeat or confirmatory tests on the specimen because of the small amount of the sample, compared with a urine sample.

Sweat

The two most common collection devices for sweat specimens are the patch and the swipe; however, only the sweat patch is approved by the U.S. FDA. The sweat collected with the patch detects drug use that occurred shortly before the patch was applied and while the device remains on the skin. It should be worn for at least 3 days, but no longer than 7 days, although most drugs will have been excreted within the first 48 hours (Barnes et al., 2009; Huestis et al., 2008; Kacinko et al., 2005; Schwilke et al., 2006).

The skin should be thoroughly cleaned with soap and water and then swabbed well with alcohol. The patch should then be applied to the skin by a staff member, not the patient (Watson et al., 2006). After 7 days, the patch is removed by the practitioner and sent to the laboratory for analysis.

Drugs and drug metabolites that have been detected in sweat include tetrahydrocannabinol (THC), amphetamine, methamphetamine, methylenedioxymethamphetamine (MDMA, or "Ecstasy"), codeine, morphine, heroin metabolite, phencyclidine (PCP), and cocaine and its metabolites (e.g., benzoylecgonine, ecgonine methyl ester) (Barnes et al., 2009; Dasgupta, 2008).

Because sweat can be collected only in limited quantities, there may not be sufficient specimen for repeat or confirmatory testing. Sweat is less susceptible to tampering or adulteration than is urine. However, the accuracy of sweat testing is not standardized and remains somewhat controversial (Chawarski, Fiellin, O'Connor, Bernard, & Schottenfeld, 2007; Watson et al., 2006). However, the sweat patch is used extensively in the criminal justice system to identify relapse or violations of conditions of probation and has been upheld by the courts.

Blood

Blood testing detects alcohol or drug use starting shortly after use, depending on the substance and the route of administration. In general, blood has a shorter detection period than urine (Warner, 2003). Blood collection is more invasive than other procedures and requires trained personnel to collect the specimen and perform laboratory testing. For people who inject drugs, or those with poor venous access, drawing blood may be difficult.

Hair

Hair testing is suited to:

- Detecting chronic drug use (Dolan et al., 2004; Warner, 2003);
- Providing a view of the patient's long-term substance use pattern; and
- Indicating periods of abstinence (Pragst & Balikova, 2006).

Hair is unique in that it may provide retrospective information on drug use with a longer window of detection, versus the point-of-time information provided by urine, blood, and breath. (Kintz, Villain, & Ludes, 2004; Boumba, Ziavrou, & Vougiouklakis, 2006). Hair follicles absorb the drug and/or metabolites from the bloodstream and from secretions of the sebaceous and sweat glands in the scalp (Cone, 1996; Musshoff & Madea, 2006). Trace amounts of drug become entrapped in the core of the hair as it grows, at a rate of approximately 1 cm per month (Dolan et al., 2004). Drug metabolites can be detected in the hair shaft approximately 7–10 days after drug ingestion. However, hair testing is not useful in monitoring opioid pain or other addictive medications when frequent (weekly or monthly) drug testing is desired. Because the timing of the drug use is difficult to determine by testing hair, it is not very useful clinically. In addition, interpreting hair test results of drugs and their metabolites is complicated as drugs may be incorporated into hair by simple environmental drug exposure and concentrations of drugs in hair can be affected by variations in hair structure, growth rate, melanin content, hygiene, and cosmetic hair treatments, such as bleaching (Ropero-Miller & Stout, 2008; Wang & Cone, 1995; Dasgupta, 2008). Hair testing can be done only in a laboratory; no POCTs are available.

The hair sample is usually taken from the back of the head, cut with scissors as close to the skin as possible, but can be collected from other parts of the body (e.g., face, armpit) of patients who are bald or have shaved heads (Wong & Tse, 2005).

Hair testing appears to be most reliable for detecting prior frequent, heavy use of cocaine, opioids, amphetamine, PCP, and Ecstasy, but is not suited for detection of very recent use, or occasional drug use. Musshoff and Madea (2006) report that hair tests can detect the presence of the THC metabolite, tetrahydrocannabinol carboxylic acid. Hair testing for alcohol is inappropriate; alcohol does not incorporate into hair. However, the minor metabolites of ethanol, ethyl glucuronide, and ethyl sulfate in hair show promise as markers of alcohol use (Wurst, Skipper, & Weinmann, 2003).

Breath

Several simple-to-use, but accurate, breath- testing devices are available for detecting very recent alcohol use. Breath also may be employed for the identification and quantitation of a variety of other volatiles, especially in industrial hygiene situations. However, breath testing is commonly used in alcohol treatment programs, but not in primary care.

The benefits of breath alcohol analyzers are that they:

- Are simple to use;
- Are inexpensive;
- Give instant results; and
- Are noninvasive.

Collection Devices

The collection device must be single use. It will normally be individually packaged with collection aids and a tamper-evident security seal. The collection device must not alter or affect the specimen. The device should have the following features for each specimen matrix:

- **Blood**. Sterile tubes that usually contain sodium fluoride to inhibit breakdown of drugs. The use of "gel" or "serum separator tubes for specimen collection for any type of drug analysis is highly discouraged.
- **Hair**. Foil or a plastic bag to store the sample with an indication of proximal and distal ends.
- **Oral fluid**. Device that allows accurate determination of the volume collected (usually 1.0±0.1 mL) and that contains an elution solvent to efficiently elute the adsorbed drugs.
- **Sweat**. A patch, placed on the skin, typically composed of an adhesive layer, release liner, and sweat-collection pad.
- **Urine**. A plastic collection container typically with a temperature strip outside the container to determine specimen temperature.

Shipping materials, documentation, and order forms will be needed if the specimen is to be sent to a laboratory.

Laboratory Tests

Laboratories perform screening, confirmatory, and validity tests. Laboratory testing is more accurate than POCT and provides quantitative information on what drugs and/or metabolites were detected. Laboratories use high-volume immunoassay tests to separate negative specimens from those that require confirmation testing.

Table 4: Comparison of Laboratory Tests and POCTs

Criterion	Laboratory Test	POCT
Time to Results	Initial test can be available within hours, but the confirmatory test takes days	Minutes
Ease of Use	Requires complex equipment	Relatively simple to use
Training	Requires trained technicians or technologists	Minimal training required
Breadth of Tests	Wide range of test menus	Limited test menu
Interpretation	Objective quantitative results; variations in laboratory cutoff concentrations may influence interpretation	Subjective results; requires interpretation, not quantitative

Sources: Melanson (2005); Watson et al. (2006).

Confirmation tests use either liquid chromatography (LC) or gas chromatography (GC) in combination with mass spectrometry (MS) for detection and measurement of drugs and metabolites. Tandem mass spectrometry (MS/MS) is a more sensitive form of MS. These tests provide a laboratory with the ability to identify and measure drugs and/or metabolites in biological fluids at low concentrations.

Most laboratories usually perform initial drug tests for commonly abused drugs, including 6-acetylmorphine (heroin metabolite), opioids, cocaine, amphetamines, barbiturates, PCP, and THC. Some laboratories offer extended opioid panels; these laboratory tests can detect and confirm several opioids including morphine, codeine, hydrocodone, hydromorphone, oxycodone, and oxymorphone. Some laboratories offer, upon request, panels that will differentiate individual benzodiazepines and their metabolites. Other extended panels include buprenorphine, carisoprodol, methadone, fentanyl, meperidine, and propoxyphene, among others. Not all laboratories are capable of identifying all known benzodiazepines and, where necessary or appropriate, their metabolites. The requirement for additional testing depends in large part on the patient population served by the facilities using the laboratory (e.g., a methadone clinic or a detoxification facility might require methadone, EDDP [methadone metabolite], burprenorphine/ norbuprenorphine, and/or other drug or metabolite analyses). POCTs or laboratory- based tests may be used for the initial testing, but only laboratories can perform confirmatory testing.

Advantages and Disadvantages of Testing in a Laboratory

Advantages: Laboratory tests have several important advantages over POCTs. Laboratory tests:

- Generally have a higher degree of precision.
- May offer quantitation of drugs and/or metabolites and a reasonable estimate of the timeframe in which the drug was used.
- Can provide information on specific drugs used.
- Can be directly sent for confirmatory GC/MS on the same sample.
- Are performed by trained laboratory professionals.

Disadvantages: The disadvantage of laboratory-based tests is turnaround time. The time required for laboratory-based testing includes transportation of the specimen to the laboratory, specimen aliquot preparation, and instrument analysis time – steps that are not required for POCTs. Results from POCT can be available while the patient is still in the office, so the practitioner can immediately discuss them with the patient. Depending on the laboratory, clinical screening results may be available in less than 1 hour after receipt or the next day, unless further testing, such as confirmation or reflexive testing, is required.

Considerations for Selecting a Laboratory

Before selecting a laboratory, practitioners should contact the laboratory and speak directly to the director or toxicologist to (White & Black, 2007):

- Determine the laboratory's analytic capabilities (laboratories may use the Federal Five as the testing menu for drug screens, which may or may not include the clinical drugs of interest);
- Inquire about other panels that test for drugs and drug classes of clinical interest;
- Confirm that the laboratory follows established Federal and State regulations (Table 5);
- Determine whether the laboratory's testing procedures are appropriate for clinical use; and
- Ensure that the laboratory provides technical assistance so the practitioner can obtain help with interpreting test results or determining which panel to order.

Practitioners need to talk to laboratory personnel about:

- Appropriate in-office specimen collection, handling, and storage procedures for each matrix used;
- Each test ordered, at least until the practitioner knows exactly what they are ordering and the limitations of any particular test;
- Unexpected results, whether positive or negative; and
- Referral testing for drugs not offered by the primary testing clinical laboratory.

Table 5: Federal and State Regulations

- The Clinical Laboratory Improvement Amendments (CLIA) of 1967 and of 1988 set forth conditions that all laboratories must meet to be certified to perform testing on biological specimens (http://www.cms.gov).
- The U.S. Department of Health and Human Services (HHS) Mandatory Guidelines for Federal Workplace Drug Testing Programs specify the requirements for a laboratory to be certified by the HHS National Laboratory
- Certification Program. Information is available at http://workplace.samhsa.gov/Dtesting.html
- Private and professional organizations (e.g., College of American Pathologists) have established voluntary laboratory accreditation programs. The American Association of Bioanalysts has private personnel standards.
- State clinical laboratory programs operate under individual State laws; State programs are usually authorized through the Centers for Medicare & Medicaid Services.

Several different types of POCTs are available. Generally, POCTs:

- Use well-established immunoassay technologies for drug detection;
- Determine the presence of parent drugs or their metabolites;
- Sometimes can determine the validity of a specimen, which is to be highly recommended as an integral part of the testing process;
- Identify drug classes (e.g., opioids, benzodiazepines, barbiturates), single drugs, or metabolites (e.g; benzoylecgonine, a cocaine metabolite); and
- Require a few drops of a specimen.

FDA has approved POCT devices for urine, breath, and oral fluid testing, but devices for urine drug testing are most widely used.

Various POCTs are available:

- Breath-testing devices, which are rare in primary care practice (the patient blows into the device)
- Cards or cassettes (drops of urine are placed on a card or in wells on a cassette)
- Dipsticks (an absorbent strip is dipped into the specimen)
- Combination collection/test cups (the testing strip is integrated into the collection cup, and results can be read on the outside of the cup)

A few devices double as both collection and testing devices. After the specimen is collected, the tester initiates the test, carefully times the test, and interprets and records the results. The test component of non-instrumented POCTs is an absorbent strip with an antibody-dye complex. The test is done by inserting the absorbent strip, card, or cassette into the specimen or adding the specimen to the testing device. When the strip or cassette comes into contact with the specimen, it reacts to the drug or drug class that the POCT can detect. Generally, a line or dot appears in the zone labeled for a specific drug if the drug is not present (negative test result); no line or dot appears when a specific drug is present (positive test result). A photocopy of the portion of the POCT device that is read can be made and placed in the patient's chart. Enough fluid (urine or oral fluid) should be retained for any reflexive or confirmatory testing that may be required.

It is critical that practitioners read package inserts carefully to know how to perform the test and read the results. Positive POCT results should usually be followed by a laboratory confirmatory test if the patient denies drug use when confronted with the positive results. A confirmatory test must be done if legal or employment ramifications for the patient will result.

Advantages and Disadvantages of POCTs

The principal advantage of POCTs is that the results are available in approximately 10 minutes. This fast turnaround allows practitioners to discuss the results with the patient during that office visit and make clinical decisions and act appropriately that day. This early intervention may prevent other health problems, hospitalization, or treatment episodes. It is also in keeping with behavioral principles: the immediacy of the intervention in relation to a behavior makes reinforcement more useful. Several manufacturers have developed drug-of-abuse assays for POCT that offer similar, but not exact, sensitivity and specificity to the methodologies used by central laboratories (Melanson, 2009). A variety of testing panels with different cutoff concentrations is available for these testing devices, but they are not as varied as laboratory testing. Increasingly, vendors are offering point-of-care devices that test for a wider range of drugs and with more sensitivity and specificity. POCTs are available to test for amphetamine, methamphetamine, barbiturates, benzodiazepines, cocaine, methadone, opioids, PCP, propoxyphene, Ecstasy, oxycodone, tricyclic antidepressants, buprenorphine, and THC acid metabolite (Melanson, 2005).

Generally, most studies suggested that POCTs are a reliable method to screen for drugs of abuse and that the results are comparable to those from automated immunoassays and GC/MS. However, no POCT device yields perfect agreement with more sophisticated testing, such as GC/MS or high-performance liquid chromatography (Watson et al., 2006). Disagreement between methods was highest for samples near the cutoffs.

Cross-reactivity differs among POCT devices because of differing antibody specificity. The manufacturer provides a list of compounds tested and their degree of cross-reactivity, including those medications outside the drug class, which may cause false-positive results (Melanson, 2009).

George and Braithwaite (2002) caution that the apparent benefit of POCTs – rapid assessment of a patient's drug use – can be detrimental if treatment decisions are based on these rapid, but unconfirmed, results. Disadvantages include:

- Most test only for drug classes, not for specific drugs within a class (Gourlay, Caplan, & Heit, 2010), which is what is needed more often in clinical applications.
- A limited test menu. Clinical settings may need a more complete panel, or separate tests, to assess for specific drugs.
- Do not provide quantitative drug or metabolite information.
- Presumptive results only; confirmatory testing may be needed at a laboratory.
- Cutoffs employed may not provide adequate sensitivity.
- Result interpretation may be subjective, making performance operator-dependent (Melanson, 2009).

Considerations for Selecting POCT Devices

Matrices. POCT devices should be FDA approved and usually CLIA-waived to test urine, breath (for alcohol), and oral fluid for substances of abuse. None are available yet for hair, sweat, or blood for drugs of abuse, although some POCT devices do exist for therapeutic drugs in blood or blood products. POCTs for urine remain the most commonly used, despite advances in testing of other matrices. Cutoff levels, cross-reactivity, and other possible interferences have been studied more for POCT urinalysis than for any other matrix (Watson et al., 2006). Most POCT devices are used in an environment that is external to a clinical laboratory.

Regulatory Issues. The use of POCTs is covered by two Federal regulations. The Medical Devices Act requires that all in vitro medical diagnostic devices be evaluated and cleared for use by FDA for commercial distribution before use with patients. CLIA regulates the use of POCTs and requires that medical diagnostic tests and devices be used only in laboratories that meet CLIA standards and are certified to perform those specific tests. However, tests may be waived from CLIA regulatory oversight if they meet certain requirements, primarily if they are simple to use and interpret and have a low error risk.

Practitioners should be aware of the following specific requirements when considering using a POCT device:

- **FDA approval**. The FDA Center for Devices and Radiological Health provides information on test categorization and approval or clearance of testing devices. (http://www.fda.gov/MedicalDevices/default.htm).
- **Waived tests.** FDA maintains a list of CLIA waived tests cleared by FDA for commercial distribution. POCT manufacturers will also state whether a test is waived by CLIA. (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCLIA/testswaived. cfm).
- **Certificate of waiver**. All sites performing waived tests must have a CLIA-waiver certificate and adhere to the manufacturer's instructions for performing the test. Facilities or physicians' offices performing waived tests must enroll in CLIA, pay the applicable fee, and follow the manufacturer's instructions. An explanation of the procedures to obtain a CLIA certificate is available at https://www.cms.gov/Regulations-and- Guidance/Legislation/CLIA/downloads/ HowObtainCertificateofWaiver.pdf.
- **State regulatory issues**. Many States have their own regulations regarding POCTs that practitioners or their designees must learn before they start to test.

Cost. The information on the economics of POCT for drugs and ethanol is limited, although cost issues should be important in deciding to initiate a point-of-care drug-testing program. The fixed unit price of POCTs often exceeds those of laboratory-based test methods. However, the cost of devices also depends in large part on the number of drugs included in the test panel, the difficulty in identifying the substances included in the panel, the number of devices ordered, and the volume of testing. In general, as the demand for POCTs grows, the cost per device decreases. In addition, the extra staff time and space to perform the test, staff training, quality assurance procedures, and documentation need to be taken into account when considering the cost. Then again, staff already collect specimens and perform POCTs to test for other conditions in many physician practices. These costs should be carefully reviewed prior to initiating POCT for drug testing.

Other Considerations: Practitioners should research the point-of-care devices being considered for use in terms of (Melanson, 2005):

- **Analytic performance**. Differences in sensitivity, specificity, and accuracy must be evaluated.
- **Cross-reactivity**. Some devices may not be able to distinguish between the substance being tested for and other chemically similar substances.
- **Validation studies**. Lot-specific evaluation information is usually summarized in package inserts, with more extensive verification documentation available on request.
- **Ease of use**. Most POCT devices can be operated by an individual with little laboratory experience. However, some devices may entail following fairly complex instructions for use, which can contribute to human errors that will affect test results.

- **Ease of reading and interpreting the results**. Most devices require visual interpretation of a color response. Clear, distinguishable results are necessary for accurate interpretation. It is also necessary to know which substances will cross-react and produce a false-positive result or a false negative result .
- Q**uality assurance and control procedures**. Devices differ in the amount of time needed for staff to learn quality control procedures, such as completing documentation to ensure adherence to the manufacturer's instructions for maintenance (if any) and assay of the appropriate control specimens at the required intervals. Maintenance and quality control procedures also must meet CLIA, State, and local regulations. Positive and negative quality control samples must be included to verify accurate testing.
- **Laboratory testing for verification**. It is suggested that a percentage (i.e., 5 percent) of specimens that screen negative or positive be sent to a laboratory to verify accurate performance of POCT results, and that all positive results that are contested by patients be submitted to a laboratory for confirmation testing.

Implementing Point-of-Care Testing

Based on surveys of sites holding CLIA waivers, Howerton, Anderson, Bosse, Granade, and Westbrook (2005) suggest that practitioners consider the following questions when deciding whether to use any type of POCT device:

- Who will manage and be accountable for testing oversight? Can this person receive the appropriate training?
- Are there sufficient personnel to conduct testing?
- How will testing affect workflow?
- How will staff be trained to conduct a POCT?
- Can the site adequately comply with Federal, State, and local regulations regarding the POCT?
- What are the safety considerations for both personnel and patients?
- Can personnel reasonably follow quality control procedures?
- Does the site meet physical requirements for testing (e.g., space for collection, testing, storage, security)?
- What are the benefits and costs of POCTs to the practitioner?
- How will testing records be maintained?
- What written documentation is needed?
- What are the plans for quality control testing and quality assurance?

Preparing Clinical and Office Staffs for Testing

Once a practitioner has decided which matrices and types of tests to use, the clinical and office staffs need to be prepared to begin testing. Preparation may include:

- Obtaining a CLIA waiver;
- Developing written policies and procedures for testing, including ongoing staff training, and establishing quality control procedures;
- Developing and implementing testing protocols, including guidelines for specimen collection, use of POCT, confirmatory testing, and laboratory technical assistance;
- Establishing confidentiality safeguards;
- Training staff in use of the selected POCT devices and in collecting specimens for laboratory testing;
- Establishing record keeping procedures;
- Preparing appropriate storage sites for completed POCTs and laboratory tests; and
- Arranging pickup or transportation for laboratory tests.

Preparing a Specimen Collection Site

The collection site is a designated area where a patient provides the specimen for a drug test. Collection of most specimen matrices does not require special arrangements. Urine collection in primary care settings needs to be configured for privacy while a patient provides a specimen if direct observations are not required. Water for drinking needs to be available in the event the patient cannot provide sufficient urine (shy bladder). Measures need to be taken to prevent adulteration or substitution, such as putting a bluing agent in the toilet, not providing access to soap and water in the collection room, and directly observing specimen provision are needed in clinical situations only if adulteration or substitution is suspected. Once specimens are collected and labeled, there must be space and proper conditions for securely and appropriately storing them. A refrigerator is a convenient, appropriate storage place, especially when samples are picked up by a laboratory courier on a daily or less frequent basis.

Section 4—Drug Testing in Chronic Non-Terminal Pain Management

Uses of Drug Testing in Chronic Non-Terminal Pain Management

Primary care practitioners often provide medical management for patients taking opioids for chronic pain. Long-term pain treatment with opioids requires monitoring for continuing effectiveness for pain relief and the potential for misuse, addiction, or diversion. Current clinical guidelines recommend the use of drug tests for pain management with opioids to help guide decisions about prescribing scheduled medications, revising treatment regimens, and when to initiate or refer for substance abuse treatment (Chou et al., 2009; Fishman, 2007).

Gourlay, Caplan, and Heit (2010) suggest that drug testing may be useful for:

- New patients as part of regular care to identify the use of illicit or non-prescribed drugs;
- Patients being prescribed a controlled substance;
- Patients who present with a condition that warrants a prescription for a controlled substance and who resist a full evaluation or who request a specific medication with addictive potential;
- Patients with aberrant behavior (e.g., patients who consistently want appointments toward the end of office hours, arrive after office hours, insist on being seen immediately, repeatedly report losing prescriptions or medications, are reluctant to change medication, do not adhere to the treatment plan);
- Patients who are suspected of diversion;
- Patients who need advocacy to verify their abstinence;
- Patients in recovery from SUDs; and
- Patients who need a change in their treatment.

A 3-year study on behavioral monitoring and urine drug testing in patients receiving long-term opioid therapy for pain found that urine drug testing was much more effective than behavioral monitoring alone in identifying patients who were taking drugs other than the prescribed opioid (Katz et al, 2003).

Drug testing is useful for monitoring patient treatment compliance with prescribed medications that have addictive properties (e.g., opioid pain medication, sedatives, ADHD medication). Test results can reveal whether patients have recently taken their prescribed medication and if non-prescribed or illicit drugs have been used. Drug testing can help practitioners identify and reduce diversion of scheduled drugs by patients.

The results of drug tests can clarify situations in which non-apparent substance use complicates the management of chronic Non-Terminal pain. Patients may not disclose:

- All the medications prescribed by other providers or over-the-counter (OTC) medications and herbal products;
- That they take medications prescribed for other people;
- Use of illicit drugs or how much alcohol they consume; or
- If they have stopped taking their medications.

Talking with Patients about Drug Testing

Prior to testing, important tasks for the practitioner are to explain to patients: (1) the reasons for performing drug testing, (2) use of the test results, and (3) the practitioner's duty to maintain confidentiality. It should also be explained to the patient that the drug tests and the results will become part of the patient's record.

Before testing, the practitioner needs to emphasize to patients the importance of revealing all prescription and nonprescription drugs (including OTC medications and herbal preparations) they are taking. Patients may not realize that OTC or herbal products can affect drug test results.

Discussing drug testing results can be difficult. Patients need clear and thoughtful explanations of the test results and the terms positive, negative, adulterated, dilute, or substituted. They need to understand why the test was positive or negative and what that means for the patient and their treatment. All results should be presented in a straightforward, nonjudgmental manner using terms the patient understands.

The ease or difficulty in establishing and maintaining a therapeutic alliance is affected by many factors, including the amount of time the practitioner can spend with the patient, the backgrounds of both the practitioner and the patient, the patient's ability to speak English, and acculturation levels (if the patient is from another country). Drug testing with some patients from diverse groups can be challenging due to their cultural beliefs, history, and heritage. Some patients may distrust the medical profession because of past abuses by the medical community. They might feel additional shame about SUDs because of the strong stigma in their community, they might fear disclosure to law enforcement, or they might possess a different idea of what constitutes normal drinking versus problematic drinking.

Monitoring Patients

Urine drug tests are becoming more common to monitor patients receiving chronic opioid analgesics. In pain management, drug tests can be useful, but they need to be used thoughtfully. The plan and reasoning for drug testing for these patients needs to be discussed thoroughly with the patient. Some patients may find drug tests intrusive; others accept the practice. Drug tests tend to be associated with drug abuse treatment and some patients may be offended when asked to participate in drug testing as part of pain treatment.

Drug tests do not monitor therapeutic drug levels; they provide information regarding medication adherence to the prescribed medication and/or the ingestion of illicit drugs. The only exception is the use of serum methadone levels. If the drug test shows the use of illicit drugs in addition to the prescribed medications, the patient needs to be educated regarding the danger of using illicit substances and opioid pain medications and that substance abuse is not helpful to long-term pain management. Some patients may need to be referred to specialists in both addiction and pain management.

To properly interpret urine drug screens, a detailed understanding of the pharmacology of the prescribed opioid and its relationship to the urine-testing technique must be understood by the prescribing provider. A negative test result when a positive one was expected (e.g., pain medication) may also trigger patient resistance or feelings of guilt, shame, or anger. In these cases, it is important that the practitioner avoid arguing with the patient and remain nonjudgmental.

Ensuring Confidentiality and 42 CFR Part 2

In most primary care settings, 42 CFR Part 2, the regulation protecting information about a patients' substance abuse, does not *usually* apply to a general medical care facility unless that facility (or person) "holds itself out as providing, and provides, alcohol or drug abuse diagnosis, treatment or referral for treatment" (42 CFR§2.11). If a healthcare practice includes someone whose primary function is to provide substance abuse assessment or treatment, and the practice benefits from Federal assistance (including Medicare or Medicaid payments), that practice must comply with the 42 CFR Part 2 law and regulations and implement special rules for handling information about patients who may have substance abuse problems (CSAT, 1997). The results of a patient's drug test and substance use history are then confidential and may not be revealed to a third party without the patient's consent, except in certain circumstances.

Many states offer varying levels of additional protection to medical information about patients that is as strict or stricter than 42 CFR Part 2. Whether a laboratory test result is privileged or protected information may depend upon several factors:

- The type of professional holding the information and whether he or she is licensed or certified by the state;
- The context in which the information was communicated;
- The context in which the information will be or was disclosed; and
- Exceptions to any general rule protecting information.

Which practitioners are covered depends on the state within which the clinician practices.

Preparing for Implementing Drug Testing

Before starting a drug testing program, discuss the needs of the program with the laboratory toxicologist or other knowledgeable laboratory staff. Some important areas to obtain information about and to understand include:

- The strengths and limitations of the different tests;
- Standard collection procedures;
- Possible cross-reactivities with the targeted drugs that could affect test results;
- Limitations of the tests offered by the laboratory;
- Windows of detection for different specimens;
- Confirmatory testing, which can be done automatically, or only with specific request of the practitioner;
- Cutoff levels and whether they are appropriate for clinical purposes; and
- Cost of clinical drug test panels.

When ordering a laboratory test to detect substances of abuse, practitioners and staff needs to know exactly what a test is – and is not – measuring. For example:

- The specific drugs or metabolites that can be detected by the test
- The cutoff concentration used by the laboratory or the point-of-care test (POCT)
- The specific substance, class of substances, cross-reacting drugs, and/or metabolites that may yield a positive test result
- The drugs, drug classes, and/or their metabolites for which the test is being done
- The drugs/drug classes that will not be detected by the test

Collecting Specimens

Clinical drug testing should have established collection procedures for that facility or office that follow the College of American Pathologists, Clinical Laboratory Improvement Amendments, and local and State regulations. A properly collected specimen is essential to a obtaining an accurate test result,. The person responsible for specimen collection needs proper training. The duties include:

- Establishing the identity of the patient;
- Explaining clearly the collection procedure to the patient;
- Ensuring that the collection container is appropriate for the specimen matrix;
- Labeling the specimen properly;
- Collecting a sufficient amount of the specimen;
- Ensuring that the specimen collection method prevents substitution, dilution, or adulteration;
- Preventing contamination from environmental sources;
- Storing the specimen according to the manufacturer's or laboratory's recommendations;
- Preventing loss of or tampering with specimen by storing it in a secure area;
- Properly recording information; and
- Following universal precautions.

Collection procedures for drug testing should be conducted in ways that preserve patients' dignity. The procedures should be written and explained to patients before collection

The results of a drug test will not provide a diagnosis of an SUD.

Conducting POCTs

Personnel assigned to conduct the POCTs need to:

- Have access to current product inserts for the laboratory collection device and for the POCT device, if it is a combined collection and testing device;
- Pay close attention to the instructions provided with the test, particularly regarding timing and reading the results accurately;
- Understand possible cross-reactivities with other substances, especially if they are interpreting the results;
- Assay appropriate positive and negative quality control samples;
- Decide under what circumstances laboratory confirmatory tests will be ordered; and
- Record test results according to the protocols established by the practice.

If giving immediate feedback to a patient – a major benefit of using POCTs – the practitioner needs to be confident about what the test is measuring, its results, and the limitations of the test. POCT manufacturers generally have a technical assistance telephone line to answer questions. Section 5 provides details about using urine drug tests for specific drugs, including windows of detection, cross-reactivities, limitations, and special considerations for interpreting results.

Interpreting Drug Test Results

A drug test indicates whether a substance or a prescribed medication is present at levels below (negative) or above (positive) the test cutoff concentration. A test result can reveal that a specimen is negative, positive, adulterated, substituted, or dilute. Generally, drug testing cannot tell the practitioner the amount of drug ingested by the patient, whether a therapeutic level has been achieved (e.g., opioids for pain relief), or frequency of use, nor can it indicate the patient's level of intoxication, impairment, or severity of abuse, when trying to determine whether a patient may have an SUD. The results of a drug test will not provide a diagnosis of an SUD.

When interpreting drug test results, the practitioner must know exactly what a test is – and is not – measuring. The practitioner must consider:

- The purpose of the drug test;
- The limitations of the test used;
- The drugs or drug metabolites being detected and those not being detected;
- Potential cross-reactivities; and
- The limitations of the selected matrix.

Many other factors need to be considered when interpreting drug test results (e.g., specific substance, class of substances, cross-reacting drugs and/or metabolites that may yield a positive result). Drug test results may raise clinical concerns for practitioners, or provide reassurance about patient adherence to treatment. Testing may provide unexpected information, but should never be the sole basis for diagnosis and treatment decision making. Test results should be used to supplement the information obtained from a comprehensive patient interview, the physical examination, and consideration of the patient's overall health.

Result: Negative Specimen

A negative test result means that a particular substance was not detected at or above the cutoff concentration in the specimen. A negative screening test result is rarely followed by a confirmatory test, but can be done if requested by the practitioner. Laboratories perform confirmatory tests on positive results, either routinely or only for certain drug/drug class positives (e.g., amphetamines, opiates) (White & Black, 2007), depending on the laboratory.

The response to a negative drug test result is based on the patient's diagnosis and reason for testing. If the patient is being prescribed medications with addictive potential (e.g., opioids, sedatives), a negative drug test warrants a reassessment that may lead to more frequent drug testing and office visits.

A negative drug test does not necessarily mean the patient has not used a particular substance or taken the prescribed medication. Negative test results can occur if:

- Errors were made in interpretation of the test.
- The patient may eliminate the medication more rapidly than usual.
- The patient does not absorb the drug sufficiently for detection.
- The patient ran out of medication.
- The patient took the medication but not when expected or during the window of detection for the ordered test.
- The patient was thirsty and drank sufficient water to dilute the specimen or consumed an excessive amount of fluids to deliberately dilute a urine specimen.
- The appropriate test was not performed.
- The cutoff concentration used in the test was set too high.
- The test was performed outside the detection window.
- The specimen may have been adulterated or substituted.

If a negative confirmatory test result is a surprise based on the patient's self-report, collateral report, or other evidence, the practitioner should reconsider the testing procedures and assessing the patient's behavior. The practitioner could contact the laboratory and discuss the results, especially to see whether the negative report came from values that were just below the laboratory's cutoff concentration. Repeated urine testing could be done, or oral fluid could be tested.

The practitioner could also consider:

- Changing or including additional drugs for testing.
- Adding specimen validity testing or testing the original negative specimen for validity.
- Changing the matrix tested.
- Testing repeated serial urines.
- Changing the drug-testing methods.
- Determining whether the testing occurred outside of the detectable window for the substance.

A confirmed negative test result for a patient receiving a prescribed medication, such as in pain treatment, is of concern. Check with the laboratory about the validity of the test: Was the cutoff concentration low enough to measure therapeutic levels of the medication? Was the correct test performed to detect the prescribed?

If the negative test result is valid for prescribed scheduled medications, the practitioner must decide how to proceed with the patient who is, at best, not adhering to his or her prescribed medication regimen or, at worst, diverting the medication.

Result: Positive Specimen

A positive screening test result means that a particular substance was detected at or above the administrative cutoff concentration in the specimen. Confirmatory tests are frequently performed for specimens with positive screening results. If the patient admits drug use when informed of positive results from a POCT, a confirmatory test is not needed.

False-positive results are possible with screening tests. If a presumptive positive is confirmed by a second methodology,, a false positive is highly unlikely if the test is performed correctly. If a positive result is surprising and the patient vehemently denies use, order a laboratory confirmatory test if such a test is not already part of the laboratory's testing agreement.

Interpretation of positive tests can sometimes be complex, especially if a patient is being monitored for abstinence following heavy drug use. With frequent use, significant bodily accumulation of drugs can occur with the consequence that drug metabolite(s) may be excreted for extended periods. This is especially true for highly lipid soluble drugs, such as marijuana (tetrahydrocannabinol) and phencyclidine, but it also applies to other drugs, such as cocaine and heroin. A patient who is recently abstinent may continue to test positive for days to weeks depending upon the drug and pattern of use. Distinguishing this normal pattern of body elimination of drugs from new drug use can be difficult. Methods to predict new marijuana and cocaine use have been described. (Huestis and Cone, 1998, Smith, Barnes, & Huestis, 2009, Preston, Silverman, Schuster, and Cone, 1997).

If the confirmatory test result is positive for nonprescribed substances, the practitioner should review the patient's use of prescribed medications, OTC products, and herbal products to determine whether any of these may be the source of the positive. The practitioner may also retest using a different matrix. However changing matrices makes interpretation difficult. If the second specimen using the same or a different matrix is negative, it does not refute the scientific validity of the first test.

Drug test results should never be the sole criteria used for diagnosis of an SUD or making treatment decisions. The practitioner should consider them along with behavioral and physical assessments and any collateral information obtained.

Other possible changes in drug-testing procedures include:

- Increasing the testing frequency to discourage illicit drug use by the patient, or possible diversion of prescribed medications;
- Changing the drugs tested for (e.g., test for another class of drugs) to detect the full scope of the patient's drug use; and
- Changing the drug-testing methods (e.g., use a laboratory test instead of a POCT or request a confirmatory test for all initial test(s) to rule out false-positive results.

Other changes to treatment are discussed in the section on monitoring patients in Section 4.

Result: Adulterated or Substituted Specimen

Urine is the easiest specimen to adulterate, and commercial formulas of synthetic urine are available for substitution. Other fluids, including water, also have been used for substitution. If the test result indicates that the specimen has been adulterated or substituted, collect another specimen and determines whether the temperature and pH of specimens are being checked immediately after collection. For patients who seem to have several test results of adulterated or substituted urine, stricter collection procedures could be instituted for that patient. These could include:

- Ensuring that adulterants, such as soap, ammonia, or bleach are not readily available in the collection area;
- Prohibiting personal belongings in the bathroom;
- Turning off the source of running water during collection and putting blue dye in the toilet; and
- Observing specimen collection.

Result: Dilute Specimen

A dilute urine specimen can be negative or positive, depending upon the degree of dilution and amount of drug excreted. If the test result shows that the specimen has been diluted, the practitioner should discuss both the dilution and the negative or positive test result with the patient. In addition:

- Test a different matrix, if possible;
- Collect and test a new specimen;
- Review the specimen collection site and ensure no access to materials that could be used to adulterate or substitute the specimen; or
- Consider medical reasons for diluted urine.

Result: Invalid Urine Specimen

An invalid result is one in which scientifically supportable analytical test results cannot be established for a specimen. An invalid laboratory test result for urine can be caused by many factors, such as:

- A physiological inconsistency between the patient's urine creatinine and specific gravity;
- An interference in the screening or initial test analysis;
- An interference in the confirmatory assay;
- The presence of oxidizing compounds at or above a cutoff set by the laboratory;
- A urine pH between 3.0 and 4.5 or outside other range set by the laboratory or POCT manufacturer;
- A urine pH between 9.0, and 11.0 or outside other range set by the laboratory or POCT manufacturer;
- The presence of nitrites in urine at or greater than 200 µg/mL but less than 500 µg/mL, or above a level set by the laboratory or POCT manufacturer;
- The possible presence of chromium (VI);
- The possible presence of a halogen (e.g., bleach, iodine, fluoride);
- The possible presence of surfactant (e.g., soap);
- The physical appearance of a specimen is such that the laboratory feels analysis of the specimen might damage its instruments; and
- Other factors determined by the laboratory for an invalid specimen.

An invalid test result is not definitive proof of specimen tampering. Consider other possible causes before assuming that the patient has attempted to subvert the test. Try to determine the reason for the report or discuss possible causes with the laboratory. A review of the patient's history may reveal a medical explanation. And, the practitioner could also have another specimen collected and tested and ensure that the collector follows proper procedures.

Results are also reported as indeterminate or inconclusive. The practitioner should consider the possible causes, including storage and transport irregularities, and potential medical explanations. If this happens often, ask the patient to return for further discussion and repeat the test.

Frequency of Testing

Drug testing can be done as a baseline when prescribing medications with addictive potential. The subsequent frequency of drug testing depends on the practitioner, the individual patient, the diagnosis, and the reason for drug testing.

In opioid pain management, testing can be done both to ensure compliance with prescribed medications and to identify abuse of illicit substances. Drugs of interest in this instance include benzodiazepines and opioids (e.g., oxycodone, methadone, fentanyl, hydrocodone, hydromorphone, morphine). Drug tests can be done before providing initial prescriptions or refills (White & Black, 2007) or for other medications with addictive potential. Testing can also be done if the patient exhibits aberrant behavior, if diversion of prescribed medications is suspected, or randomly to monitor treatment.

For the patients receiving medications, particularly opioids, with abuse potential, drug tests can be done during every visit, randomly, before providing prescription refills, or if the patient exhibits aberrant behavior. The frequency can also change with several drug tests that show that the patient is taking the medication as prescribed and is not positive for illicit drugs.

A drug test may not be needed if the patient admits illicit drug use or treatment noncompliance for prescribed medications when coming to his or her appointment.

Documentation and Reimbursement

Proper documentation is needed for both patient record keeping and to obtain reimbursement.

Documentation

In addition to keeping accurate patient medical records, practitioners must ensure proper documentation of the use of POCTs. This includes (Howerton et al., 2005):

- Written procedures for performing POCTs;
- Inventory control – lot numbers and expiration dates for POCTs;
- Documentation of staff training and reassessment;
- Quality assurance test results;
- Documentation of problems and problem resolution; and
- Copies of laboratory test orders and results.

Patient medical records should document:

- The medical necessity for drug testing;
- Tests performed and test results;
- Changes made to the treatment plan based on test results; and
- Referrals made.

Reimbursement

Testing for alcohol or drugs is billed by the specific biological tests conducted according to the Current Procedural Terminology (CPT) codebook. Insurance coverage for alcohol or drug testing varies by carrier. Careful documentation of the need for testing assists with obtaining reimbursement. The current issue of the CPT codebook should be consulted to obtain proper reimbursement.

Some CPT codes that are used for testing include:

- 80100: For qualitative screening tests used to detect the presence of *multiple* drug classes.
- 80101: For qualitative screening tests used to detect the presence of *one* drug class.
- 80102: For each *confirmatory* test.
- 82055: Alcohol testing (any method other than breath).
- 82075: Alcohol testing (breath).

Centers for Medicare & Medicaid Services uses different codes:

- G0430-QW: When multiple drug classes are tested and the testing methodology does not use the chromatographic method
- 80100-QW: When testing for multiple drug classes that do use the chromatographic method
- G0431: Used, per drug class, when performing a test for a single drug class

The medical necessity for testing can be documented by using International Classification of Diseases codes (i.e., harmful use or dependence syndrome) from the *International Statistical Classification of Diseases and Related Health Problems, Volume 1: 10th Revision* (World Health Organization, 1992). However, the patient may want to pay for a drug test and not submit the cost to the health insurance company. This should be discussed with the patient.

Section 5—Urine Drug Testing for Specific Substances

Urine is the most rigorously evaluated and most commonly used matrix for drug testing (Watson et al., 2006). All results are affected by laboratory test or point-of-care test (POCT) cutoff concentrations. Therefore, practitioners should always consult with laboratory staff when ordering laboratory tests or carefully read POCT package inserts before using the test. Numerous POCTs are available for urine drug testing.

Window of Detection

The window of detection for urine falls in the intermediate range, compared with the detection period or window for other matrices. Many factors influence the window of detection for a substance. Factors include, but are not limited to, the frequency of use (chronic or acute), amount taken, rate at which the substance is metabolized, cutoff concentration of the test, patient's physical condition and, in many cases, body fat. Some hepatic, renal, endocrine, and other pathologies may extend the detection window.

Drugs are present in urine from within minutes of use to several days after, depending on the substance; quantity ingested; the degree to which the bladder was filled with drug-free urine at the start of drug use; the patient's hepatic, cardiac, and renal function; the patient's state of hydration; and drug type. Drugs that are smoked or injected are detectable in urine samples almost immediately. Detection rates for drugs taken orally are slower, taking up to several hours and peaking at about 6 hours (Dolan et al., 2004).

The window-of-detection estimates used in this section are from several sources: Cone (1997), Dasgupta (2008), Verstraete (2004), Warner (2003), White and Black (2007), Wolff et al. (1999), and Wong and Tse (2005).

Many urine drug tests detect the drug metabolite, rather than the drug itself. As a general rule, drug metabolites remain in the body for a longer period than does the parent drug, allowing for a longer detection period.

It may be difficult to detect illegal substances in urine specimens of patients who stop use for several days before providing a specimen. Most substances of abuse are detectable in urine for approximately 2–4 days (Center for Substance Abuse Treatment [CSAT], 2006b; Cone, 1997). However, the detection time may be prolonged when large, frequent doses are taken over a long period (CSAT, 2006b). For example, one dose of intranasal cocaine may be detectable in urine for 3–5 days using a cutoff of 300 ng/mL after ingestion, but daily, heavy cocaine use may be detected for additional days following discontinuation of use (Verstraete, 2004). Chronic use of marijuana may be detectable for up to 30 days after use is stopped.

Specimen Collection

Urine collection usually is easier than collecting blood, and samples are available in sufficient quantities (Warner, 2003). Urine sample collection is not usually observed in primary care settings. However, if it is suspected that a patient is tampering, diluting, or adulterating urine specimens, some measures used in forensic or workplace testing can be used to prevent this, including:

- Directly observing specimen provision;
- Turning the water off to the taps and adding a bluing agent to the toilet tank to avoid sample dilution;
- Not providing hand soap in the restroom where the sample is being done;
- Not storing cleaning agents in the restroom (e.g., ammonia-containing products, bleach, toilet cleaning products); and
- Not allowing coats, purses, or bags into the restroom with the patient.

Patients who exhibit "shy bladder syndrome" (inability to void) may need to consume liquids to provide a specimen (e.g., 8 oz. of water every 30 minutes, but not to exceed a maximum of 40 oz. over a period of 3 hours, or until the patient has provided a sufficient urine specimen).

Once the specimen is collected and labeled:

- The appearance and color of the urine sample should be documented.
- The use of primary collection containers with a temperature-sensitive strip on the outside is recommended, rather than placing a thermometer or temperature strip into the urine.
- The urine specimen temperature should be recorded within 4 minutes of collection; the temperature should be between 90°F and 100°F.

Additional clinical testing, such as a routine urinalysis (e.g., pH and tests to detect the presence of oxidizing components and adulterants) can be conducted on an aliquot separate from that used for urine drug testing to avoid any argument that a positive was the result of a foreign object being placed in the patient's urine specimen.

Adulteration, Substitution, and Dilution

Urine tests can be reported as adulterated, substituted, or dilute.

Adulteration

An adulterated urine specimen is one containing a substance that is not normally found in urine or that is normally found, but is in abnormal concentrations. Adulterants work by interfering with immunoassay and/ or confirmatory assay function, or they convert the target drug to compounds not detected by the test (Jaffee, Trucco, Levy, & Weiss, 2007). Ordinary household products (e.g., laundry bleach, toilet bowl cleaner, hand soap, vinegar, ammonia, eye drops) have been used for many years to adulterate urine specimens to obtain a negative drug test result (Dasgupta, 2007). Household products that alter the pH of urine to a value outside the physiologic range can be easily detected by determining the pH of the sample (Dasgupta, 2007). Products such as bleach and other oxidizing agents can be detected with a general oxidants assay.

Numerous commercial adulterants are available via the Internet. The following list is a summary of such products by active ingredient (Jaffee et al., 2007):

- Glutaraldehyde (e.g., “Clean X”) can interfere with absorbance rates on immunoassay tests, masking the presence of many substances.
- Sodium or potassium nitrite (e.g., “Klear,” “Whizzies”) can mask the presence of marijuana metabolite in immunoassay and confirmatory tests..
- Pyridinium chlorochromate (PCC, commercially known as “Urine Luck”) is an oxidizing agent that masks the presence of THCCOOH and, depending on the pH of the urine, can affect test results for morphine. Cocaine metabolites, amphetamine, and PCP are not affected by PCC (Dasgupta, 2007).
- Peroxide/peroxidase (e.g., “Stealth”) can oxidize drugs and their metabolites, making THCCOOH and lysergic acid diethylamide (LSD) undetectable by immunoassay tests.

The effectiveness of an adulterant depends on the amount of the adulterant added and, in some instances, the concentration of the drug in the sample. Specimen validity tests can detect many adulterants.

Substitution

Synthetic urine products can be submitted when collection of a urine specimen is not observed. These products are premixed liquids with the characteristics of natural urine (i.e., correct pH, specific gravity, and creatinine levels). To achieve the temperature of recently voided urine, synthetic urine products can be heated in a microwave or taped next to a heating pad in a pocket. Sometimes, another person's urine is submitted.

More commonly, water or a saline solution is substituted for urine. Thus, a urine specimen is considered substituted when the creatinine concentration on both the initial and the confirmatory tests is less than 2.0 mg/dL and the specific gravity is less than or equal to 1.0010 or greater than or equal to 1.0200 (Substance Abuse and Mental Health Service Administration [SAMHSA], 2010b).

Dilute Specimens

Diluting the urine sample to the point where the targeted drug is below the cutoff concentration is another way to obtain a negative test result. For instance, consuming water in more-than-normal quantity and taking diuretics can dilute the urine sample. Individuals may also add water from the tap or toilet bowl to dilute specimens if tap water is available in the restroom and/or bluing has not been added to the commode water. Commercial products are available that promise to "cleanse the urine." These products advocate consuming large amounts of tea or other fluids, increasing urine volume, thereby diluting drugs in the urine. Reducing the amount of time between notice that a specimen will be collected and the time of collection reduces the potential for the patient to consume enough fluids to dilute the urine.

Dilution may raise suspicion of tampering, but does not necessarily confirm tampering. Other factors need to be considered, such as whether the patient is taking a diuretic, eating a strict vegetarian diet, or maintaining a high state of hydration. Other factors include whether the patient was working in hot weather conditions and drank large amounts of fluid or drank fluids immediately before providing the specimen.

Cross-Reactivity

The cross-reactivity of urine immunoassay tests varies by drug class. For example, tests for cocaine measuring its principal metabolite, benzoylecgonine, have low cross- reactivity with other substances. However, tests for amphetamine/methamphetamine usually are extremely cross-reactive, and further laboratory testing using a method different in principle from immunoassay (i.e., not a second immunoassay) is required to confirm amphetamine use (Gourlay et al., 2010). As stated above, cross-reactivity is many times viewed as a negative aspect of immunoassay. However, cross-reactivity does have a positive side. An immunoassay that is specific for morphine will detect only morphine and will miss other opiates (e.g., hydrocodone) that a patient might be using without the treating physician's knowledge. Thus, a general opiates screen is preferred over a specific test when looking for opiate-type drugs. Lack of cross-reactivity also may affect testing, such as that performed for oxycodone, as discussed under "opioids."

Alcohol

The window of detection for alcohol is 7–12 hours. Because of rapid metabolism, blood tests or the standard hand-held breath devices (breathalyzers) are often used.

Urine drug tests for alcohol indicate only recent ingestion; they cannot identify long- term abuse. Alcohol in blood or a blood product (e.g., serum, plasma) or a breath alcohol is required to show impairment and the degree of impairment.

Biomarkers, such as the gamma-glutamyl- peptidase, carbohydrate-deficient transferrin, aspartate amino transferase (measured in serum), and erythrocyte mean cell volume tests may confirm a suspicion of long-term alcohol abuse or dependence. Ethyl glucuronide EtG) and ethyl sulfate are direct metabolites of ethanol that can be measured in urine. More research is needed to establish standards to rule out possible exposure to alcohol in commercial products, such as mouthwash and hand sanitizers, versus drinking of alcoholic beverages (CSAT, 2006a).

Amphetamines

The SAMHSA workplace cutoff concentration for amphetamines is 500 ng/mL for initial testing, 250 ng/mL for confirmatory testingand equal to or greater than 100 ng/mL for methamphetamines (SAMHSA, 2008).

The window of detection varies. A single dose of amphetamine or methamphetamine can be detected in the urine for approximately 4 hours, depending upon urine pH and individual metabolic differences. People who use chronically and at high doses may continue to have positive urine specimens for 2–4 days after last use (SAMHSA, 2010b). Methylenedioxyamphetamine (MDA), methylenedioxymethamphetamine (MDMA), and methylenedioxyethylamphetamine (MDEA) can be detected for 1–2 days (Moeller et al., 2008; SAMHSA, 2010b).

Drug tests for the presence of amphetamine are among the hardest to interpret. Methamphetamine is the target analyte for amphetamine/ methamphetamine testing. Immunoassay tests are highly cross-reactive and may detect other sympathomimetic amines, such as diet agents, decongestants and medications to treat attention deficit/hyperactivity disorder, narcolepsy, and Parkinson's disease.

Methamphetamine exists as two optical isomers (stereoisomers): the *d*-form has high abuse potential while the *l*-form is found in some OTC products (Kwong, 2008a, 2008b).

Typical immunoassay tests do not distinguish methamphetamine and/or amphetamine use from use of OTC products containing sympathomimetic amines. All presumptively positive urine "amphetamines" results should be confirmed by an alternate methodology different in principle from the immunoassay used to produce the screening result (White & Black, 2007). A separate test is available that is offered by most laboratories that distinguishes illicit methamphetamine (*d*-methamphetamine) from OTC nasal inhaler (*l*-methamphetamine).

Tests for amphetamine cross-react with many other substances and are too numerous to present a comprehensive list. A confirmed test for amphetamine or methamphetamine can occur because a number of other medications metabolize to these. The product inserts should be consulted for the current list of cross-reacting drugs.

Barbiturates

The incidence of barbiturate abuse is low compared with abuse of other drugs or alcohol (SAMHSA, 2009). Barbiturates (sans phenobarbital) are detected easily using a variety of immunoassays, even though only a small amount of the parent drug is found in the urine. The use of barbiturates may be confirmed readily using several different methods (Levine, 2010). The window of detection depends on the type of barbiturate (see Table 6).

Benzodiazepines

Like barbiturates, benzodiazepines are classified by their elimination half-lives False-negative results can occur if a test is set to detect only one benzodiazepine or its primary metabolite(s), and the clinician is trying to monitor a non-cross-reacting benzodiazepine. Drug-screening immunoassay tests are usually designed to detect a specific benzodiazepine metabolite

Benzodiazepines can be divided into several groups, based on their metabolites:

- Some benzodiazepines (e.g., chlordiazepoxide, diazepam, temazepam) are metabolized to oxazepam and then to the inactive glucuronide metabolite.
- Nitrobenzodiazepines (e.g., clonazepam) are usually reduced to the corresponding amino compound, but are not converted into oxazepam.
- The triazolobenzodiazepines (e.g., alorazepam, estazolam, and triazolam) tend to form hydroxyl derivatives that are separate and distinct from oxazepam.
- Other benzodiazepines (e.g., lorazepam, flurazepam) have a unique metabolism that does not result in the formation of oxazepam.

Clinical laboratories usually use cutoff concentrations which may not necessarily detect a low therapeutic doses (e.g., triazolam) (Warner, 2003). See Table 6 for estimated windows of detection of some of the most commonly prescribed benzodiazepines.

Cocaine

Urine drug tests for cocaine detect cocaine's major metabolite, benzoylecgonine. The body quickly metabolizes cocaine to its major metabolite, benzoylecgonine, and neither is stored in the body. Therefore, even with chronic use, the window of detection is short (Jufer, Walsh, Cone, & Sampson-Cone, 2006), with the clinical test cutoff of 300 ng/mL. The detection window may be longer using the federally mandated cutoffs. Immunoassay tests are highly specific for the cocaine metabolite (benzoylecgonine) and do not cross-react with other substances. See Table 6 for cutoff values and window of detection.

Marijuana/Cannabis

Marijuana, the most commonly used illicit drug, can be detected for prolonged periods after regular use. The active principle of marijuana, tetrahydrocannabinol (or THC) has high lipid solubility. The THC that is stored in fatty tissue gradually reenters the bloodstream at very low levels, permitting metabolism and eventual excretion. THC is metabolized extensively in the liver.

The window of detection is highly dependent on the quality of the marijuana, the individual's body fat content and metabolism, chronicity of use, the individual's state of hydration when the urine sample is collected, and the cutoff used by the laboratory (White & Black, 2007). See Table 6 for approximate window of detection times. Marijuana is easily detected by immunoassay detecting THC-COOH (11-nor- Δ9-tetrahydrocannabinol-9-carboxylic acid; commonly referenced as THC acid or THCA), the major inactive metabolite of THC.

Confirmation by GC/MS tests should be performed if the positive screening test results have legal or other serious implications for the patient. Some legal food products are made from hemp seeds (e.g., hemp seed oil, flour, liquor, ale). However, usually the THC concentrations in the food products are too low to produce a positive urine drug test result (Bosy & Cole, 2000). Some proton-pump inhibitors have caused positive tests on immunoassay (Gourlay et al., 2010).

Under extreme conditions (e.g., the person rides in a closed car with people smoking marijuana), passive exposure can lead to positive results with a screening cutoff of 20 ng/mL. However, the levels of marijuana metabolites found in urine under less extreme passive exposure conditions are below cutoff concentrations and would not be detected (Cone et al., 1987; Perez-Reyes, Di Guiseppi, & Davis, 1983). Marinol and Sativex cause positive results because they contain THC.

Opioids

Practitioners need to be particularly careful when interpreting urine drug test results for opioids. It is essential to understand the metabolism of this class of drugs to interpret drug tests.

The term *opioids* includes both opiates and opioids. Opioids are a group of compounds that have pharmacological properties similar to morphine and have affinity toward the opiate receptors in the brain (Dasgupta, 2008). The term *opiates* refers to naturally occurring alkaloids (morphine and codeine) obtained from the opium poppy and semisynthetic alkaloids that are partially derived from the opium poppy (i.e., buprenorphine, dihydrocodeine, heroin, hydrocodone, hydromorphone, levorphanol, oxycodone, and oxymorphone) (Dasgupta, 2008). Opioids include the synthetic compounds that are structurally unrelated to morphine (i.e., fentanyl, meperidine, methadone, pentazocine, propoxyphene, tramadol) (Dasgupta, 2008).

Opiate immunoassay tests were originally designed to detect morphine and codeine as target analytes to identify heroin use as morphine is a metabolite of heroin ((Kwong, 2008a, 2008b, Warner, 2003). Many laboratories use SAMHSA's Federal workplace cutoff concentrations for opiates and test for morphine, codeine, and 6-acetylmorphone (6-AM). However, for opiates, a cutoff of 300 ng/mL is commonly preferred clinically (White & Black, 2007). As heroin is metabolized, 6-AM is produced, which is then hydrolyzed to morphine. Thus, the detection of 6-AM in the urine proves heroin use, but 6-AM is eliminated quickly from the body, making detection in urine possible for only a few hours (Gourlay et al., 2010).

A typical opiate screen reports the presence of only codeine and morphine. An expanded opiate panel may also include hydrocodone and hydromorphone and/or oxycodone and oxymorphone.

Distinguishing between illicit opioid use and the use of prescribed opioid medications can be difficult. Immunoassay tests have variable cross-reactivity with semisynthetic opioids (i.e., hydrocodone, hydromorphone) and may or may not detect their use. The synthetic opioids (e.g., meperidine, fentanyl, methadone) are structurally dissimilar enough from morphine that they are not detected in standard opioid urine immunoassay tests, although some cross-reactivity – especially with the metabolites – may exist. Separate immunoassay tests specifically designed for their detection must be used. Oxycodone and its active metabolite, oxymorphone, require a drug-specific test. Specific assays for oxycodone are available as both POCTs and laboratory tests. Specialized tests for synthetic opioids must be ordered when concerns exist about abuse or diversion of synthetic opioid pain medications or to monitor patients' use of buprenorphine or methadone. Many laboratories have specific pain medication panels that test for codeine, morphine, hydrocodone, hydromorphone, oxycodone, fentanyl, and buprenorphine (Gourlay et al., 2010). Buprenorphine has potential for abuse, especially in the stand- alone preparation—Subutex (Smith, Bailey, Woody, & Kleber, 2007).

Poppy seeds can contain morphine and codeine. Ingesting large amounts of poppy seed or products containing poppy seeds can cause a positive urine drug test result.

Methadone is not detected in standard opioid drug tests. Specific tests for methadone and its major metabolite EDDP (or 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine) exist and are used to monitor adherence to medication-assisted treatment and to check for illicit drug use. These methadone immunoassay tests have little cross-reactivity with other opioids. Therefore, a positive opioid drug test result for a patient on methadone suggests the use of other opioids. To confirm that the patient has taken methadone and is not simply adding it to a urine specimen, the test for the methadone metabolite, EDDP, can be ordered.

Other Substances of Abuse

Testing information for other substances is presented below.

PCP

Federally regulated laboratories are required to test for PCP; other laboratories are not. Directors of clinical laboratories may add PCP to their screening drug panel if PCP use is prevalent in the community. The metabolite of dextromethorphan can cross-react with PCP and could cause a false positive.

When used to adulterate urine specimens, table salt, sodium hypochlorite, sodium hydroxide, detergent, and soap cause false- negative test results (Jaffee et al., 2007). However, these adulterants can be detected if the pH and specific gravity of the urine samples are checked.

Club Drugs

Club drugs generally include gamma-hydroxybutyrate (GHB), ketamine, flunitrazepam (Rohypnol, or "Roofies"), MDMA, MDA, and MDEA. Urine drug screening tests do not generally screen for club drugs. However, please see the section above on amphetamines for information about MDMA, MDA, and MDEA, and flunitrazepam (Rohypnol, or "Roofies") has excellent cross reactivity with many commercial benzodiazepine assays. New drug tests may screen for some club drugs, but routine drug tests cannot detect ketamine or GHB. Testing for GHB can be done by using GC or high-performance LC (LeBeau et al., 2006). The window of detection for GHB is generally less than 12 hours. Two commercial enzyme-linked immunosorbent assays (ELISAs) that test for ketamine are available (Huang et al., 2007). For a single dose of ketamine, detection is possible for about 3 days at a cutoff of 50 ng/mL (Baselt, 2004; Cone & Huestis, 2007).

LSD

Very little of the parent drug, LSD, is excreted in urine and it can be detected for only approximately 4 hours. The most abundant metabolite is nor-LSD (N-desmethyl-LSD), which is generally detected at a cutoff level of 0.5 ng/mL. Confirmatory testing is usually done with LC/MS or LC/MS/MS.

Inhalants

No standard drug test can detect inhalant use. Most inhalants contain many compounds, and no single assay can test for all of them. Some laboratories can test for inhalants using specially ordered tests, primarily with GC. Collection of a specimen for inhalants requires that the specimen be appropriately and rapidly sealed to ensure that the volatile inhalants are not lost.

Toluene is the main substance in many inhalants. It is cleared from the body quickly, leaving a short period to detect exposure. Most laboratories are unable to test for this substance. Urinary hippuric acid (UHA) measurements can be adapted to detect toluene inhalation, but they should be used cautiously because a person's metabolism can raise the levels of UHA. Thiesen, Noto, and Barros (2007) report that UHA levels higher than 3.0 g/g creatinine indicate intentional exposure.

Table 6: Window of Detection Estimates for Various Substances

Drug	Detection Limit	Detection Time
Amphetamines	500 ng/mL (S) 250 ng/mL (C)	4 hours(A) 2-4 days(C)
MDA/MDMA/MDEA		1-2 days
Short Acting Barbiturates (pentobarbital, secobarbital)	300 ng/mL (S)	4-6 days
Intermediate Acting Barbiturates (amobarbital, butalibital)	300 ng/mL (S)	3-8 days
Long Acting Barbiturates (phenobarbital)	300 ng/mL (S)	10-30 days
Short Acting Benzodiazepines (e.g., triazolam)	200 ng/mL or 300 ng/mL (S)	Up to 24 hours
Intermediate Acting Benzodiazepines (e.g., alprazolam, clonazepam, lorazepam, temazepam)	200 ng/mL or 300 ng/mL (S)	1–12.5 days
Long Acting Benzodiazepines (diazepam)	200 ng/mL or 300 ng/mL (S)	Diazepam: 5–8 days Nordiazepam: 6–24 days
Chronic abuse of Benzodiazepines	200 ng/mL or 300 ng/mL (S)	Up to 30 days after last dose
Cocaine	150 ng/mL (S) 100 ng/mL (C)	1-3 days
Marijuana/Cannabis	20-50 ng/mL (S) 15 ng/mL (C)	Single Use: Up to 3 days Moderate Use: Up to 4 days Heavy use: Up to 10 days Chronic Heavy use: 30-36 days
Buprenorphine	0.5 ng/mL (S)	Up to 4 days
Codeine	300 ng/mL (S)	1–2 days
Heroin metabolite (6-acetylmorphine [6-AM])	10 ng/mL (S)	1–3 days
Hydrocodone	100 ng/mL (S)	1–2 days
Hydromorphone	300 ng/mL (S)	1–2 days
Methadone (maintenance dose)	300 ng/mL (S)	3–11 days
Morphine	300 ng/mL (S)	1–2 days
Oxycodone (immediate-release formulation)	100 ng/mL (S)	1–1.5 days
Oxycodone (controlled-release formulation)	100 ng/mL (S)	1.5–3 days
Oxymorphone (immediate-release formulation)	100 ng/mL (S)	1.5–2.5 days
Oxymorphone (extended-release formulation)	100 ng/mL (S)	1–4 days
PCP	25 ng/mL (S,C)	1.5-10 days (A) Several weeks (C)
	S=Screening; C=Confirmatory	A=Acute; C=Chronic

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