# Oklahoma Health Care Authority
## Medical Professional Services
## Prior Authorization Guideline

Medical Authorization Director Sig/Date

Physician Medical Director Sig/Date 12/21/16

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**NOTE:** Drug screening and testing is indicated in several populations, including neonates suspected prenatal drug exposure; symptomatic patients with possible multiple drug ingestion or unreliable history (usually seen in the emergency room); those patients undergoing substance abuse treatment; or patients in chronic pain management with chronic opioid therapy. **THIS GUIDELINE IS APPLICABLE TO URINE DRUG SCREENING/TESTING IN THOSE PATIENTS IN CHRONIC PAIN MANAGEMENT WITH CHRONIC OPIOID THERAPY (COT).**

**SUBJECT:** Presumptive Drug Testing (80305, 80306, 80307)
Definitive Drug Testing (G0659; G0480-G0483)
Therapeutic Drug Assays (80150-80299)

**NOTE:** Urine drug testing may not be limited to codes listed above; thus, all codes/tests submitted for drug testing on laboratory specimens must meet medical necessity requirements per OHCA policy, or as determined by OHCA physician review.

**REVISION DATE:** **January 1, 2017**
**REVIEW DATE:** **December 21, 2016**
**ORIGINAL DATE:** January 1, 2015

**OBJECTIVE:** To provide guidelines to assist in clinical decision making regarding medical necessity and consistency in the prior authorization process.

**DISCLAIMER:** This document is not a contract, and these guidelines do not reflect or represent every conceived situation. Although all items contained in these guidelines may be met, this does not reflect, or imply, any responsibility of this agency or department to change the plan provision to include the stated service as an eligible benefit.

## BACKGROUND:

Urine drug testing provides objective information to assist clinicians in identifying the absence or presence of drugs or drug classes in the body to assist with making treatment decisions. Testing for drugs of abuse to monitor treatment compliance should be included in the treatment plan for pain management when chronic opioid therapy is involved. Some indications for testing for patients on Chronic Opioid Therapy (COT) include:

- Identifies absence of prescribed medication and potential for abuse, misuse, and diversion;
- Identifies undisclosed substances, unsanctioned prescription medication, or illicit substances;
- Identifies substances that contribute to adverse events or drug-drug interactions;
- Provides objectivity to the treatment plan;
- Reinforces therapeutic compliance with the patient;
- Provides additional documentation demonstrating compliance with patient evaluation and monitoring.

## DEFINITIONS:

**PRESUMPTIVE DRUG TESTING**: Presumptive drug testing is used to identify possible use or non-use of a drug or drug class. A presumptive test may be followed by a definitive test in order to specifically identify drugs or metabolites. Urine is the best specimen for presumptive screening as blood is relatively insensitive for many common drugs, including psychotropic agents, opioids and stimulants. When obtained, results can be expressed as a negative/positive result or as a numerical result. Multiple methods can be utilized to perform presumptive testing, including direct optical observation, instrument assisted direct optical observation or utilization of chemical analyzers.

**DEFINITIVE DRUG TESTING:** Definitive drug tests are qualitative or quantitative and may be used to identify possible use or non-use of a specific drug. These tests identify specific drugs and associated metabolites, if performed. A presumptive test is not always required in order to proceed to definitive drug testing. Definitive drug testing is performed when it is medically necessary to identify specific medications, illicit substances and metabolites. Urine is typically the sample used to obtain these results. Results are reported as absent or present and listed in concentrations of nanograms per milliliter (ng/ml). Testing methods are limited to gas chromatography-mass spectrometry (GC-MS) or Liquid chromatography-mass spectrometry (LC-MS, or HPLC-MS).

**THERAPEUTIC DRUG ASSAYS:** Therapeutic assays are used to monitor clinical responses to a known, prescribed medication. These assays are usually quantitative tests and the *specimen is whole blood, serum, plasma or cerebrospinal fluid.* Routine testing of *therapeutic* drug levels when there is no impact to the patient's treatment plan is not allowed. The use of these codes for urine drug testing is inappropriate and not allowed. Therapeutic drug assays do not require prior authorization, but are only allowed when the member is being treated with a specific medication listed in the assay section.

**SPECIMEN VALIDITY TESTING** - is used to determine if a urine specimen is diluted or has been adulterated or substituted. Most basic urine immunoassays have specimen validity checks built into the screening process and allow for basic determination of urine sample tampering. Specimen validity testing (SVT), consisting of pH, specific gravity, oxidants, creatinine, or other test, is considered to be a quality measure and **coverage is excluded**. If the physician believes the patient has produced adulterated or substituted urine, and no alternative matrix sampling is available (i.e., blood), the treating provider should consider witnessed urine collection.

# URINE DRUG SCREENING/TESTING GUIDELINES:

## POLICY

OHCA will reimburse for *medically indicated laboratory* services. Medical necessity criteria is defined in **OAC 317:30-3-1(f).** Drug screening for medico-legal purposes (e.g., court-ordered drug screening) and for employment purposes (e.g., as a pre-requisite for employment or as a requirement for continuation of employment) is **not considered medically necessary** by OHCA. Testing is not covered for patient sample/sources such as saliva, oral fluids, and hair. Urine is the preferred biologic specimen for testing because of the ease of collection, storage, and cost-effectiveness. Urine drug testing cannot detect the amount of drug ingested/used, the time of use, or the means of delivery. **There is no coverage of testing of two different specimen types (blood and urine) from the same patient on the same date of service.**

## MEDICAL NECESSITY

**PRESUMPTIVE DRUG TESTING** is allowed once per day without authorization utilizing one of the 3 CPT codes 80305, 80306 or 80307. This test is billed depending on the methodology used for the test, regardless of the number of classes tested. This testing is used when there is a medical need to determine the presence or absence of drugs or drug classes in a urine sample. Reasons providers perform presumptive drug testing include:

- To identify an absence of a prescribed medication and potential for abuse, misuse and diversion;
- To identify non disclosed substances, such as alcohol, unsanctioned prescriptions or illicit substances;
- To identify substances that could contribute to adverse reactions or drug-drug interactions;
- To assist the provider with assessing compliance of the patient with his/her treatment plan.

**DEFINITIVE DRUG TESTING** may be reasonable and necessary based on patient specific indications, including historical use, medication response, and clinical assessment, when accurate results are necessary to make clinical decisions. The clinician's rationale for the definitive urine drug testing and the tests ordered must be documented in the patient's medical record. Definitive drug testing may be medically indicated for the following:

- To Identify a specific substance or metabolite that is inadequately detected or not detected by a presumptive drug test, such as fentanyl, meperidine, synthetic cannabinoids or other synthetic/analog drugs;
- To definitively identify specific drugs in a large family of drugs;
- To identify drugs when a definitive concentration of a drug is needed to guide management (e.g., discontinuation of THC use according to a treatment plan);
- To identify a negative, or confirm a positive, presumptive drug test result that is inconsistent with a patient's self-report, presentation, medical history, or current prescribed pain medication plan;
- To rule out an error as the cause of a presumptive drug test result;
- To identify non-prescribed medication or illicit use for ongoing safe prescribing of controlled substances when medically necessary, as evidenced by risk assessment, PMP database search results, random pill counts, aberrant behavior and overall clinical presentation; and
- For use in a differential assessment of medication efficacy, side effects, or drug-drug interactions.

**In all cases, drugs or drug classes for which *definitive* testing is performed should reflect only those likely to be present, based on the patient's medical history, current clinical presentation and illicit drugs that are in common use. In other words, it is NOT medically necessary or reasonable to routinely test for substances (licit or illicit), which are not used in the patient treatment population or, in the instance of illicit drugs, in the community at large. The ordering/referring provider must issue a written order for all drugs to be tested individualized to the patient.** Copies of the test results alone without a proper clinician order for the test are not sufficient documentation to support a claim for the testing services.

Based on the patient-specific treatment, clinicians must select and order the specific drug(s) or drug classes for testing. The rationale for this selection must be documented and available in the patient record. **Routine definitive testing or non-specific panel testing for all of the drugs/drug classes is excluded from coverage as not medically indicated. Automatic definitive testing for any drug is not reasonable and necessary without patient specific indications. The test must be utilized only if it is going to affect patient care.** If a previous presumptive drug test is negative, no further testing is necessary unless the clinician provides documentation of aberrant behavior to support the medical necessity of performing subsequent definitive testing. It is generally not appropriate to order definitive testing of a drug if the presumptive drug screen result is negative for an illicit substance.

**Only patient-specific orders documented in the medical record are considered reasonable and necessary**. Nonspecific orders, aka "standing orders," are not considered reasonable and necessary for patient management. When presumptive urine drug testing is performed at a site other than the point of contact (physician office), and an unexpected drug(s) or metabolite(s) is observed on a single procedure (single solid/mobile phase procedure), the laboratory is required to contact the ordering physician to obtain an order for definitive drug testing. If the physician determines the drug/metabolite has clinical significance for the management of the given patient, definitive drug testing may be necessary. Not all incidental drug(s) or metabolite(s) require quantitation or further testing. Standing orders for identification of incidental drug(s) or metabolite(s) are not allowed by OHCA.

## DOCUMENTATION

When patients are under the care of a physician for chronic pain management and/or opioid treatment, the medical record *should* include the following information; however, not all documents may be included in the medical documentation and the nurse reviewer should utilize clinical judgment in what is pertinent to the provider's request:

- Treatment plan which adheres to the appropriate state regulatory requirements;
- Patient history and physical;
- Review of previous medical records if treated by other previous physician for pain management;
- Review of all radiographs and/or laboratory studies, pertinent to the patient's condition;
- Current treatment plan;
- Opioid agreement and informed consent of urine drug testing;
- List of prescribed medications;
- Risk assessment, as identified by use of a validated risk assessment interview or questionnaire tool, with appropriate risk stratification noted and utilized;
- Documentation of review of prescription drug monitoring data or pharmacy profile as warranted;
- Office/provider monitoring protocols, such as random pill counts, etc.

## FREQUENCY

**NOTE: In general, the *recommended* frequency of testing is at the initiation of opioid treatment, compliance monitoring within one – three months later, and random monitoring every 6-12 months. These recommendations are based on multiple professional literature review recommendations and medical policy decisions. However, frequency must be individualized to the patient based on personal history, risk and behaviors.** The frequency of definitive drug testing is based on a complete clinical assessment of the individual's risk potential for abuse and diversion using a validated risk assessment interview or questionnaire and should include the patient's response to prescribed medications and the side effects of medications. Ongoing testing may be medically necessary based on the patient history, clinical assessment, including medication side effects or inefficacy, suspicious behaviors, self-escalation of doses, doctor-shopping, indications or symptoms of illegal drug use, evidence of diversion, or other documented clinical change in the patient's behavior.

- ### Frequency of Presumptive Drug Testing:

  One unit of **80305, 80306 or 80307** is allowed per member per day. There are no annual limits set on these tests. However, it would not be appropriate to perform these tests on every visit. These tests do not require prior authorization.

### Frequency of Definitive Drug Testing:

HCPCS **G0659** is a definitive test utilizing methods to identify individual drugs and distinguish between structural isomers, not necessarily stereoisomers, performed without calibrations or quality

control sampling, **regardless of the number of drug classes**. G0659 is not allowed as OHCA expects quality services provided to their members.

**G0480, G0481, G0482** and **G0483** are based on the number of ***drug classes*** tested, regardless of the methodology. (See attached for a list of drug classes). Only one test is allowed per day. Requests for more than one **G0483** per twelve month period should be referred to the physician for medical review. Providers requesting more than 5 units of a combination of HCPCS **G0659, G0480, G0481** or **G0482** in a twelve month period should be referred to the physician for review. The indications for the frequency and number of drug classes being tested should be reflected in the member's medical record. All records/documentation as noted above must be submitted for consideration.

The **frequency of drug testing** should be based, in part, on the assessed risk that the chronic opioid therapy patient will engage in medication-aberrant behavior (or illicit drug use behavior). Stratifying patients into different risk categories is essential to appropriate pain management treatment and opioid prescribing. Several risk assessment tools are available for stratifying risk factors. The Opioid Risk Tool (ORT); Pain Medication Questionnaire (PMQ); Diagnosis, Intractability, Risk, Efficacy Score (DIRE); and the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) are widely accepted tools for opioid risk assessment. A formal psychological assessment can be used as well. Risk assessments typically categorize patients into low-, moderate-, and high-risk groups. This risk should be utilized to assist in determining the frequency of urine drug testing.

- **LOW RISK**, based on a validated risk assessment tool, the **frequency of periodic definitive** testing should be **every one to two years**.
- **MODERATE RISK,** based on a validated risk assessment tool, the **frequency of periodic definitive** testing should be **every six to twelve months**.
- **HIGH RISK,** based on a validated risk assessment tool, the **frequency of periodic definitive** testing should be **every three to six months**.
- Patients considered at low to moderate risk who subsequently have aberrant urine drug testing results or display aberrant behaviors should be moved into the high-risk category.

Once the risk assessment has been completed and the risk category has been determined, a baseline testing should be performed. **BASELINE TESTING** should be used to identify the presence of illicit substances *prior to initiating treatment* involving controlled medications, and to confirm the presence or absence of the prescribed drug/drug class where possible and in accordance with the patient's documented treatment history. Patient baseline drug testing should be conducted and reviewed prior to the initial issuance or dispensing of a controlled substance prescription if possible. When a patient enters chronic opioid therapy with a new provider, baseline testing should be performed. ***(For the purpose of this guideline, baseline testing may not be relevant to the review and the patient most likely has already had baseline testing performed. However, if a patient changes pain management providers, and has exceeded the annual limit of drug tests prompting medical review, this may be necessary to allow if the new provider cannot obtain previous laboratory results or history.)***

**Chronic opioid therapy patients assessed at a higher risk for medication misuse and illicit drugs require more frequent testing than chronic pain patients assessed at a lower risk.** In the absence of specific symptoms of medication aberrant behavior or misuse, definitive drug testing is only reasonable and necessary when titrated to patient risk potential. Patients with a history of aberrant drug-related behaviors, psychiatric co-morbidities or substance abuse may require more frequent testing.

It is important to note, urine drug testing is one component of treating the chronic opioid patient. Other components should include random pill counting, checking the Prescription Monitoring Program database and reviewing the patient's prescription history.

Testing should be random, not necessarily at each scheduled office visit and not necessarily for the same drug tests at each testing event. When performing urine drug testing on a **random basis**, drug testing should be ordered in a way that minimizes the patient's ability to prepare for the test.

As the nurse reviewer, it may be necessary to perform a claims history review to determine the frequency at which the patient has previously been tested. Claims identified as being submitted each month, or at routine intervals, for testing of the same multiple quantitative levels implies random drug testing is not being performed.

## PANELS

A drug test panel is a list (or menu) of drugs or drug classes that can be tested for in a specimen. These can be ordered to identify drugs of abuse or drugs utilized in pain management. No single drug panel is suitable for all clinical uses, and test options should be adapted to clinical needs through proper exercise of clinical decision-making. Marketing test panels by independent clinical laboratories may result in medically unnecessary and unreasonable testing and should be carefully evaluated by the ordering practitioner. Nonspecific orders, aka "standing orders" or routine utilization of panels is not considered reasonable and necessary for patient management.

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## DEFINITIVE DRUG CLASSES LISTING

| Codes | Classes | Drugs |
|---|---|---|
| 80320 | Alcohol(s) | Acetone, ethanol, ethchlorvynol, ethylene glycol, isopropanol, isopropyl alcohol, methanol |
| 80321-80322 | Alcohol Biomarkers | Ethanol conjugates (ethyl glucuronide [ETG], ethyl sulfate [ETS], fatty acid ethyl esters, phosphatidylethanol) |
| 80323 | Alkaloids, not otherwise specified | 7-Hydroxymitragynine, atropine, cotinine, lysergic acid diethylamide (LSD), mescaline, mitragynine, nicotine, psilocin, psilocybin, scopolamine |
| 80324-80326 | Amphetamines | Amphetamine, ephedrinelisdexamphetamine, methamphetamine, phentermine, phenylpropanolamine, pseudoephedrine |
| 80327-80328 | Anabolic steroids | 1-Androstenediol, 1-androstenedione, 1-testosterone, 4-hydroxy-testosterone, 6-oxo, 19-norandrostenedione, androstenedione, androstanolone, bolandiol, bolasterone, boldenone, boldione, calusterone, clostebol, danazol, dehydrochlormethyltestosterone, dihydrotestosterone, drostanolone, epiandrosterone, epitestosterone, fluoxymesterone, furazabol, mestanolone, mesterolone, methandienone, methandriol, methenolone, methydienolone, methyl-1-testosterone, methylnortestosterone, methyltestosterone, mibolerone, nandrolone, norbolethone, norclostebol, norethandrolone, norethindrone, oxabolone, oxandrolone, oxymesterone, oxymetholone, stanozolol, stenbolone, tibolone, trenbolone, zeranol |
| 80329-80331 | Analgesics, non-opioid | Acetaminophen, diclofenac ibuprofen, ketoprofen, naproxen, oxaprozin, salicylate |
| 80332-80334 | Antidepressants, serotonergic class | Citalopram, duloxetine, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline |
| 80335-80337 | Antidepressants, Tricyclic and other cyclicals | Amitriptyline, amoxapine, clomipramine, demexiptiline, desipramine, doxepin, imipramine, maprotiline, mirtazpine, nortriptyline, protriptyline |
| 80338 | Antidepressants, not otherwise specified | Bupropion, desyenlafaxine, isocarboxazid, nefazodone, phenelzine, selegiline, tranylcypromine, trazodone, venlafaxine |
| 80339-80341 | Antiepileptics, not otherwise specified | Carbamazepine, clobazam, diamethadione, ethosuximide, ezogabine, lamotrigine, levetiracetam, methsuximide, oxcarbazepine, phenytoin, primidone, rufinamide, tiagabine, topiramate, trimethadione, valproic acid, zonisamide |
| 80342-80344 | Antipsychotics, not otherwise specified | Aripiprazole, chlorpromazine, clozapine, fluphenazine, haloperidol, loxapine, mesoridazine, molindone, olanzapine, paliperidone, perphenazine, phenothiazine, pimozide, prochlorperazine, quetiapine, risperidone, trifluoperazine, thiothixene, thoridazine, ziprasidone |
| 80345 | Barbiturates | Amobarbital, aprobarbital, butalbital, cyclobarbital, mephobarbital, pentobarbital, phenobarbital, secobarbital, talbutal, thiopental |
| 80346, 80347 | Benzodiazepines | Alprazolam, chlordiazepoxide, clonazepam, clorazepate, diazepam, estazolam, flunitrazepam, flurazepam, halazepamlorazepammidazolam, nitrazepam, nordazepam, oxazepam, prazepam, quazepam, temazepam |
| 80348 | Buprenorphine | Buprenorphine |
| 80349 | Cannabinoids, natural | Marijuana, dronabinol carboxy-THC |
| 80350-80352 | Cannabinoids, synthetic | CP-47,497, CP497 C8-homolog, JWH-018 and AM678, JWH-073, JWH-019, JWH-200, JWH-210, JWH-250, JWH-081, JWH-122, HWH-398, AM-2201, AM-694, SR-19 and RCS-4, SR-18 and RCS-8, JWH-203, UR-144, XLR-11, MAM-2201, AKB-48 |
| 80353 | Cocaine | Benzoylecgonine, cocaethylene, cocaine, ecgonine methyl ester, norcocaine |
| 80354 | Fentanyls | Acetylfentanyl, alfentanil, fentanyl, remifentanil, sufentanil |
| 80355 | Gabapentin, non-blood | Gabapentin |
| 80356 | Heroin metabolite | 6-acetylmorphine, acetylcodeine, diacetylmorphine |
| 80368 | Hypnotics, sedative (non-benzodiazepines) | See Sedative Hypnotics |

**DEFINITIVE DRUG CLASSES LISTING** *(Continued)*

| Codes | Classes | Drugs |
|---|---|---|
| 80357 | Ketamine and Norketamine | Ketamine, norketamine |
| 80358 | Methadone | Methadone and EDDP |
| 80359 | Methylenedioxyamphetamines | MDA, MDEA, MDMA |
| 80360 | Methylphenidate | Methylphenidate, ritalinic acid |
| 80357 | Norketamine | See Ketamine |
| 80368 | Non-Benzodiazepines | See Hypnotics, sedative |
| 80361 | Opiates | Codeine, dihydrocodeine, hydrocodone, hydromorphone, morphine |
| 80362-80364 | Opioids and opiate analogs | Butorphanol, desomorphine, dextromethorphan, dextrorphan, levorphanol, meperidine, naloxone, naltrexone, normeperidine, pentazocine |
| 80365 | Oxycodone | Oxycodone, oxymorphone |
| 83992 | Phencyclidine | Phencyclidine |
| 80366 | Pregabalin | Pregabalin |
| 80367 | Propoxyphene | Norpropoxyphene, propoxyphene |
| 80368 | Sedative Hypnotics (non-benzodiazepines) | Eszopiclone, zaleplon, zolpidem |
| 80369, 80370 | Skeletal muscle relaxants | Baclofen, carisoprodol, cyclobenzaprine, meprobamate, metaxalone, methocarbamol, orphenadrine, tizanidide |
| 80371 | Stimulants, synthetic | 2C-B, 2C-E, 2C-I, 2C-H, 3TFMPP, 4-methylethcathinone, alpha-PVP, benzylpiperazine, bromodragonfly, cathinone, m-CPP, MDPBP, MDPPP, MDPV, mephedrone, methcathinone, methylone, phenethylamines, salvinorin, tryptamines |
| 80372 | Tapentadol | Tapentadol |
| 80373 | Tramadol | Tramadol |

# Therapeutic Drug Assays

Therapeutic Drug Assays are performed to monitor clinical response to a known, prescribed medication.

The material for examination is whole blood, serum, plasma, or cerebrospinal fluid. Examination is quantitative. Coding is by parent drug; measured metabolites of the drug are included in the code, if performed.

**80150** Amikacin

- *CPT Changes: An Insider's View* 2015
- *CPT Assistant* Aug 05:9, Oct 10:7, Dec 10:7, Mar 11:10, Apr 15:3

(80152 has been deleted. To report definitive drug testing for amitryptyline, see 80335, 80336, 80337)

(80154 has been deleted. To report definitive drug testing for benzodiazepines, see 80346, 80347)

**80155** Caffeine

- *CPT Changes: An Insider's View* 2014

**80156** Carbamazepine; total

- *CPT Changes: An Insider's View* 2001
- *CPT Assistant* Oct 10:7, Mar 11:10

**80157** free

- *CPT Changes: An Insider's View* 2001
- *CPT Assistant* Oct 10:7, Mar 11:10

**80158** Cyclosporine

- *CPT Assistant* Oct 10:7, Mar 11:10

**80159** Clozapine

- *CPT Changes: An Insider's View* 2014

(80160 has been deleted. To report definitive drug testing for desipramine, see 80335, 80336, 80337)

**80162** Digoxin; total

- *CPT Changes: An Insider's View* 2015
- *CPT Assistant* Oct 10:7, Mar 11:10, Apr 15:3

**80163** free

- *CPT Changes: An Insider's View* 2015
- *CPT Assistant* Apr 15:3

**80164** Code is out of numerical sequence. See 80150-80299

**80165** Code is out of numerical sequence. See 80150-80299

(80166 has been deleted. To report definitive drug testing for doxepin, see 80335, 80336, 80337)

**80168** Ethosuximide

- *CPT Assistant* Oct 10:7, Mar 11:10

Oklahoma HealthCare Authority

# Controlled Substance Monitoring and Drugs of Abuse Testing

New HCPCS codes effective January 1, 2016

- Elimination of HCPCS G0431, G0434 and G6030-G6058 effective January 1, 2016. These are previous CMS HCPCS codes and will be deleted.

- G0477, G0478 and G0479 for Presumptive Drug Testing – allow one of any per day. Codes are based on the methodology of testing, regardless of the number of drug classes (point of care testing)

| CODE | DESCRIPTION |
|---|---|
| G0477 | Drug tests(s), presumptive, any number of drug classes; any number of devices or procedures, (e.g., immunoassay) capable of being read by direct optical observation only (e.g., dipsticks, cups, cards, cartridges), includes sample validation when performed, per date of service. |
| G0478 | Drug tests(s), presumptive, any number of drug classes; any number of devices or procedures, (e.g., immunoassay) read by instrument-assisted direct optical observation (e.g., dipsticks, cups, cards, cartridges), includes sample validation when performed, per date of service. |
| G0479 | Drug tests(s), presumptive, any number of drug classes; any number of devices or procedures by instrumented chemistry analyzers (e.g., immunoassay, enzyme assay, TOF, MALDI, LDTD, DESI, DART, GHPC, GC mass spectrometry), includes sample validation when performed, per date of service. |

- G0480, G0481, G0482 and G0483 for Definitive Drug Testing – Specific code is billed based on the number of drug classes being tested, regardless of the methodology, is quantitative or qualitative. **Will require prior authorization confirming medical necessity (for up to one year) effective ***March 1, 2016***. Documentation required for prior authorization consideration will include the patient's treatment plan, H&P, pertinent office notes, pertinent lab/radiological studies, opioid agreement, list of medications, risk assessment forms, documentation of PMP review and office monitoring protocols

| CODE | DESCRIPTION |
|---|---|
| G0480 | Drug test(s), definitive, utilizing drug identification methods able to identify individual drugs and distinguish between structural isomers (but not necessarily stereoisomers), including, but not limited to GC/MS (any type, single or tandem) and LC/MS (any type, single or tandem and excluding immunoassays (e.g., IA, EIA, ELISA, EMIT, FPIA) and enzymatic methods (e.g., alcohol dehydrogenase)); qualitative or quantitative, all sources, includes specimen validity testing, per day, 1-7 drug class(es), including metabolite(s) if performed. |
| G0481 | 8-14 drug class(es) |
| G0482 | 15-21 drug class(es) |
| G0483 | 22 or more drug class(es) |

# Oklahoma Health Care Authority

## Controlled Substance Monitoring and Drugs of Abuse Testing

## Definitive Urine Drug Testing

**Documentation to submit:**

1. Treatment plan which adheres to the appropriate state regulatory requirements
2. Patient history and physical
3. Review of previous medical records if treated by other previous physician for pain management
4. Review of all radiographs and/or laboratory studies, pertinent to the patient's condition
5. Current treatment plan
6. Opioid agreement and informed consent of urine drug testing
7. List of prescribed medications
8. Risk assessment, as identified by use of a validated risk assessment interview or questionnaire tool, with appropriate risk stratification noted and utilized
9. Documentation of review of prescription drug monitoring data or pharmacy profile as warranted
10. Office/provider monitoring protocols, such as random pill counts, etc.

*The items highlighted in red must be submitted for review before authorization can be completed. Any request where these items are not documented are subject to denial.

Per the OHCA Controlled Substance Monitoring and Drugs of Abuse Testing Guideline:

"When patients are under the care of a physician for chronic pain management and/or opioid treatment, the medical record *should* include the following information; however, not all documents may be included in the medical documentation and the nurse reviewer should utilize clinical judgment in what is pertinent to the provider's request, "

**Treatment plan which adheres to the appropriate state regulatory requirements;**

- **Oklahoma Administrative Code 435:10-7-11**
- **Oklahoma Administrative Code 510:5-9-2**
- CDC Guideline for Prescribing Opioids for Chronic Pain, US, 2016 pages 19 and 20
- CMS Local Coverage Determination, Novitas, "Controlled Substance Monitoring and Drugs of Abuse Testing", page 9
- "Prevention of Opioid Abuse in Chronic Non-Cancer Pain: An Algorithmic, Evidence Based Approach", Pain Physician 2012; page 7 and 8
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, pages 1 and 2

**Patient history and physical;**

- **Oklahoma Administrative Code 435:10-7-11 (1)(6A)**
- **Oklahoma Administrative Code 510:5-9-2 (2)**
- CDC Guideline for Prescribing Opioids for Chronic Pain, US, 2016 page 18
- CMS Local Coverage Determination, Novitas, "Controlled Substance Monitoring and Drugs of Abuse Testing", page 9
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, pages 1 and 2

**Review of previous medical records if treated by other previous physician for pain management;**

- **Oklahoma Administrative Code 435:10-7-11 (1)(6C)**
- **Oklahoma Administrative Code 510:5-9-2 (2)**
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, pages 1 and 2

**Review of all radiographs and/or laboratory studies, pertinent to the patient's condition;**

- **Oklahoma Administrative Code 435:10-7-11 (6B)**
- **Oklahoma Administrative Code 510:5-9-2 (2)(4)**
- CMS Local Coverage Determination, Novitas, "Controlled Substance Monitoring and Drugs of Abuse Testing", page 9

**Current treatment plan;**

- **Oklahoma Administrative Code 435:10-7-11 (2)(6D)(6G)**
- **Oklahoma Administrative Code 510:5-9-2 (3)**
- CMS Local Coverage Determination, Novitas, "Controlled Substance Monitoring and Drugs of Abuse Testing", page 9
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, pages 1 and 2

**Opioid agreement and informed consent of urine drug testing;**

- **Oklahoma Administrative Code 435:10-7-11 (3) (6F)**
- **Oklahoma Administrative Code 510:5-9-2 (5)(6)**
- "Prevention of Opioid Abuse in Chronic Non-Cancer Pain: An Algorithmic, Evidence Based Approach", Pain Physician 2012; page 6 and 9
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, page 2

**List of prescribed medications;**

- **Oklahoma Administrative Code 435:10-7-11 (6H)**
- **Oklahoma Administrative Code 510:5-9-2 (3)**
- CDC Guideline for Prescribing Opioids for Chronic Pain, US, 2016 page 29
- CMS Local Coverage Determination, Novitas, "Controlled Substance Monitoring and Drugs of Abuse Testing", page 9
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, pages 1 and 2

**Risk assessment, as identified by use of a validated risk assessment interview or questionnaire tool, with appropriate risk stratification noted and utilized;**

- **Oklahoma Administrative Code 435:10-7-11 (6B)( 6E)**
- CDC Guideline for Prescribing Opioids for Chronic Pain, US, 2016 page 16 and 26
- CMS Local Coverage Determination, Novitas, "Controlled Substance Monitoring and Drugs of Abuse Testing", page 9
- "Prevention of Opioid Abuse in Chronic Non-Cancer Pain: An Algorithmic, Evidence Based Approach", Pain Physician 2012; pages 4-8
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, pages 1 and 2

**Documentation of review of prescription drug monitoring data or pharmacy profile as warranted;**

- **63 O.S. 2011, 2-309D G**
- CDC Guideline for Prescribing Opioids for Chronic Pain, US, 2016 page 16, 29 and 32
- "Prevention of Opioid Abuse in Chronic Non-Cancer Pain: An Algorithmic, Evidence Based Approach", Pain Physician 2012; page 6

- “Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting”, Oklahoma Medical Board, October 2013, pages 1 and 2

**Office/provider monitoring protocols, such as random pill counts, etc.**

- **Oklahoma Administrative Code 435:10-7-11 (6I)( 6J)**
- “Prevention of Opioid Abuse in Chronic Non-Cancer Pain: An Algorithmic, Evidence Based Approach”, Pain Physician 2012; pages 7 and 8
- “Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting”, Oklahoma Medical Board, October 2013, pages 10 and 16

**Treatment plan which adheres to the appropriate state regulatory requirements;**

- **Oklahoma Administrative Code 435:10-7-11**
- **Oklahoma Administrative Code 510:5-9-2**
- CDC Guideline for Prescribing Opioids for Chronic Pain, US, 2016 pages 19 and 20
- CMS Local Coverage Determination, Novitas, "Controlled Substance Monitoring and Drugs of Abuse Testing", page 9
- "Prevention of Opioid Abuse in Chronic Non-Cancer Pain: An Algorithmic, Evidence Based Approach", Pain Physician 2012; page 7 and 8
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, pages 1 and 2

## 435:30-7-11. Use of controlled substances for the management of chronic pain

The Board has recognized that principles of quality medical practice dictate that the people of the State of Oklahoma have access to appropriate and effective pain relief and has adopted the following criteria when evaluating the physician's treatment of pain, including the use of controlled substances:

(1) **Evaluation of the patient.** A medical history and physical examination must be obtained, evaluated and documented in the medical record. The medical record should document the nature and intensity of the pain, current and past treatments for pain, underlying or coexisting diseases or conditions, the effect of the pain on physical and psychological function and history of substance abuse. The medical record also should document the presence of one or more recognized medical indications for the use of a controlled substance.

(2) **Treatment plan.** The written treatment plan should state objectives that will be used to determine treatment success, such as pain relief and improved physical and psychosocial function, and should indicate if any further diagnostic evaluations or other treatments are planned. After treatment begins, the physician should adjust drug therapy to the individual medical needs of each patient. Other treatment modalities or a rehabilitation program may be necessary depending on the etiology of the pain and the extent to which the pain is associated with physical and psychosocial impairment.

(3) **Informed consent and agreement for treatment.** The physician should discuss the risks and benefits of the use of controlled substances with the patient, persons designated by the patient or with the patient's surrogate or guardian if the patient is without medical decision-making capacity. The patient should receive prescriptions from one physician and one pharmacy whenever possible. If the patient is at high risk for medication abuse or has a history of substance abuse, the physician should consider the use of a written agreement between physician and patient outlining patient responsibilities, including:

(A) urine/serum medication levels screening when requested;
(B) number and frequency of all prescription refills; and
(C) reasons for which drug therapy may be discontinued (e.g. violation of agreement)

(4) **Periodic review.** The physician should periodically review the course of pain treatment and any new information about the etiology of the pain or the patient's state of health. Continuation or modification of controlled substances for pain management therapy depends on the physician's evaluation of progress toward treatment objectives. Satisfactory response to treatment may be indicated by the patient's decreased pain, increased level of function or improved quality of life. Objective evidence of improved or diminished function should be monitored and information from family members or other caregivers should be considered in determining the patient's response to treatment. If the patient's progress is unsatisfactory, the physician should assess the appropriateness of continued use of the current treatment plan and consider the use of other therapeutic modalities.

(5) **Consultation.** The physician should be willing to refer the patient, as necessary, for additional evaluation and treatment in order to achieve treatment objectives. Special attention should be given to those patients with pain who are at risk for medication misuse, abuse or diversion. The management of pain in patients with a history of substance abuse or with a comorbid psychiatric disorder may require extra care, monitoring, documentation and consultation with or referral to an expert in the management of such patients.

(6) **Medical records.** Records should remain current and be maintained in an accessible manner, readily available for review. The physician should keep accurate and complete records to include:

(A) the medical history and physical examination (including vital signs),
(B) diagnostic, therapeutic and laboratory results,
(C) evaluations, consultations and follow-up evaluations,
(D) treatment objectives,
(E) discussion of risks and benefits,
(F) informed consent,
(G) treatments,
(H) medications (including date, type, dosage and quantity prescribed),
(I) instructions and agreements and
(J) periodic reviews.

(7) **Compliance with controlled substances laws and regulations.** To prescribe, dispense or administer controlled substances, the physician must be licensed in Oklahoma and comply with applicable federal and state regulations. Physicians are referred to the Physicians Manual of the U.S. Drug Enforcement Administration for specific rules governing controlled substances as well as applicable state regulations.

[Source: Amended at 16 Ok Reg 2003, eff 6-14-99; Added at 22 Ok Reg 2096, eff 6-25-05]

## 510:5-9-2 Guidelines and requirements

This rule requires that diagnosis be documented, it requires that certain records be maintained, and it requires that the physician must discuss the risks and benefits with the patient or the patient's guardian.

(1) To treat a patient's intractable pain, as long as the benefit of the expected relief outweighs the risk, even if the use of the drug increases the risk of death, so long as it is not furnished for the purpose of causing, or the purpose of assisting in causing death, the physician may prescribe or administer Schedule II, III, IV or V controlled dangerous substances or other pain relieving drugs in higher than normal dosages when, in that physician's judgment, the higher dosages are necessary to produce the desired therapeutic effect.

(2) The determination of intractable pain must include a complete medical history and physical examination which includes an assessment of the patient's pain, physical and psychological function, substance abuse history, underlying or co-existing diseases or conditions and the presence of a recognized medical indication for the use of an analgesic.

(3) The treatment plan must state objectives by which treatment success can be evaluated, such as pain relief and or improved physical and psychological function, and must indicate what further diagnostic evaluations or other treatments are planned. The drug therapy must be tailored to the individual needs of each patient.

(4) The course of treatment and any new information about the etiology of the intractable pain must be reviewed periodically, at least annually, with consideration given to referral for a current second opinion. The continuation or modification of treatment will depend on the results of this review and the evaluation of the patient's progress toward the treatment objectives. If the patient has not improved, the physician must assess the appropriateness of continuing the current therapy and the trial of other modalities.

(5) The management of intractable pain in patients with a history of substance abuse requires extra care, monitoring, documentation and consultation with addiction medicine specialists, and may include the use of agreements between the physician and patient specifying rules for medication use and consequences for its misuse.

(6) The physician must discuss the risks and benefits of the use of controlled substances with the patient or the patient's guardian and obtain informed consent prior to proceeding if it substantially increases the risk of death.

(7) Accurate and complete records documenting these requirements must be kept.

(8) To prescribe controlled substances, the physician must be licensed in Oklahoma, have a valid controlled substances registration and comply with federal and state regulations for issuing controlled substances prescriptions.

(9) Expert clinical testimony may be used to prove a violation of this rule. As used herein, a "clinical expert" is a physician who, by reason of specialized education or substantial relevant experience in pain management, has knowledge regarding current standards, practices and guidelines.

(10) Nothing in this rule shall limit a physician's authority to prescribe or administer prescription drug products beyond the customary indications as noted in the manufacturer's package insert for use in treating intractable pain, provided the drug is recognized for treatment of intractable pain in standard reference compendia or medical literature.

[Source: Added at 16 Ok Reg 2539, eff 6-25-99]

for improved pain or function with long-term use of opioids for several chronic pain conditions for which opioids are commonly prescribed, such as low back pain (*182*), headache (*183*), and fibromyalgia (*184*). Although NSAIDs can be used for exacerbations of nociceptive pain, other medications (e.g., tricyclics, selected anticonvulsants, or transdermal lidocaine) generally are recommended for neuropathic pain. In addition, improvement of neuropathic pain can begin weeks or longer after symptomatic treatment is initiated (*179*). Medications should be used only after assessment and determination that expected benefits outweigh risks given patient-specific factors. For example, clinicians should consider falls risk when selecting and dosing potentially sedating medications such as tricyclics, anticonvulsants, or opioids, and should weigh risks and benefits of use, dose, and duration of NSAIDs when treating older adults as well as patients with hypertension, renal insufficiency, or heart failure, or those with risk for peptic ulcer disease or cardiovascular disease. Some guidelines recommend topical NSAIDs for localized osteoarthritis (e.g., knee osteoarthritis) over oral NSAIDs in patients aged ≥75 years to minimize systemic effects (*176*).

Experts agreed that opioids should not be considered first-line or routine therapy for chronic pain (i.e., pain continuing or expected to continue >3 months or past the time of normal tissue healing) outside of active cancer, palliative, and end-of-life care, given small to moderate short-term benefits, uncertain long-term benefits, and potential for serious harms; although evidence on long-term benefits of nonopioid therapies is also limited, these therapies are also associated with short-term benefits, and risks are much lower. This does not mean that patients should be required to sequentially "fail" nonpharmacologic and nonopioid pharmacologic therapy before proceeding to opioid therapy. Rather, expected benefits specific to the clinical context should be weighed against risks before initiating therapy. In some clinical contexts (e.g., headache or fibromyalgia), expected benefits of initiating opioids are unlikely to outweigh risks regardless of previous nonpharmacologic and nonopioid pharmacologic therapies used. In other situations (e.g., serious illness in a patient with poor prognosis for return to previous level of function, contraindications to other therapies, and clinician and patient agreement that the overriding goal is patient comfort), opioids might be appropriate regardless of previous therapies used. In addition, when opioid pain medication is used, it is more likely to be effective if integrated with nonpharmacologic therapy. Nonpharmacologic approaches such as exercise and CBT should be used to reduce pain and improve function in patients with chronic pain. Nonopioid pharmacologic therapy should be used when benefits outweigh risks and should be combined with nonpharmacologic therapy to reduce pain and improve function. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate, to provide greater benefits to patients in improving pain and function.

2. **Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety (recommendation category: A, evidence type: 4).**

The clinical evidence review found insufficient evidence to determine long-term benefits of opioid therapy for chronic pain and found an increased risk for serious harms related to long-term opioid therapy that appears to be dose-dependent. In addition, studies on currently available risk assessment instruments were sparse and showed inconsistent results (KQ4). The clinical evidence review for the current guideline considered studies with outcomes examined at ≥1 year that compared opioid use versus nonuse or placebo. Studies of opioid therapy for chronic pain that did not have a nonopioid control group have found that although many patients discontinue opioid therapy for chronic noncancer pain due to adverse effects or insufficient pain relief, there is weak evidence that patients who are able to continue opioid therapy for at least 6 months can experience clinically significant pain relief and insufficient evidence that function or quality of life improves (*185*). These findings suggest that it is very difficult for clinicians to predict whether benefits of opioids for chronic pain will outweigh risks of ongoing treatment for individual patients. Opioid therapy should not be initiated without consideration of an "exit strategy" to be used if the therapy is unsuccessful.

Experts agreed that before opioid therapy is initiated for chronic pain outside of active cancer, palliative, and end-of-life care, clinicians should determine how effectiveness will be evaluated and should establish treatment goals with patients. Because the line between acute pain and initial chronic pain is not always clear, it might be difficult for clinicians to determine when they are initiating opioids for chronic pain rather than treating acute pain. Pain lasting longer than 3 months or past the time of normal tissue healing (which could be substantially shorter than 3 months, depending on the condition) is generally no longer considered acute. However, establishing treatment goals with a patient who has already received opioid therapy for 3 months would defer this discussion well past the point of

initiation of opioid therapy for chronic pain. Clinicians often write prescriptions for long-term use in 30-day increments, and opioid prescriptions written for ≥30 days are likely to represent initiation or continuation of long-term opioid therapy. Before writing an opioid prescription for ≥30 days, clinicians should establish treatment goals with patients. Clinicians seeing new patients already receiving opioids should establish treatment goals for continued opioid therapy. Although the clinical evidence review did not find studies evaluating the effectiveness of written agreements or treatment plans (KQ4), clinicians and patients who set a plan in advance will clarify expectations regarding how opioids will be prescribed and monitored, as well as situations in which opioids will be discontinued or doses tapered (e.g., if treatment goals are not met, opioids are no longer needed, or adverse events put the patient at risk) to improve patient safety.

Experts thought that goals should include improvement in both pain relief and function (and therefore in quality of life). However, there are some clinical circumstances under which reductions in pain without improvement in physical function might be a more realistic goal (e.g., diseases typically associated with progressive functional impairment or catastrophic injuries such as spinal cord trauma). Experts noted that function can include emotional and social as well as physical dimensions. In addition, experts emphasized that mood has important interactions with pain and function. Experts agreed that clinicians may use validated instruments such as the three-item "Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale (*186*) to track patient outcomes. Clinically meaningful improvement has been defined as a 30% improvement in scores for both pain and function (*187*). Monitoring progress toward patient-centered functional goals (e.g., walking the dog or walking around the block, returning to part-time work, attending family sports or recreational activities) can also contribute to the assessment of functional improvement. Clinicians should use these goals in assessing benefits of opioid therapy for individual patients and in weighing benefits against risks of continued opioid therapy (see Recommendation 7, including recommended intervals for follow-up). Because depression, anxiety, and other psychological co-morbidities often coexist with and can interfere with resolution of pain, clinicians should use validated instruments to assess for these conditions (see Recommendation 8) and ensure that treatment for these conditions is optimized. If patients receiving opioid therapy for chronic pain do not experience meaningful improvements in both pain and function compared with prior to initiation of opioid therapy, clinicians should consider working with patients to taper and discontinue opioids (see Recommendation 7) and should use nonpharmacologic and nonopioid pharmacologic approaches to pain management (see Recommendation 1).

3. **Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy (recommendation category: A, evidence type: 3).**

The clinical evidence review did not find studies evaluating effectiveness of patient education or opioid treatment plans as risk-mitigation strategies (KQ4). However, the contextual evidence review found that many patients lack information about opioids and identified concerns that some clinicians miss opportunities to effectively communicate about safety. Given the substantial evidence gaps on opioids, uncertain benefits of long-term use, and potential for serious harms, patient education and discussion before starting opioid therapy are critical so that patient preferences and values can be understood and used to inform clinical decisions. Experts agreed that essential elements to communicate to patients before starting and periodically during opioid therapy include realistic expected benefits, common and serious harms, and expectations for clinician and patient responsibilities to mitigate risks of opioid therapy.

Clinicians should involve patients in decisions about whether to start or continue opioid therapy. Given potentially serious risks of long-term opioid therapy, clinicians should ensure that patients are aware of potential benefits of, harms of, and alternatives to opioids before starting or continuing opioid therapy. Clinicians are encouraged to have open and honest discussions with patients to inform mutual decisions about whether to start or continue opioid therapy. Important considerations include the following:

- Be explicit and realistic about expected benefits of opioids, explaining that while opioids can reduce pain during short-term use, there is no good evidence that opioids improve pain or function with long-term use, and that complete relief of pain is unlikely (clinical evidence review, KQ1).
- Emphasize improvement in function as a primary goal and that function can improve even when pain is still present.
- Advise patients about serious adverse effects of opioids, including potentially fatal respiratory depression and development of a potentially serious lifelong opioid use disorder that can cause distress and inability to fulfill major role obligations.
- Advise patients about common effects of opioids, such as constipation, dry mouth, nausea, vomiting, drowsiness, confusion, tolerance, physical dependence, and withdrawal symptoms when stopping opioids. To prevent constipation associated with opioid use, advise patients to increase

a. Identifies absence of prescribed medication and potential for abuse, misuse, and diversion;
b. Identifies undisclosed substances, such as alcohol, unsanctioned prescription medication, or illicit substances;
c. Identifies substances that contribute to adverse events or drug-drug interactions;
d. Provides objectivity to the treatment plan;
e. Reinforces therapeutic compliance with the patient;
f. Provides additional documentation demonstrating compliance with patient evaluation and monitoring;
g. Provides diagnostic information to help assess individual patient response to medications (e.g., metabolism, side effects, drug-drug interaction, etc.) over time for ongoing management of prescribed medications.

2. Medical Necessity Guidance:

Criteria to establish medical necessity for drug testing must be based on patient- specific elements identified during the clinical assessment, and documented by the clinician in the patient's medical record and minimally include the following elements:

- Patient history, physical examination and previous laboratory findings;
- Current treatment plan;
- Prescribed medication(s); and
- Risk assessment plan.

National pain organizations, physician societies, and the Federation of State Medical Boards recommend a practical approach to definitive UDT for COT.

Frequency of testing beyond the baseline presumptive UDT must be based on individual patient needs substantiated by documentation in the patient's medical record. Recommendations for the ordering of presumptive and definitive UDT for patients on COT are as follows:

a. COT Baseline Testing:

Initial presumptive or definitive COT patient testing may include amphetamine/methamphetamine, barbiturates, benzodiazepines, cocaine, methadone, oxycodone, tricyclic antidepressants, tetrahydrocannabinoid, opioids, opiates, heroin, and synthetic/analog or "designer" drugs.

b. COT Monitoring Testing:

Ongoing testing may be medically reasonable and necessary based on the patient history, clinical assessment, including medication side effects or inefficacy, suspicious behaviors, self -escalation of dose, doctor-shopping, indications/symptoms of illegal drug use, evidence of diversion, or other clinician documented change in affect or behavioral pattern.

The frequency of testing must be based on a complete clinical assessment of the individual's risk potential for abuse and diversion using a validated risk assessment interview or questionnaire and should include the patient's response to prescribed medications and the side effects of medications.

The clinician should perform random UDT at random intervals, in order to properly monitor a patient. UDT testing does not have to be associated with an office visit.

**Drug Testing Panels**

MED. Braden et al (113) found that patients (Arkansas Medicaid and HealthCore commercially insured enrollees) receiving MEDs of more than 120 mg/d are more likely to have drug-related encounters than those getting lower doses. There were no differences between these 2 groups regarding emergency department visits. Gomes et al (57) found that patients from Ontario's public drug plan receiving "very high" doses (> 400 mg MED) and "high" doses (200-400 mg MED) had a much higher overdose death than those getting "moderate" doses (< 200 mg MED). In "very high" and "high" dose patients the opioid-related mortality rates were 9.94/1,000 for "very high" and 7.92/1,000 for "high." Comparatively, the opioid-related mortality rate was 1.63/1,000 in those with "moderate" doses. Also, the overall death rate (from any cause) was much higher in patients receiving opioids (20.05/1,000) when compared to those who were not getting any opioids (4.00/1,000).

In the above 5 studies, the doses which are related to an emergency department admission for overdoses or death are 40 mg MED (104), 50 mg MED (111,112), 120 mg MED (113), and 200 mg MED (57). We did not find any study in which a higher dose did not correlate with increased mortality and only one study where there was no correlation between higher opioid dose and emergency department visits. Moreover, Paulozzi et al (15) reported that in 80% of all patients receiving opioids, the dose was less than 100 mg MED and was obtained from one physician. This patient pool constituted 20% of the overall overdose deaths. Even though only 10% of all patients were receiving a dose of greater than 100 mg MED from a single prescriber, the overdose death rate in this population was as high as 40%. Patients receiving more than 100 mg MED from multiple physicians constituted the rest of the 10%. The percentage of overdose deaths was 40% in this segment. In other words, patients receiving more than 100 mg MED (from single or multiple prescribers), contributed to 80% of all the overdose deaths, whereas patients on doses of less than 100 mg MED contributed to only 20% of the overall overdose deaths, implying that 100 mg MED is a dangerous dose. There has been a call for establishing a maximum daily dose in order to guide physicians treating patients with chronic pain (114). Based on the current available evidence presented above, defining 50 mg MED/d as a high dose does not seem unreasonable. The dose limits recommended earlier by Washington State (120 mg MED) (109) and the Canadian guideline (200 mg MED) (110) seem excessive. Defining 200 mg MED by APS and AAPM as a high dose also appears to be harmful. We agree with Katz (114) that having dose limits will provide a guide for practicing physicians, reduce harm by eliminating high doses, assist in the negotiation process between physicians and patients pressing for higher doses and finally, impel high dose prescribers to exercise more caution. We concur with Manchikanti et al (20) that commencing long-acting opioid therapy is often the starting point for high dose opioid therapy, a practice that growing evidence suggests is harmful to patients and increases the black market availability of opioids through diversion. Many argue that chronic pain is undertreated and opioids must be used more liberally. We agree that chronic pain is undertreated, but we completely disagree, based on evidence, that aggressive opioid use is the answer to alleviating undertreated chronic pain. Given our awareness of the inadequacy and adverse effects of using opioids for the treatment of chronic pain, the failure to set dose limits is irresponsible and hazardous both to the individual and to society.

## Algorithmic Approach to Prevent Opioid Abuse

Opioids play an important but limited role in treating chronic pain. The challenge for the physician is to make opioids available for those who are truly in need, and to withhold them from those who are either abusing or diverting. Although difficult, this can be achieved in most cases. If all nonopioid measures fail in alleviating pain, and if opioids are being used, the following steps would be very helpful. The 3 cornerstones for responsible prescribing are stratifying patients by using screening tools into high, medium and low risk groups; monitoring patients by using UDS, PMPs and pill counts; and lastly, establishing dose limits (Fig. 1).

Stratification of patients into different risk categories is the first step. This requires the use of existing screening tools designed specifically to screen for opioid misuse (subjective tools like SOAPP (67), PMQ (68), PUDQP (70) or objective tools like ABC checklist (71), DIRE Score (72) and the tool by Atluri and Sudarshan (73) to classify patients as high risk, medium risk and low risk. As mentioned earlier, objective tools may be better than subjective tools. Those who are categorized as "high risk" should be monitored closely by performing UDS every 3 to 6 months and PMP every 2-4 months. Opioids should be either avoided or prescribed in low doses. Doses of more than 50 mg MED should be very rarely used and only under specialized settings in conjunction, when available, with addiction specialists. Pa-

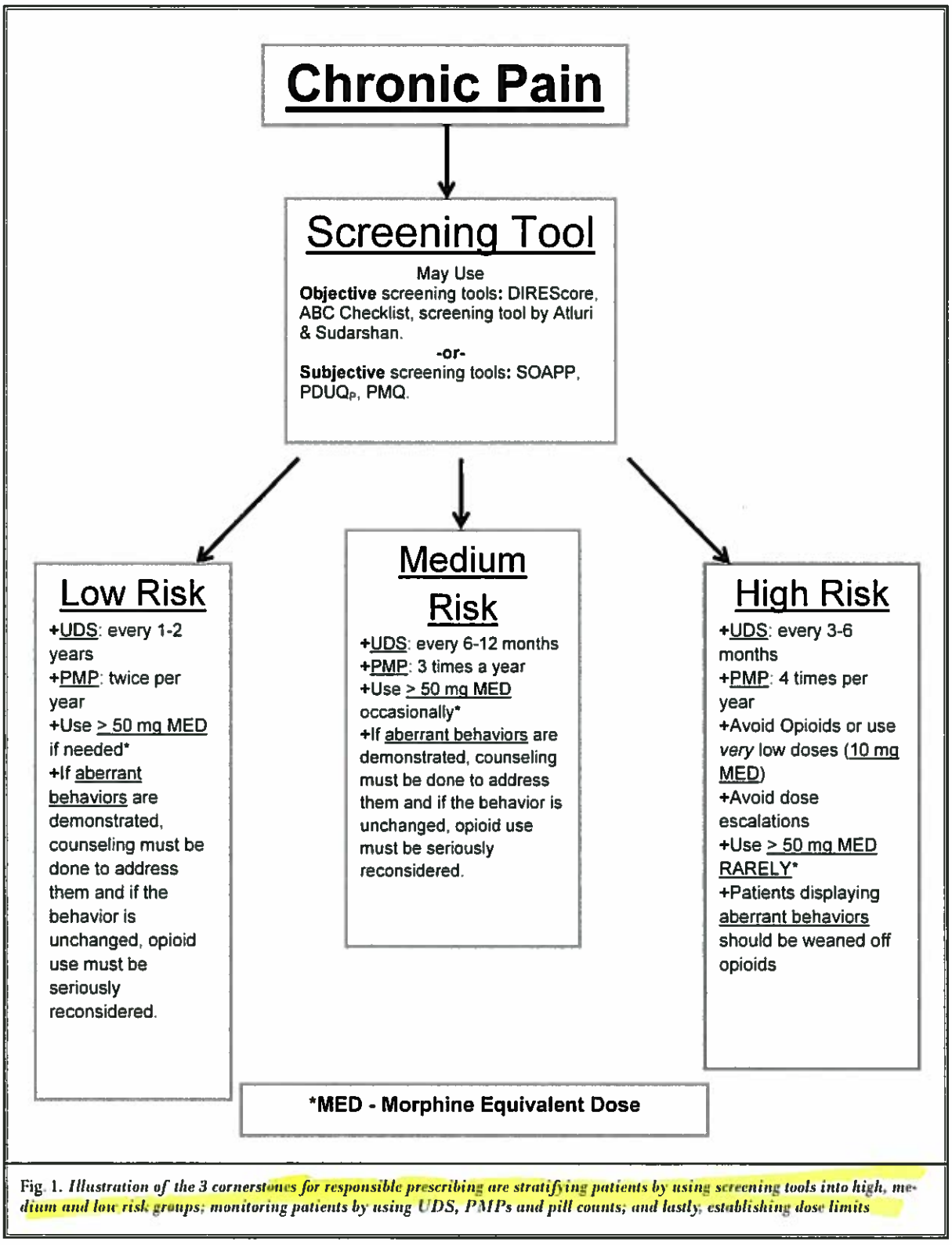


Fig. 1. *Illustration of the 3 cornerstones for responsible prescribing are stratifying patients by using screening tools into high, medium and low risk groups; monitoring patients by using UDS, PMPs and pill counts; and lastly, establishing dose limits*

# Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting

*Note: These guidelines do not replace clinical judgment in the appropriate care of patients. They are not intended as standards of care or as templates for legislation, nor are they meant for patients in palliative care programs or with cancer pain. The recommendations are an educational tool based on the expert opinion of numerous physicians and other health care providers, medical/nursing boards, mental and public health officials, and law enforcement personnel in Oklahoma and throughout the United States. The guidelines are available at* http://poison.health.ok.gov.

## Opioid Treatment for Acute Pain

1. Opioids should only be used for treatment of acute pain when the severity of the pain warrants that choice and after determining that other non-opioid pain medications or therapies will not provide adequate pain relief.
2. Providers should query the Oklahoma Prescription Monitoring Program (PMP) for patients presenting with acute pain, prior to prescribing an opioid medication. In circumstances where a patient's pain is resulting from an objectively diagnosed disease process or injury, a provider may prudently opt not to review the Oklahoma PMP.
3. When opioids are prescribed for treatment of acute pain, the number of doses dispensed should be no more than the number of doses needed based on the usual duration of pain severe enough to require opioids for that condition.
4. When opioids are prescribed for treatment of acute pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.
5. Long duration-of-action opioids (e.g., methadone, buprenorphine, fentanyl, extended release oxycodone, and morphine) are rarely indicated for treatment of acute pain.
6. The use of opioids should be re-evaluated carefully, including assessing the potential for abuse, if persistent pain suggests the need to continue opioids beyond the anticipated time period of acute pain treatment for that condition. Health care providers should query the Oklahoma PMP as part of this re-evaluation process.
7. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.

## Opioid Treatment for Chronic Pain

1. Alternatives to opioid treatment should be tried, or previous attempts documented, before initiating opioid treatment.
2. A comprehensive evaluation should be performed before initiating opioid treatment for chronic pain. For chronic pain patients transferring their care to new health care providers, new opioid prescriptions should generally not be written until the previous provider's records have been reviewed or the previous health care provider has been notified of the transfer of care.
3. The health care provider should screen for risk of abuse or addiction before initiating opioid treatment.
4. Prior to the initial prescribing of opioid medications, health care providers should query the Oklahoma Prescription Monitoring Program (PMP).
5. When opioids are used for the treatment of chronic pain, a written treatment plan should be established that includes measurable goals for reduction of pain and improvement of function. One health care provider should coordinate a patient's comprehensive pain care plan and provide all opioid prescriptions required for the plan.

6. The patient should be informed of the risks, benefits, and terms for continuation of opioid treatment, ideally using a written and signed treatment agreement.
7. Opioids should be initiated as a short-term trial to assess the effects of opioid treatment on pain intensity, function, and quality of life. In most instances, the trial should begin with a short-acting opioid medication.
8. Regular visits for evaluation of progress toward goals should be scheduled during the period when the dose of opioids is being adjusted (titration period). During the titration period, and until the patient is clinically stable and judged to be compliant with therapy, it is recommended that the health care provider check the Oklahoma PMP more frequently.
9. Once a stable dose has been established (maintenance period), regular monitoring should be conducted at face-to-face visits during which treatment goals, analgesia, activity, adverse effects, and aberrant behaviors are monitored. The Oklahoma PMP should be queried at least once per year for patients receiving opioid treatment for chronic pain.
10. Continuing opioid treatment should be a deliberate decision that takes into consideration the risks and benefits of chronic opioid treatment for that patient. Patients and health care providers should periodically reassess the need for continued opioid treatment, weaning whenever possible, as part of the comprehensive pain care plan. A second opinion or consultation may be useful in making that decision.
11. Opioid treatment should be discontinued if adverse effects outweigh benefits or if aberrant, dangerous, or illegal behaviors are demonstrated.
12. Health care providers treating chronic pain patients with opioids should maintain records, in accordance with state and federal law, documenting patient evaluation, treatment plan, discussion of risks and benefits, informed consent, treatments prescribed, results of treatment, and any aberrant behavior observed.
13. Health care providers should consider consultation for patients with complex pain conditions, serious co-morbidities and mental illness, a history or evidence of current drug addiction or abuse, or when the provider is not confident of his/her ability to manage the treatment.
14. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.
15. The administration of intravenous and intramuscular opioids for the relief of exacerbations of chronic pain is discouraged, except in special circumstances.
16. Long-acting opioids are associated with an increased risk of overdose death, and should only be prescribed by health care providers familiar with their indications, risks, and need for careful monitoring.
17. When opioids are prescribed for treatment of chronic pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.

TAKE AS PRESCRIBED

**Patient history and physical;**

- **Oklahoma Administrative Code 435:10-7-11 (1)(6A)**
- **Oklahoma Administrative Code 510:5-9-2 (2)**
- CDC Guideline for Prescribing Opioids for Chronic Pain, US, 2016 page 18
- CMS Local Coverage Determination, Novitas, "Controlled Substance Monitoring and Drugs of Abuse Testing", page 9
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, pages 1 and 2

## 435:30-7-11. Use of controlled substances for the management of chronic pain

The Board has recognized that principles of quality medical practice dictate that the people of the State of Oklahoma have access to appropriate and effective pain relief and has adopted the following criteria when evaluating the physician's treatment of pain, including the use of controlled substances:

(1) **Evaluation of the patient.** A medical history and physical examination must be obtained, evaluated and documented in the medical record. The medical record should document the nature and intensity of the pain, current and past treatments for pain, underlying or coexisting diseases or conditions, the effect of the pain on physical and psychological function and history of substance abuse. The medical record also should document the presence of one or more recognized medical indications for the use of a controlled substance.

(2) **Treatment plan.** The written treatment plan should state objectives that will be used to determine treatment success, such as pain relief and improved physical and psychosocial function, and should indicate if any further diagnostic evaluations or other treatments are planned. After treatment begins, the physician should adjust drug therapy to the individual medical needs of each patient. Other treatment modalities or a rehabilitation program may be necessary depending on the etiology of the pain and the extent to which the pain is associated with physical and psychosocial impairment.

(3) **Informed consent and agreement for treatment.** The physician should discuss the risks and benefits of the use of controlled substances with the patient, persons designated by the patient or with the patient's surrogate or guardian if the patient is without medical decision-making capacity. The patient should receive prescriptions from one physician and one pharmacy whenever possible. If the patient is at high risk for medication abuse or has a history of substance abuse, the physician should consider the use of a written agreement between physician and patient outlining patient responsibilities, including:

(A) urine/serum medication levels screening when requested;
(B) number and frequency of all prescription refills; and
(C) reasons for which drug therapy may be discontinued (e.g. violation of agreement)

(4) **Periodic review.** The physician should periodically review the course of pain treatment and any new information about the etiology of the pain or the patient's state of health. Continuation or modification of controlled substances for pain management therapy depends on the physician's evaluation of progress toward treatment objectives. Satisfactory response to treatment may be indicated by the patient's decreased pain, increased level of function or improved quality of life. Objective evidence of improved or diminished function should be monitored and information from family members or other caregivers should be considered in determining the patient's response to treatment. If the patient's progress is unsatisfactory, the physician should assess the appropriateness of continued use of the current treatment plan and consider the use of other therapeutic modalities.

(5) **Consultation.** The physician should be willing to refer the patient, as necessary, for additional evaluation and treatment in order to achieve treatment objectives. Special attention should be given to those patients with pain who are at risk for medication misuse, abuse or diversion. The management of pain in patients with a history of substance abuse or with a comorbid psychiatric disorder may require extra care, monitoring, documentation and consultation with or referral to an expert in the management of such patients.

(6) **Medical records.** Records should remain current and be maintained in an accessible manner, readily available for review. The physician should keep accurate and complete records to include:

(A) the medical history and physical examination (including vital signs),
(B) diagnostic, therapeutic and laboratory results,
(C) evaluations, consultations and follow-up evaluations,
(D) treatment objectives,
(E) discussion of risks and benefits,
(F) informed consent,
(G) treatments,
(H) medications (including date, type, dosage and quantity prescribed),
(I) instructions and agreements and
(J) periodic reviews.

(7) **Compliance with controlled substances laws and regulations.** To prescribe, dispense or administer controlled substances, the physician must be licensed in Oklahoma and comply with applicable federal and state regulations. Physicians are referred to the Physicians Manual of the U.S. Drug Enforcement Administration for specific rules governing controlled substances as well as applicable state regulations.

[**Source:** Amended at 16 Ok Reg 2003, eff 6-14-99; Added at 22 Ok Reg 2096, eff 6-25-05]

## 510:5-9-2 Guidelines and requirements

This rule requires that diagnosis be documented, it requires that certain records be maintained, and it requires that the physician must discuss the risks and benefits with the patient or the patient's guardian.

(1) To treat a patient's intractable pain, as long as the benefit of the expected relief outweighs the risk, even if the use of the drug increases the risk of death, so long as it is not furnished for the purpose of causing, or the purpose of assisting in causing death, the physician may prescribe or administer Schedule II, III, IV or V controlled dangerous substances or other pain relieving drugs in higher than normal dosages when, in that physician's judgment, the higher dosages are necessary to produce the desired therapeutic effect.

(2) The determination of intractable pain must include a complete medical history and physical examination which includes an assessment of the patient's pain, physical and psychological function, substance abuse history, underlying or co-existing diseases or conditions and the presence of a recognized medical indication for the use of an analgesic.

(3) The treatment plan must state objectives by which treatment success can be evaluated, such as pain relief and or improved physical and psychological function, and must indicate what further diagnostic evaluations or other treatments are planned. The drug therapy must be tailored to the individual needs of each patient.

(4) The course of treatment and any new information about the etiology of the intractable pain must be reviewed periodically, at least annually, with consideration given to referral for a current second opinion. The continuation or modification of treatment will depend on the results of this review and the evaluation of the patient's progress toward the treatment objectives. If the patient has not improved, the physician must assess the appropriateness of continuing the current therapy and the trial of other modalities.

(5) The management of intractable pain in patients with a history of substance abuse requires extra care, monitoring, documentation and consultation with addiction medicine specialists, and may include the use of agreements between the physician and patient specifying rules for medication use and consequences for its misuse.

(6) The physician must discuss the risks and benefits of the use of controlled substances with the patient or the patient's guardian and obtain informed consent prior to proceeding if it substantially increases the risk of death.

(7) Accurate and complete records documenting these requirements must be kept.

(8) To prescribe controlled substances, the physician must be licensed in Oklahoma, have a valid controlled substances registration and comply with federal and state regulations for issuing controlled substances prescriptions.

(9) Expert clinical testimony may be used to prove a violation of this rule. As used herein, a "clinical expert" is a physician who, by reason of specialized education or substantial relevant experience in pain management, has knowledge regarding current standards, practices and guidelines.

(10) Nothing in this rule shall limit a physician's authority to prescribe or administer prescription drug products beyond the customary indications as noted in the manufacturer's package insert for use in treating intractable pain, provided the drug is recognized for treatment of intractable pain in standard reference compendia or medical literature.

[Source: Added at 16 Ok Reg 2539, eff 6-25-99]

are not generally associated with substance use disorder, and the numbers of fatal overdoses associated with nonopioid medications are a fraction of those associated with opioid medications (contextual evidence review). For example, acetaminophen, NSAIDs, and opioid pain medication were involved in 881, 228, and 16,651 pharmaceutical overdose deaths in the United States in 2010 (*178*). However, nonopioid pharmacologic therapies are associated with certain risks, particularly in older patients, pregnant patients, and patients with certain co-morbidities such as cardiovascular, renal, gastrointestinal, and liver disease (see contextual evidence review). For example, acetaminophen can be hepatotoxic at dosages of >3–4 grams/day and at lower dosages in patients with chronic alcohol use or liver disease (*109*). NSAID use has been associated with gastritis, peptic ulcer disease, cardiovascular events (*111,112*), and fluid retention, and most NSAIDs (choline magnesium trilisate and selective COX-2 inhibitors are exceptions) interfere with platelet aggregation (*179*). Clinicians should review FDA-approved labeling including boxed warnings before initiating treatment with any pharmacologic therapy.

Although opioids can reduce pain during short-term use, the clinical evidence review found insufficient evidence to determine whether pain relief is sustained and whether function or quality of life improves with long-term opioid therapy (KQ1). While benefits for pain relief, function, and quality of life with long-term opioid use for chronic pain are uncertain, risks associated with long-term opioid use are clearer and significant. Based on the clinical evidence review, long-term opioid use for chronic pain is associated with serious risks including increased risk for opioid use disorder, overdose, myocardial infarction, and motor vehicle injury (KQ2). At a population level, more than 165,000 persons in the United States have died from opioid pain-medication-related overdoses since 1999 (see Contextual Evidence Review).

Integrated pain management requires coordination of medical, psychological, and social aspects of health care and includes primary care, mental health care, and specialist services when needed (*180*). Nonpharmacologic physical and psychological treatments such as exercise and CBT are approaches that encourage active patient participation in the care plan, address the effects of pain in the patient's life, and can result in sustained improvements in pain and function without apparent risks. Despite this, these therapies are not always or fully covered by insurance, and access and cost can be barriers for patients. For many patients, aspects of these approaches can be used even when there is limited access to specialty care. For example, previous guidelines have strongly recommended aerobic, aquatic, and/or resistance exercises for patients with osteoarthritis of the knee or hip (*176*) and maintenance of activity for patients with low back pain (*110*). A randomized trial found no difference in reduced chronic low back pain intensity, frequency or disability between patients assigned to relatively low-cost group aerobics and individual physiotherapy or muscle reconditioning sessions (*181*). Low-cost options to integrate exercise include brisk walking in public spaces or use of public recreation facilities for group exercise. CBT addresses psychosocial contributors to pain and improves function (*97*). Primary care clinicians can integrate elements of a cognitive behavioral approach into their practice by encouraging patients to take an active role in the care plan, by supporting patients in engaging in beneficial but potentially anxiety-provoking activities, such as exercise (*179*), or by providing education in relaxation techniques and coping strategies. In many locations, there are free or low-cost patient support, self-help, and educational community-based programs that can provide stress reduction and other mental health benefits. Patients with more entrenched anxiety or fear related to pain, or other significant psychological distress, can be referred for formal therapy with a mental health specialist (e.g., psychologist, psychiatrist, clinical social worker). Multimodal therapies should be considered for patients not responding to single-modality therapy, and combinations should be tailored depending on patient needs, cost, and convenience.

To guide patient-specific selection of therapy, clinicians should evaluate patients and establish or confirm the diagnosis. Detailed recommendations on diagnosis are provided in other guidelines (*110,179*), but evaluation should generally include a focused history, including history and characteristics of pain and potentially contributing factors (e.g., function, psychosocial stressors, sleep) and physical exam, with imaging or other diagnostic testing only if indicated (e.g., if severe or progressive neurologic deficits are present or if serious underlying conditions are suspected) (*110,179*). For complex pain syndromes, pain specialty consultation can be considered to assist with diagnosis as well as management. Diagnosis can help identify disease-specific interventions to reverse or ameliorate pain; for example, improving glucose control to prevent progression of diabetic neuropathy; immune-modulating agents for rheumatoid arthritis; physical or occupational therapy to address posture, muscle weakness, or repetitive occupational motions that contribute to musculoskeletal pain; or surgical intervention to relieve mechanical/compressive pain (*179*). The underlying mechanism for most pain syndromes can be categorized as neuropathic (e.g., diabetic neuropathy, postherpetic neuralgia, fibromyalgia), or nociceptive (e.g., osteoarthritis, muscular back pain). The diagnosis and pathophysiologic mechanism of pain have implications for symptomatic pain treatment with medication. For example, evidence is limited or insufficient

a. Identifies absence of prescribed medication and potential for abuse, misuse, and diversion;
b. Identifies undisclosed substances, such as alcohol, unsanctioned prescription medication, or illicit substances;
c. Identifies substances that contribute to adverse events or drug-drug interactions;
d. Provides objectivity to the treatment plan;
e. Reinforces therapeutic compliance with the patient;
f. Provides additional documentation demonstrating compliance with patient evaluation and monitoring;
g. Provides diagnostic information to help assess individual patient response to medications (e.g., metabolism, side effects, drug-drug interaction, etc.) over time for ongoing management of prescribed medications.

2. Medical Necessity Guidance:

Criteria to establish medical necessity for drug testing must be based on patient- specific elements identified during the clinical assessment, and documented by the clinician in the patient's medical record and minimally include the following elements:

- Patient history, physical examination and previous laboratory findings;
- Current treatment plan;
- Prescribed medication(s); and
- Risk assessment plan.

National pain organizations, physician societies, and the Federation of State Medical Boards recommend a practical approach to definitive UDT for COT.

Frequency of testing beyond the baseline presumptive UDT must be based on individual patient needs substantiated by documentation in the patient's medical record. Recommendations for the ordering of presumptive and definitive UDT for patients on COT are as follows:

a. COT Baseline Testing:

Initial presumptive or definitive COT patient testing may include amphetamine/methamphetamine, barbiturates, benzodiazepines, cocaine, methadone, oxycodone, tricyclic antidepressants, tetrahydrocannabinoid, opioids, opiates, heroin, and synthetic/analog or "designer" drugs.

b. COT Monitoring Testing:

Ongoing testing may be medically reasonable and necessary based on the patient history, clinical assessment, including medication side effects or inefficacy, suspicious behaviors, self -escalation of dose, doctor-shopping, indications/symptoms of illegal drug use, evidence of diversion, or other clinician documented change in affect or behavioral pattern.

The frequency of testing must be based on a complete clinical assessment of the individual's risk potential for abuse and diversion using a validated risk assessment interview or questionnaire and should include the patient's response to prescribed medications and the side effects of medications.

The clinician should perform random UDT at random intervals, in order to properly monitor a patient. UDT testing does not have to be associated with an office visit.

**Drug Testing Panels**

# Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting

*Note: These guidelines do not replace clinical judgment in the appropriate care of patients. They are not intended as standards of care or as templates for legislation, nor are they meant for patients in palliative care programs or with cancer pain. The recommendations are an educational tool based on the expert opinion of numerous physicians and other health care providers, medical/nursing boards, mental and public health officials, and law enforcement personnel in Oklahoma and throughout the United States. The guidelines are available at* http://poison.health.ok.gov.

## Opioid Treatment for Acute Pain

1. Opioids should only be used for treatment of acute pain when the severity of the pain warrants that choice and after determining that other non-opioid pain medications or therapies will not provide adequate pain relief.
2. Providers should query the Oklahoma Prescription Monitoring Program (PMP) for patients presenting with acute pain, prior to prescribing an opioid medication. In circumstances where a patient's pain is resulting from an objectively diagnosed disease process or injury, a provider may prudently opt not to review the Oklahoma PMP.
3. When opioids are prescribed for treatment of acute pain, the number of doses dispensed should be no more than the number of doses needed based on the usual duration of pain severe enough to require opioids for that condition.
4. When opioids are prescribed for treatment of acute pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.
5. Long duration-of-action opioids (e.g., methadone, buprenorphine, fentanyl, extended release oxycodone, and morphine) are rarely indicated for treatment of acute pain.
6. The use of opioids should be re-evaluated carefully, including assessing the potential for abuse, if persistent pain suggests the need to continue opioids beyond the anticipated time period of acute pain treatment for that condition. Health care providers should query the Oklahoma PMP as part of this re-evaluation process.
7. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.

## Opioid Treatment for Chronic Pain

1. Alternatives to opioid treatment should be tried, or previous attempts documented, before initiating opioid treatment.
2. A comprehensive evaluation should be performed before initiating opioid treatment for chronic pain. For chronic pain patients transferring their care to new health care providers, new opioid prescriptions should generally not be written until the previous provider's records have been reviewed or the previous health care provider has been notified of the transfer of care.
3. The health care provider should screen for risk of abuse or addiction before initiating opioid treatment.
4. Prior to the initial prescribing of opioid medications, health care providers should query the Oklahoma Prescription Monitoring Program (PMP).
5. When opioids are used for the treatment of chronic pain, a written treatment plan should be established that includes measurable goals for reduction of pain and improvement of function. One health care provider should coordinate a patient's comprehensive pain care plan and provide all opioid prescriptions required for the plan.

6. The patient should be informed of the risks, benefits, and terms for continuation of opioid treatment, ideally using a written and signed treatment agreement.
7. Opioids should be initiated as a short-term trial to assess the effects of opioid treatment on pain intensity, function, and quality of life. In most instances, the trial should begin with a short-acting opioid medication.
8. Regular visits for evaluation of progress toward goals should be scheduled during the period when the dose of opioids is being adjusted (titration period). During the titration period, and until the patient is clinically stable and judged to be compliant with therapy, it is recommended that the health care provider check the Oklahoma PMP more frequently.
9. Once a stable dose has been established (maintenance period), regular monitoring should be conducted at face-to-face visits during which treatment goals, analgesia, activity, adverse effects, and aberrant behaviors are monitored. The Oklahoma PMP should be queried at least once per year for patients receiving opioid treatment for chronic pain.
10. Continuing opioid treatment should be a deliberate decision that takes into consideration the risks and benefits of chronic opioid treatment for that patient. Patients and health care providers should periodically reassess the need for continued opioid treatment, weaning whenever possible, as part of the comprehensive pain care plan. A second opinion or consultation may be useful in making that decision.
11. Opioid treatment should be discontinued if adverse effects outweigh benefits or if aberrant, dangerous, or illegal behaviors are demonstrated.
12. Health care providers treating chronic pain patients with opioids should maintain records, in accordance with state and federal law, documenting patient evaluation, treatment plan, discussion of risks and benefits, informed consent, treatments prescribed, results of treatment, and any aberrant behavior observed.
13. Health care providers should consider consultation for patients with complex pain conditions, serious co-morbidities and mental illness, a history or evidence of current drug addiction or abuse, or when the provider is not confident of his/her ability to manage the treatment.
14. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.
15. The administration of intravenous and intramuscular opioids for the relief of exacerbations of chronic pain is discouraged, except in special circumstances.
16. Long-acting opioids are associated with an increased risk of overdose death, and should only be prescribed by health care providers familiar with their indications, risks, and need for careful monitoring.
17. When opioids are prescribed for treatment of chronic pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.

**Review of previous medical records if treated by other previous physician for pain management;**

- **Oklahoma Administrative Code 435:10-7-11 (1)(6C)**
- **Oklahoma Administrative Code 510:5-9-2 (2)**
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, pages 1 and 2

## 435:30-7-11. Use of controlled substances for the management of chronic pain

The Board has recognized that principles of quality medical practice dictate that the people of the State of Oklahoma have access to appropriate and effective pain relief and has adopted the following criteria when evaluating the physician's treatment of pain, including the use of controlled substances:

(1) **Evaluation of the patient.** A medical history and physical examination must be obtained, evaluated and documented in the medical record. The medical record should document the nature and intensity of the pain, current and past treatments for pain, underlying or coexisting diseases or conditions, the effect of the pain on physical and psychological function and history of substance abuse. The medical record also should document the presence of one or more recognized medical indications for the use of a controlled substance.

(2) **Treatment plan.** The written treatment plan should state objectives that will be used to determine treatment success, such as pain relief and improved physical and psychosocial function, and should indicate if any further diagnostic evaluations or other treatments are planned. After treatment begins, the physician should adjust drug therapy to the individual medical needs of each patient. Other treatment modalities or a rehabilitation program may be necessary depending on the etiology of the pain and the extent to which the pain is associated with physical and psychosocial impairment.

(3) **Informed consent and agreement for treatment.** The physician should discuss the risks and benefits of the use of controlled substances with the patient, persons designated by the patient or with the patient's surrogate or guardian if the patient is without medical decision-making capacity. The patient should receive prescriptions from one physician and one pharmacy whenever possible. If the patient is at high risk for medication abuse or has a history of substance abuse, the physician should consider the use of a written agreement between physician and patient outlining patient responsibilities, including:

(A) urine/serum medication levels screening when requested;
(B) number and frequency of all prescription refills; and
(C) reasons for which drug therapy may be discontinued (e.g. violation of agreement)

(4) **Periodic review.** The physician should periodically review the course of pain treatment and any new information about the etiology of the pain or the patient's state of health. Continuation or modification of controlled substances for pain management therapy depends on the physician's evaluation of progress toward treatment objectives. Satisfactory response to treatment may be indicated by the patient's decreased pain, increased level of function or improved quality of life. Objective evidence of improved or diminished function should be monitored and information from family members or other caregivers should be considered in determining the patient's response to treatment. If the patient's progress is unsatisfactory, the physician should assess the appropriateness of continued use of the current treatment plan and consider the use of other therapeutic modalities.

(5) **Consultation.** The physician should be willing to refer the patient, as necessary, for additional evaluation and treatment in order to achieve treatment objectives. Special attention should be given to those patients with pain who are at risk for medication misuse, abuse or diversion. The management of pain in patients with a history of substance abuse or with a comorbid psychiatric disorder may require extra care, monitoring, documentation and consultation with or referral to an expert in the management of such patients.

(6) **Medical records.** Records should remain current and be maintained in an accessible manner, readily available for review. The physician should keep accurate and complete records to include:

(A) the medical history and physical examination (including vital signs),
(B) diagnostic, therapeutic and laboratory results,
(C) evaluations, consultations and follow-up evaluations,
(D) treatment objectives,
(E) discussion of risks and benefits,
(F) informed consent,
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(H) medications (including date, type, dosage and quantity prescribed),
(I) instructions and agreements and
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(7) **Compliance with controlled substances laws and regulations.** To prescribe, dispense or administer controlled substances, the physician must be licensed in Oklahoma and comply with applicable federal and state regulations. Physicians are referred to the Physicians Manual of the U.S. Drug Enforcement Administration for specific rules governing controlled substances as well as applicable state regulations.

[**Source:** Amended at 16 Ok Reg 2003, eff 6-14-99; Added at 22 Ok Reg 2096, eff 6-25-05]

## 510:5-9-2 Guidelines and requirements

This rule requires that diagnosis be documented, it requires that certain records be maintained, and it requires that the physician must discuss the risks and benefits with the patient or the patient's guardian.

(1) To treat a patient's intractable pain, as long as the benefit of the expected relief outweighs the risk, even if the use of the drug increases the risk of death, so long as it is not furnished for the purpose of causing, or the purpose of assisting in causing death, the physician may prescribe or administer Schedule II, III, IV or V controlled dangerous substances or other pain relieving drugs in higher than normal dosages when, in that physician's judgment, the higher dosages are necessary to produce the desired therapeutic effect.

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(10) Nothing in this rule shall limit a physician's authority to prescribe or administer prescription drug products beyond the customary indications as noted in the manufacturer's package insert for use in treating intractable pain, provided the drug is recognized for treatment of intractable pain in standard reference compendia or medical literature.

[Source: Added at 16 Ok Reg 2539, eff 6-25-99]

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6. The patient should be informed of the risks, benefits, and terms for continuation of opioid treatment, ideally using a written and signed treatment agreement.
7. Opioids should be initiated as a short-term trial to assess the effects of opioid treatment on pain intensity, function, and quality of life. In most instances, the trial should begin with a short-acting opioid medication.
8. Regular visits for evaluation of progress toward goals should be scheduled during the period when the dose of opioids is being adjusted (titration period). During the titration period, and until the patient is clinically stable and judged to be compliant with therapy, it is recommended that the health care provider check the Oklahoma PMP more frequently.
9. Once a stable dose has been established (maintenance period), regular monitoring should be conducted at face-to-face visits during which treatment goals, analgesia, activity, adverse effects, and aberrant behaviors are monitored. The Oklahoma PMP should be queried at least once per year for patients receiving opioid treatment for chronic pain.
10. Continuing opioid treatment should be a deliberate decision that takes into consideration the risks and benefits of chronic opioid treatment for that patient. Patients and health care providers should periodically reassess the need for continued opioid treatment, weaning whenever possible, as part of the comprehensive pain care plan. A second opinion or consultation may be useful in making that decision.
11. Opioid treatment should be discontinued if adverse effects outweigh benefits or if aberrant, dangerous, or illegal behaviors are demonstrated.
12. Health care providers treating chronic pain patients with opioids should maintain records, in accordance with state and federal law, documenting patient evaluation, treatment plan, discussion of risks and benefits, informed consent, treatments prescribed, results of treatment, and any aberrant behavior observed.
13. Health care providers should consider consultation for patients with complex pain conditions, serious co-morbidities and mental illness, a history or evidence of current drug addiction or abuse, or when the provider is not confident of his/her ability to manage the treatment.
14. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.
15. The administration of intravenous and intramuscular opioids for the relief of exacerbations of chronic pain is discouraged, except in special circumstances.
16. Long-acting opioids are associated with an increased risk of overdose death, and should only be prescribed by health care providers familiar with their indications, risks, and need for careful monitoring.
17. When opioids are prescribed for treatment of chronic pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.

TAKE AS PRESCRIBED

**Review of all radiographs and/or laboratory studies, pertinent to the patient's condition;**

- **Oklahoma Administrative Code 435:10-7-11 (6B)**
- **Oklahoma Administrative Code 510:5-9-2 (2)(4)**
- CMS Local Coverage Determination, Novitas, "Controlled Substance Monitoring and Drugs of Abuse Testing", page 9

(6) **Medical records.** Records should remain current and be maintained in an accessible manner, readily available for review. The physician should keep accurate and complete records to include:

(A) the medical history and physical examination (including vital signs),
(B) diagnostic, therapeutic and laboratory results,
(C) evaluations, consultations and follow-up evaluations,
(D) treatment objectives,
(E) discussion of risks and benefits,
(F) informed consent,
(G) treatments,
(H) medications (including date, type, dosage and quantity prescribed),
(I) instructions and agreements and
(J) periodic reviews.

(7) **Compliance with controlled substances laws and regulations.** To prescribe, dispense or administer controlled substances, the physician must be licensed in Oklahoma and comply with applicable federal and state regulations. Physicians are referred to the Physicians Manual of the U.S. Drug Enforcement Administration for specific rules governing controlled substances as well as applicable state regulations.

[Source: Amended at 16 Ok Reg 2003, eff 6-14-99; Added at 22 Ok Reg 2096, eff 6-25-05]

## 510:5-9-2 Guidelines and requirements

This rule requires that diagnosis be documented, it requires that certain records be maintained, and it requires that the physician must discuss the risks and benefits with the patient or the patient's guardian.

(1) To treat a patient's intractable pain, as long as the benefit of the expected relief outweighs the risk, even if the use of the drug increases the risk of death, so long as it is not furnished for the purpose of causing, or the purpose of assisting in causing death, the physician may prescribe or administer Schedule II, III, IV or V controlled dangerous substances or other pain relieving drugs in higher than normal dosages when, in that physician's judgment, the higher dosages are necessary to produce the desired therapeutic effect.

(2) The determination of intractable pain must include a complete medical history and physical examination which includes an assessment of the patient's pain, physical and psychological function, substance abuse history, underlying or co-existing diseases or conditions and the presence of a recognized medical indication for the use of an analgesic.

(3) The treatment plan must state objectives by which treatment success can be evaluated, such as pain relief and or improved physical and psychological function, and must indicate what further diagnostic evaluations or other treatments are planned. The drug therapy must be tailored to the individual needs of each patient.

(4) The course of treatment and any new information about the etiology of the intractable pain must be reviewed periodically, at least annually, with consideration given to referral for a current second opinion. The continuation or modification of treatment will depend on the results of this review and the evaluation of the patient's progress toward the treatment objectives. If the patient has not improved, the physician must assess the appropriateness of continuing the current therapy and the trial of other modalities.

(5) The management of intractable pain in patients with a history of substance abuse requires extra care, monitoring, documentation and consultation with addiction medicine specialists, and may include the use of agreements between the physician and patient specifying rules for medication use and consequences for its misuse.

(6) The physician must discuss the risks and benefits of the use of controlled substances with the patient or the patient's guardian and obtain informed consent prior to proceeding if it substantially increases the risk of death.

(7) Accurate and complete records documenting these requirements must be kept.

(8) To prescribe controlled substances, the physician must be licensed in Oklahoma, have a valid controlled substances registration and comply with federal and state regulations for issuing controlled substances prescriptions.

(9) Expert clinical testimony may be used to prove a violation of this rule. As used herein, a "clinical expert" is a physician who, by reason of specialized education or substantial relevant experience in pain management, has knowledge regarding current standards, practices and guidelines.

(10) Nothing in this rule shall limit a physician's authority to prescribe or administer prescription drug products beyond the customary indications as noted in the manufacturer's package insert for use in treating intractable pain, provided the drug is recognized for treatment of intractable pain in standard reference compendia or medical literature.

[Source: Added at 16 Ok Reg 2539, eff 6-25-99]

a. Identifies absence of prescribed medication and potential for abuse, misuse, and diversion;
b. Identifies undisclosed substances, such as alcohol, unsanctioned prescription medication, or illicit substances;
c. Identifies substances that contribute to adverse events or drug-drug interactions;
d. Provides objectivity to the treatment plan;
e. Reinforces therapeutic compliance with the patient;
f. Provides additional documentation demonstrating compliance with patient evaluation and monitoring;
g. Provides diagnostic information to help assess individual patient response to medications (e.g., metabolism, side effects, drug-drug interaction, etc.) over time for ongoing management of prescribed medications.

2. Medical Necessity Guidance:

Criteria to establish medical necessity for drug testing must be based on patient- specific elements identified during the clinical assessment, and documented by the clinician in the patient's medical record and minimally include the following elements:

- Patient history, physical examination and previous laboratory findings;
- Current treatment plan;
- Prescribed medication(s); and
- Risk assessment plan.

National pain organizations, physician societies, and the Federation of State Medical Boards recommend a practical approach to definitive UDT for COT.

Frequency of testing beyond the baseline presumptive UDT must be based on individual patient needs substantiated by documentation in the patient's medical record. Recommendations for the ordering of presumptive and definitive UDT for patients on COT are as follows:

a. COT Baseline Testing:

Initial presumptive or definitive COT patient testing may include amphetamine/methamphetamine, barbiturates, benzodiazepines, cocaine, methadone, oxycodone, tricyclic antidepressants, tetrahydrocannabinoid, opioids, opiates, heroin, and synthetic/analog or "designer" drugs.

b. COT Monitoring Testing:

Ongoing testing may be medically reasonable and necessary based on the patient history, clinical assessment, including medication side effects or inefficacy, suspicious behaviors, self -escalation of dose, doctor-shopping, indications/symptoms of illegal drug use, evidence of diversion, or other clinician documented change in affect or behavioral pattern.

The frequency of testing must be based on a complete clinical assessment of the individual's risk potential for abuse and diversion using a validated risk assessment interview or questionnaire and should include the patient's response to prescribed medications and the side effects of medications.

The clinician should perform random UDT at random intervals, in order to properly monitor a patient. UDT testing does not have to be associated with an office visit.

**Drug Testing Panels**

**Current treatment plan;**

- **Oklahoma Administrative Code 435:10-7-11 (2)(6D)(6G)**
- **Oklahoma Administrative Code 510:5-9-2 (3)**
- CMS Local Coverage Determination, Novitas, "Controlled Substance Monitoring and Drugs of Abuse Testing", page 9
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, pages 1 and 2

## 435:30-7-11. Use of controlled substances for the management of chronic pain

The Board has recognized that principles of quality medical practice dictate that the people of the State of Oklahoma have access to appropriate and effective pain relief and has adopted the following criteria when evaluating the physician's treatment of pain, including the use of controlled substances:

(1) **Evaluation of the patient.** A medical history and physical examination must be obtained, evaluated and documented in the medical record. The medical record should document the nature and intensity of the pain, current and past treatments for pain, underlying or coexisting diseases or conditions, the effect of the pain on physical and psychological function and history of substance abuse. The medical record also should document the presence of one or more recognized medical indications for the use of a controlled substance.

(2) **Treatment plan.** The written treatment plan should state objectives that will be used to determine treatment success, such as pain relief and improved physical and psychosocial function, and should indicate if any further diagnostic evaluations or other treatments are planned. After treatment begins, the physician should adjust drug therapy to the individual medical needs of each patient. Other treatment modalities or a rehabilitation program may be necessary depending on the etiology of the pain and the extent to which the pain is associated with physical and psychosocial impairment.

(3) **Informed consent and agreement for treatment.** The physician should discuss the risks and benefits of the use of controlled substances with the patient, persons designated by the patient or with the patient's surrogate or guardian if the patient is without medical decision-making capacity. The patient should receive prescriptions from one physician and one pharmacy whenever possible. If the patient is at high risk for medication abuse or has a history of substance abuse, the physician should consider the use of a written agreement between physician and patient outlining patient responsibilities, including:

(A) urine/serum medication levels screening when requested;
(B) number and frequency of all prescription refills; and
(C) reasons for which drug therapy may be discontinued (e.g. violation of agreement)

(4) **Periodic review.** The physician should periodically review the course of pain treatment and any new information about the etiology of the pain or the patient's state of health. Continuation or modification of controlled substances for pain management therapy depends on the physician's evaluation of progress toward treatment objectives. Satisfactory response to treatment may be indicated by the patient's decreased pain, increased level of function or improved quality of life. Objective evidence of improved or diminished function should be monitored and information from family members or other caregivers should be considered in determining the patient's response to treatment. If the patient's progress is unsatisfactory, the physician should assess the appropriateness of continued use of the current treatment plan and consider the use of other therapeutic modalities.

(5) **Consultation.** The physician should be willing to refer the patient, as necessary, for additional evaluation and treatment in order to achieve treatment objectives. Special attention should be given to those patients with pain who are at risk for medication misuse, abuse or diversion. The management of pain in patients with a history of substance abuse or with a comorbid psychiatric disorder may require extra care, monitoring, documentation and consultation with or referral to an expert in the management of such patients.

(6) **Medical records.** Records should remain current and be maintained in an accessible manner, readily available for review. The physician should keep accurate and complete records to include:

(A) the medical history and physical examination (including vital signs),
(B) diagnostic, therapeutic and laboratory results,
(C) evaluations, consultations and follow-up evaluations,
(D) treatment objectives,
(E) discussion of risks and benefits,
(F) informed consent,
(G) treatments,
(H) medications (including date, type, dosage and quantity prescribed),
(I) instructions and agreements and
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(7) **Compliance with controlled substances laws and regulations.** To prescribe, dispense or administer controlled substances, the physician must be licensed in Oklahoma and comply with applicable federal and state regulations. Physicians are referred to the Physicians Manual of the U.S. Drug Enforcement Administration for specific rules governing controlled substances as well as applicable state regulations.

[Source: Amended at 16 Ok Reg 2003, eff 6-14-99; Added at 22 Ok Reg 2096, eff 6-25-05]

## 510:5-9-2 Guidelines and requirements

This rule requires that diagnosis be documented, it requires that certain records be maintained, and it requires that the physician must discuss the risks and benefits with the patient or the patient's guardian.

(1) To treat a patient's intractable pain, as long as the benefit of the expected relief outweighs the risk, even if the use of the drug increases the risk of death, so long as it is not furnished for the purpose of causing, or the purpose of assisting in causing death, the physician may prescribe or administer Schedule II, III, IV or V controlled dangerous substances or other pain relieving drugs in higher than normal dosages when, in that physician's judgment, the higher dosages are necessary to produce the desired therapeutic effect.

(2) The determination of intractable pain must include a complete medical history and physical examination which includes an assessment of the patient's pain, physical and psychological function, substance abuse history, underlying or co-existing diseases or conditions and the presence of a recognized medical indication for the use of an analgesic.

(3) The treatment plan must state objectives by which treatment success can be evaluated, such as pain relief and or improved physical and psychological function, and must indicate what further diagnostic evaluations or other treatments are planned. The drug therapy must be tailored to the individual needs of each patient.

(4) The course of treatment and any new information about the etiology of the intractable pain must be reviewed periodically, at least annually, with consideration given to referral for a current second opinion. The continuation or modification of treatment will depend on the results of this review and the evaluation of the patient's progress toward the treatment objectives. If the patient has not improved, the physician must assess the appropriateness of continuing the current therapy and the trial of other modalities.

(5) The management of intractable pain in patients with a history of substance abuse requires extra care, monitoring, documentation and consultation with addiction medicine specialists, and may include the use of agreements between the physician and patient specifying rules for medication use and consequences for its misuse.

(6) The physician must discuss the risks and benefits of the use of controlled substances with the patient or the patient's guardian and obtain informed consent prior to proceeding if it substantially increases the risk of death.

(7) Accurate and complete records documenting these requirements must be kept.

(8) To prescribe controlled substances, the physician must be licensed in Oklahoma, have a valid controlled substances registration and comply with federal and state regulations for issuing controlled substances prescriptions.

(9) Expert clinical testimony may be used to prove a violation of this rule. As used herein, a "clinical expert" is a physician who, by reason of specialized education or substantial relevant experience in pain management, has knowledge regarding current standards, practices and guidelines.

(10) Nothing in this rule shall limit a physician's authority to prescribe or administer prescription drug products beyond the customary indications as noted in the manufacturer's package insert for use in treating intractable pain, provided the drug is recognized for treatment of intractable pain in standard reference compendia or medical literature.

[Source: Added at 16 Ok Reg 2539, eff 6-25-99]

a. Identifies absence of prescribed medication and potential for abuse, misuse, and diversion;
b. Identifies undisclosed substances, such as alcohol, unsanctioned prescription medication, or illicit substances;
c. Identifies substances that contribute to adverse events or drug-drug interactions;
d. Provides objectivity to the treatment plan;
e. Reinforces therapeutic compliance with the patient;
f. Provides additional documentation demonstrating compliance with patient evaluation and monitoring;
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2. Medical Necessity Guidance:

Criteria to establish medical necessity for drug testing must be based on patient- specific elements identified during the clinical assessment, and documented by the clinician in the patient's medical record and minimally include the following elements:

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The frequency of testing must be based on a complete clinical assessment of the individual's risk potential for abuse and diversion using a validated risk assessment interview or questionnaire and should include the patient's response to prescribed medications and the side effects of medications.

The clinician should perform random UDT at random intervals, in order to properly monitor a patient. UDT testing does not have to be associated with an office visit.

**Drug Testing Panels**

# Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting

*Note: These guidelines do not replace clinical judgment in the appropriate care of patients. They are not intended as standards of care or as templates for legislation, nor are they meant for patients in palliative care programs or with cancer pain. The recommendations are an educational tool based on the expert opinion of numerous physicians and other health care providers, medical/nursing boards, mental and public health officials, and law enforcement personnel in Oklahoma and throughout the United States. The guidelines are available at* http://poison.health.ok.gov.

## Opioid Treatment for Acute Pain

1. Opioids should only be used for treatment of acute pain when the severity of the pain warrants that choice and after determining that other non-opioid pain medications or therapies will not provide adequate pain relief.
2. Providers should query the Oklahoma Prescription Monitoring Program (PMP) for patients presenting with acute pain, prior to prescribing an opioid medication. In circumstances where a patient's pain is resulting from an objectively diagnosed disease process or injury, a provider may prudently opt not to review the Oklahoma PMP.
3. When opioids are prescribed for treatment of acute pain, the number of doses dispensed should be no more than the number of doses needed based on the usual duration of pain severe enough to require opioids for that condition.
4. When opioids are prescribed for treatment of acute pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.
5. Long duration-of-action opioids (e.g., methadone, buprenorphine, fentanyl, extended release oxycodone, and morphine) are rarely indicated for treatment of acute pain.
6. The use of opioids should be re-evaluated carefully, including assessing the potential for abuse, if persistent pain suggests the need to continue opioids beyond the anticipated time period of acute pain treatment for that condition. Health care providers should query the Oklahoma PMP as part of this re-evaluation process.
7. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.

## Opioid Treatment for Chronic Pain

1. Alternatives to opioid treatment should be tried, or previous attempts documented, before initiating opioid treatment.
2. A comprehensive evaluation should be performed before initiating opioid treatment for chronic pain. For chronic pain patients transferring their care to new health care providers, new opioid prescriptions should generally not be written until the previous provider's records have been reviewed or the previous health care provider has been notified of the transfer of care.
3. The health care provider should screen for risk of abuse or addiction before initiating opioid treatment.
4. Prior to the initial prescribing of opioid medications, health care providers should query the Oklahoma Prescription Monitoring Program (PMP).
5. When opioids are used for the treatment of chronic pain, a written treatment plan should be established that includes measurable goals for reduction of pain and improvement of function. One health care provider should coordinate a patient's comprehensive pain care plan and provide all opioid prescriptions required for the plan.

6. The patient should be informed of the risks, benefits, and terms for continuation of opioid treatment, ideally using a written and signed treatment agreement.
7. Opioids should be initiated as a short-term trial to assess the effects of opioid treatment on pain intensity, function, and quality of life. In most instances, the trial should begin with a short-acting opioid medication.
8. Regular visits for evaluation of progress toward goals should be scheduled during the period when the dose of opioids is being adjusted (titration period). During the titration period, and until the patient is clinically stable and judged to be compliant with therapy, it is recommended that the health care provider check the Oklahoma PMP more frequently.
9. Once a stable dose has been established (maintenance period), regular monitoring should be conducted at face-to-face visits during which treatment goals, analgesia, activity, adverse effects, and aberrant behaviors are monitored. The Oklahoma PMP should be queried at least once per year for patients receiving opioid treatment for chronic pain.
10. Continuing opioid treatment should be a deliberate decision that takes into consideration the risks and benefits of chronic opioid treatment for that patient. Patients and health care providers should periodically reassess the need for continued opioid treatment, weaning whenever possible, as part of the comprehensive pain care plan. A second opinion or consultation may be useful in making that decision.
11. Opioid treatment should be discontinued if adverse effects outweigh benefits or if aberrant, dangerous, or illegal behaviors are demonstrated.
12. Health care providers treating chronic pain patients with opioids should maintain records, in accordance with state and federal law, documenting patient evaluation, treatment plan, discussion of risks and benefits, informed consent, treatments prescribed, results of treatment, and any aberrant behavior observed.
13. Health care providers should consider consultation for patients with complex pain conditions, serious co-morbidities and mental illness, a history or evidence of current drug addiction or abuse, or when the provider is not confident of his/her ability to manage the treatment.
14. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.
15. The administration of intravenous and intramuscular opioids for the relief of exacerbations of chronic pain is discouraged, except in special circumstances.
16. Long-acting opioids are associated with an increased risk of overdose death, and should only be prescribed by health care providers familiar with their indications, risks, and need for careful monitoring.
17. When opioids are prescribed for treatment of chronic pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.


**Oklahoma Board of Nursing** **Oklahoma Society of Interventional Pain Physicians**

**Opioid agreement and informed consent of urine drug testing;**

- **Oklahoma Administrative Code 435:10-7-11 (3) (6F)**
- **Oklahoma Administrative Code 510:5-9-2 (5)(6)**
- "Prevention of Opioid Abuse in Chronic Non-Cancer Pain: An Algorithmic, Evidence Based Approach", Pain Physician 2012; page 6 and 9
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, page 2

## 435:30-7-11. Use of controlled substances for the management of chronic pain

The Board has recognized that principles of quality medical practice dictate that the people of the State of Oklahoma have access to appropriate and effective pain relief and has adopted the following criteria when evaluating the physician's treatment of pain, including the use of controlled substances:

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(2) **Treatment plan.** The written treatment plan should state objectives that will be used to determine treatment success, such as pain relief and improved physical and psychosocial function, and should indicate if any further diagnostic evaluations or other treatments are planned. After treatment begins, the physician should adjust drug therapy to the individual medical needs of each patient. Other treatment modalities or a rehabilitation program may be necessary depending on the etiology of the pain and the extent to which the pain is associated with physical and psychosocial impairment.

(3) **Informed consent and agreement for treatment.** The physician should discuss the risks and benefits of the use of controlled substances with the patient, persons designated by the patient or with the patient's surrogate or guardian if the patient is without medical decision-making capacity. The patient should receive prescriptions from one physician and one pharmacy whenever possible. If the patient is at high risk for medication abuse or has a history of substance abuse, the physician should consider the use of a written agreement between physician and patient outlining patient responsibilities, including:

(A) urine/serum medication levels screening when requested;
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(4) **Periodic review.** The physician should periodically review the course of pain treatment and any new information about the etiology of the pain or the patient's state of health. Continuation or modification of controlled substances for pain management therapy depends on the physician's evaluation of progress toward treatment objectives. Satisfactory response to treatment may be indicated by the patient's decreased pain, increased level of function or improved quality of life. Objective evidence of improved or diminished function should be monitored and information from family members or other caregivers should be considered in determining the patient's response to treatment. If the patient's progress is unsatisfactory, the physician should assess the appropriateness of continued use of the current treatment plan and consider the use of other therapeutic modalities.

(5) **Consultation.** The physician should be willing to refer the patient, as necessary, for additional evaluation and treatment in order to achieve treatment objectives. Special attention should be given to those patients with pain who are at risk for medication misuse, abuse or diversion. The management of pain in patients with a history of substance abuse or with a comorbid psychiatric disorder may require extra care, monitoring, documentation and consultation with or referral to an expert in the management of such patients.

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[**Source:** Amended at 16 Ok Reg 2003, eff 6-14-99; Added at 22 Ok Reg 2096, eff 6-25-05]

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(2) The determination of intractable pain must include a complete medical history and physical examination which includes an assessment of the patient's pain, physical and psychological function, substance abuse history, underlying or co-existing diseases or conditions and the presence of a recognized medical indication for the use of an analgesic.

(3) The treatment plan must state objectives by which treatment success can be evaluated, such as pain relief and or improved physical and psychological function, and must indicate what further diagnostic evaluations or other treatments are planned. The drug therapy must be tailored to the individual needs of each patient.

(4) The course of treatment and any new information about the etiology of the intractable pain must be reviewed periodically, at least annually, with consideration given to referral for a current second opinion. The continuation or modification of treatment will depend on the results of this review and the evaluation of the patient's progress toward the treatment objectives. If the patient has not improved, the physician must assess the appropriateness of continuing the current therapy and the trial of other modalities.

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(10) Nothing in this rule shall limit a physician's authority to prescribe or administer prescription drug products beyond the customary indications as noted in the manufacturer's package insert for use in treating intractable pain, provided the drug is recognized for treatment of intractable pain in standard reference compendia or medical literature.

[Source: Added at 16 Ok Reg 2539, eff 6-25-99]

tients displaying aberrant behaviors (asking for early refills, frequent visits to an emergency department for opioids, doctor shopping, taking opioids from others, etc.) should be weaned off opioids. Patients falling into the "low risk" category should be subjected to UDS every 1-2 years and PMP every 6 months to 1 year. Dose escalations can be done more liberally if required, keeping in mind that doses more than 50 mg MED/d should be an exception rather than the rule. If aberrant behaviors are present, counseling must commence. If counseling does not alter the behavior, opioid use must be seriously reconsidered. Those who are deemed as "medium risk" should be monitored with UDS every 6-12 months and PMP every 3-6 months. Opioid doses and their escalations should be guarded. Doses more than 50 mg MED/d can be used occasionally in carefully selected patients. If aberrant behaviors are present, counseling must commence, with a reconsideration of opioid use if the behavior does not change. These measures, along with an opioid agreement requiring patients to use a single prescriber and a single pharmacy, discouraging self dose escalations, giving limited refills, establishing regular office follow-ups, explaining the risks and benefits of opioids along with insisting on compliance with the opioid agreement should be useful in curbing inappropriate use of opioids.

## Conclusion

To tackle the epidemic of prescription opioid abuse, the following is suggested by Paulozzi et al (15).

1. Improving legislation and enforcement of existing laws regarding doctor shopping, diversion, and unscrupulous physicians.
2. Improving medical practice in prescribing opioids through proper education. In our opinion, and in order to encourage proper prescribing, this education should be based on evidence and not influenced by pharmaceutical companies. Currently, most of the education in this field is sponsored by pharmaceutical companies. Not surprisingly, there has been an escalation of abuse despite "voluntary" education (14). There is some evidence that the risk reduction strategies are not employed by primary care physicians, even in high risk patients (115). Mandatory education for those prescribing opioids for chronic pain may be helpful.
3. Pain organizations and societies should establish guidelines based on sound science without conflict of interest. Opioid management should be based on evidence and not on consensus of experts, no matter how learned they may be (116).

Opioids have an important but limited role in chronic pain. Their use should not be curtailed. The aim of this article is to encourage opioid use for patients who need it and at the same time deny it to those who abuse it. Unless the medical community takes an active role in curbing abuse, opioid use will be subject to excessive regulation by the government, making it difficult for us to prescribe. Responsible opioid prescribing, entails employing screening tools, monitoring patients, and establishing dose limits, and is required to prevent harm and preserve access to those who need it. Lest, we should forget, "first do no harm."

## Acknowledgments

The authors would like to thank Dr. Manchikanti for his expertise in this area and his invaluable input in enhancing the quality of this manuscript; Alvaro F. Gómez, MA, and Tom Prigge, MA, for manuscript review, and Tonie M. Hatton and Diane E. Neihoff, transcriptionists, for their assistance in preparation of this manuscript. We would like to thank the editorial board of *Pain Physician* for review and criticism in improving the manuscript.

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# Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting

*Note: These guidelines do not replace clinical judgment in the appropriate care of patients. They are not intended as standards of care or as templates for legislation, nor are they meant for patients in palliative care programs or with cancer pain. The recommendations are an educational tool based on the expert opinion of numerous physicians and other health care providers, medical/nursing boards, mental and public health officials, and law enforcement personnel in Oklahoma and throughout the United States. The guidelines are available at* http://poison.health.ok.gov.

## Opioid Treatment for Acute Pain

1. Opioids should only be used for treatment of acute pain when the severity of the pain warrants that choice and after determining that other non-opioid pain medications or therapies will not provide adequate pain relief.
2. Providers should query the Oklahoma Prescription Monitoring Program (PMP) for patients presenting with acute pain, prior to prescribing an opioid medication. In circumstances where a patient's pain is resulting from an objectively diagnosed disease process or injury, a provider may prudently opt not to review the Oklahoma PMP.
3. When opioids are prescribed for treatment of acute pain, the number of doses dispensed should be no more than the number of doses needed based on the usual duration of pain severe enough to require opioids for that condition.
4. When opioids are prescribed for treatment of acute pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.
5. Long duration-of-action opioids (e.g., methadone, buprenorphine, fentanyl, extended release oxycodone, and morphine) are rarely indicated for treatment of acute pain.
6. The use of opioids should be re-evaluated carefully, including assessing the potential for abuse, if persistent pain suggests the need to continue opioids beyond the anticipated time period of acute pain treatment for that condition. Health care providers should query the Oklahoma PMP as part of this re-evaluation process.
7. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.

## Opioid Treatment for Chronic Pain

1. Alternatives to opioid treatment should be tried, or previous attempts documented, before initiating opioid treatment.
2. A comprehensive evaluation should be performed before initiating opioid treatment for chronic pain. For chronic pain patients transferring their care to new health care providers, new opioid prescriptions should generally not be written until the previous provider's records have been reviewed or the previous health care provider has been notified of the transfer of care.
3. The health care provider should screen for risk of abuse or addiction before initiating opioid treatment.
4. Prior to the initial prescribing of opioid medications, health care providers should query the Oklahoma Prescription Monitoring Program (PMP).
5. When opioids are used for the treatment of chronic pain, a written treatment plan should be established that includes measurable goals for reduction of pain and improvement of function. One health care provider should coordinate a patient's comprehensive pain care plan and provide all opioid prescriptions required for the plan.

6. The patient should be informed of the risks, benefits, and terms for continuation of opioid treatment, ideally using a written and signed treatment agreement.
7. Opioids should be initiated as a short-term trial to assess the effects of opioid treatment on pain intensity, function, and quality of life. In most instances, the trial should begin with a short-acting opioid medication.
8. Regular visits for evaluation of progress toward goals should be scheduled during the period when the dose of opioids is being adjusted (titration period). During the titration period, and until the patient is clinically stable and judged to be compliant with therapy, it is recommended that the health care provider check the Oklahoma PMP more frequently.
9. Once a stable dose has been established (maintenance period), regular monitoring should be conducted at face-to-face visits during which treatment goals, analgesia, activity, adverse effects, and aberrant behaviors are monitored. The Oklahoma PMP should be queried at least once per year for patients receiving opioid treatment for chronic pain.
10. Continuing opioid treatment should be a deliberate decision that takes into consideration the risks and benefits of chronic opioid treatment for that patient. Patients and health care providers should periodically reassess the need for continued opioid treatment, weaning whenever possible, as part of the comprehensive pain care plan. A second opinion or consultation may be useful in making that decision.
11. Opioid treatment should be discontinued if adverse effects outweigh benefits or if aberrant, dangerous, or illegal behaviors are demonstrated.
12. Health care providers treating chronic pain patients with opioids should maintain records, in accordance with state and federal law, documenting patient evaluation, treatment plan, discussion of risks and benefits, informed consent, treatments prescribed, results of treatment, and any aberrant behavior observed.
13. Health care providers should consider consultation for patients with complex pain conditions, serious co-morbidities and mental illness, a history or evidence of current drug addiction or abuse, or when the provider is not confident of his/her ability to manage the treatment.
14. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.
15. The administration of intravenous and intramuscular opioids for the relief of exacerbations of chronic pain is discouraged, except in special circumstances.
16. Long-acting opioids are associated with an increased risk of overdose death, and should only be prescribed by health care providers familiar with their indications, risks, and need for careful monitoring.
17. When opioids are prescribed for treatment of chronic pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.

**List of prescribed medications;**

- **Oklahoma Administrative Code 435:10-7-11 (6H)**
- **Oklahoma Administrative Code 510:5-9-2 (3)**
- CDC Guideline for Prescribing Opioids for Chronic Pain, US, 2016 page 29
- CMS Local Coverage Determination, Novitas, "Controlled Substance Monitoring and Drugs of Abuse Testing", page 9
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, pages 1 and 2

(6) **Medical records.** Records should remain current and be maintained in an accessible manner, readily available for review. The physician should keep accurate and complete records to include:

(A) the medical history and physical examination (including vital signs),
(B) diagnostic, therapeutic and laboratory results,
(C) evaluations, consultations and follow-up evaluations,
(D) treatment objectives,
(E) discussion of risks and benefits,
(F) informed consent,
(G) treatments,
(H) medications (including date, type, dosage and quantity prescribed),
(I) instructions and agreements and
(J) periodic reviews.

(7) **Compliance with controlled substances laws and regulations.** To prescribe, dispense or administer controlled substances, the physician must be licensed in Oklahoma and comply with applicable federal and state regulations. Physicians are referred to the Physicians Manual of the U.S. Drug Enforcement Administration for specific rules governing controlled substances as well as applicable state regulations.

[**Source:** Amended at 16 Ok Reg 2003, eff 6-14-99; Added at 22 Ok Reg 2096, eff 6-25-05]

## 510:5-9-2 Guidelines and requirements

This rule requires that diagnosis be documented, it requires that certain records be maintained, and it requires that the physician must discuss the risks and benefits with the patient or the patient's guardian.

(1) To treat a patient's intractable pain, as long as the benefit of the expected relief outweighs the risk, even if the use of the drug increases the risk of death, so long as it is not furnished for the purpose of causing, or the purpose of assisting in causing death, the physician may prescribe or administer Schedule II, III, IV or V controlled dangerous substances or other pain relieving drugs in higher than normal dosages when, in that physician's judgment, the higher dosages are necessary to produce the desired therapeutic effect.

(2) The determination of intractable pain must include a complete medical history and physical examination which includes an assessment of the patient's pain, physical and psychological function, substance abuse history, underlying or co-existing diseases or conditions and the presence of a recognized medical indication for the use of an analgesic.

(3) The treatment plan must state objectives by which treatment success can be evaluated, such as pain relief and or improved physical and psychological function, and must indicate what further diagnostic evaluations or other treatments are planned. The drug therapy must be tailored to the individual needs of each patient.

(4) The course of treatment and any new information about the etiology of the intractable pain must be reviewed periodically, at least annually, with consideration given to referral for a current second opinion. The continuation or modification of treatment will depend on the results of this review and the evaluation of the patient's progress toward the treatment objectives. If the patient has not improved, the physician must assess the appropriateness of continuing the current therapy and the trial of other modalities.

(5) The management of intractable pain in patients with a history of substance abuse requires extra care, monitoring, documentation and consultation with addiction medicine specialists, and may include the use of agreements between the physician and patient specifying rules for medication use and consequences for its misuse.

(6) The physician must discuss the risks and benefits of the use of controlled substances with the patient or the patient's guardian and obtain informed consent prior to proceeding if it substantially increases the risk of death.

(7) Accurate and complete records documenting these requirements must be kept.

(8) To prescribe controlled substances, the physician must be licensed in Oklahoma, have a valid controlled substances registration and comply with federal and state regulations for issuing controlled substances prescriptions.

(9) Expert clinical testimony may be used to prove a violation of this rule. As used herein, a "clinical expert" is a physician who, by reason of specialized education or substantial relevant experience in pain management, has knowledge regarding current standards, practices and guidelines.

(10) Nothing in this rule shall limit a physician's authority to prescribe or administer prescription drug products beyond the customary indications as noted in the manufacturer's package insert for use in treating intractable pain, provided the drug is recognized for treatment of intractable pain in standard reference compendia or medical literature.

[Source: Added at 16 Ok Reg 2539, eff 6-25-99]

(mostly due to illicit opiate use), and it is plausible that effectiveness would be observed when naloxone is provided in the clinical setting as well. Experts agreed that it is preferable not to initiate opioid treatment when factors that increase risk for opioid-related harms are present. Opinions diverged about the likelihood of naloxone being useful to patients and the circumstances under which it should be offered. However, most experts agreed that clinicians should consider offering naloxone when prescribing opioids to patients at increased risk for overdose, including patients with a history of overdose, patients with a history of substance use disorder, patients taking benzodiazepines with opioids (see Recommendation 11), patients at risk for returning to a high dose to which they are no longer tolerant (e.g., patients recently released from prison), and patients taking higher dosages of opioids (≥50 MME/day). Practices should provide education on overdose prevention and naloxone use to patients receiving naloxone prescriptions and to members of their households. Experts noted that naloxone co-prescribing can be facilitated by clinics or practices with resources to provide naloxone training and by collaborative practice models with pharmacists. Resources for prescribing naloxone in primary care settings can be found through Prescribe to Prevent at http://prescribetoprevent.org.

9. **Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months (recommendation category: A, evidence type: 4).**

PDMPs are state-based databases that collect information on controlled prescription drugs dispensed by pharmacies in most states and, in select states, by dispensing physicians as well. In addition, some clinicians employed by the federal government, including some clinicians in the Indian Health Care Delivery System, are not licensed in the states where they practice, and do not have access to PDMP data. Certain states require clinicians to review PDMP data prior to writing each opioid prescription (see state-level PDMP-related policies on the National Alliance for Model State Drug Laws website at http://www.namsdl.org/prescription-monitoring-programs.cfm). The clinical evidence review did not find studies evaluating the effectiveness of PDMPs on outcomes related to overdose, addiction, abuse, or misuse (KQ4). However, even though evidence is limited on the effectiveness of PDMP implementation at the state level on prescribing and mortality outcomes (*28*), the contextual evidence review found that most fatal overdoses were associated with patients receiving opioids from multiple prescribers and/or with patients receiving high total daily opioid dosages; information on both of these risk factors for overdose are available to prescribers in the PDMP. PDMP data also can be helpful when patient medication history is not otherwise available (e.g., for patients from other locales) and when patients transition care to a new clinician. The contextual evidence review also found that PDMP information could be used in a way that is harmful to patients. For example, it has been used to dismiss patients from clinician practices (*211*), which might adversely affect patient safety.

The contextual review found variation in state policies that affect timeliness of PDMP data (and therefore benefits of reviewing PDMP data) as well as time and workload for clinicians in accessing PDMP data. In states that permit delegating access to other members of the health care team, workload for prescribers can be reduced. These differences might result in a different balance of benefits to clinician workload in different states. Experts agreed that PDMPs are useful tools that should be consulted when starting a patient on opioid therapy and periodically during long-term opioid therapy. However, experts disagreed on how frequently clinicians should check the PDMP during long-term opioid therapy, given PDMP access issues and the lag time in reporting in some states. Most experts agreed that PDMP data should be reviewed every 3 months or more frequently during long-term opioid therapy. A minority of experts noted that, given the current burden of accessing PDMP data in some states and the lack of evidence surrounding the most effective interval for PDMP review to improve patient outcomes, annual review of PDMP data during long-term opioid therapy would be reasonable when factors that increase risk for opioid-related harms are not present.

Clinicians should review PDMP data for opioids and other controlled medications patients might have received from additional prescribers to determine whether a patient is receiving high total opioid dosages or dangerous combinations (e.g., opioids combined with benzodiazepines) that put him or her at high risk for overdose. Ideally, PDMP data should be reviewed before every opioid prescription. This is recommended in all states with well-functioning PDMPs and where PDMP access policies make this practicable (e.g., clinician and delegate access permitted), but it is not currently possible in states without functional PDMPs or in those that do not permit certain prescribers to access them. As vendors and practices facilitate integration of PDMP information into regular clinical workflow (e.g., data made available in electronic health records), clinicians' ease of access in reviewing PDMP data is expected to improve.

a. Identifies absence of prescribed medication and potential for abuse, misuse, and diversion;
b. Identifies undisclosed substances, such as alcohol, unsanctioned prescription medication, or illicit substances;
c. Identifies substances that contribute to adverse events or drug-drug interactions;
d. Provides objectivity to the treatment plan;
e. Reinforces therapeutic compliance with the patient;
f. Provides additional documentation demonstrating compliance with patient evaluation and monitoring;
g. Provides diagnostic information to help assess individual patient response to medications (e.g., metabolism, side effects, drug-drug interaction, etc.) over time for ongoing management of prescribed medications.

2. Medical Necessity Guidance:

Criteria to establish medical necessity for drug testing must be based on patient- specific elements identified during the clinical assessment, and documented by the clinician in the patient's medical record and minimally include the following elements:

- Patient history, physical examination and previous laboratory findings;
- Current treatment plan;
- Prescribed medication(s); and
- Risk assessment plan.

National pain organizations, physician societies, and the Federation of State Medical Boards recommend a practical approach to definitive UDT for COT.

Frequency of testing beyond the baseline presumptive UDT must be based on individual patient needs substantiated by documentation in the patient's medical record. Recommendations for the ordering of presumptive and definitive UDT for patients on COT are as follows:

a. COT Baseline Testing:

Initial presumptive or definitive COT patient testing may include amphetamine/methamphetamine, barbiturates, benzodiazepines, cocaine, methadone, oxycodone, tricyclic antidepressants, tetrahydrocannabinoid, opioids, opiates, heroin, and synthetic/analog or "designer" drugs.

b. COT Monitoring Testing:

Ongoing testing may be medically reasonable and necessary based on the patient history, clinical assessment, including medication side effects or inefficacy, suspicious behaviors, self -escalation of dose, doctor-shopping, indications/symptoms of illegal drug use, evidence of diversion, or other clinician documented change in affect or behavioral pattern.

The frequency of testing must be based on a complete clinical assessment of the individual's risk potential for abuse and diversion using a validated risk assessment interview or questionnaire and should include the patient's response to prescribed medications and the side effects of medications.

The clinician should perform random UDT at random intervals, in order to properly monitor a patient. UDT testing does not have to be associated with an office visit.

**Drug Testing Panels**

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6. The use of opioids should be re-evaluated carefully, including assessing the potential for abuse, if persistent pain suggests the need to continue opioids beyond the anticipated time period of acute pain treatment for that condition. Health care providers should query the Oklahoma PMP as part of this re-evaluation process.
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9. Once a stable dose has been established (maintenance period), regular monitoring should be conducted at face-to-face visits during which treatment goals, analgesia, activity, adverse effects, and aberrant behaviors are monitored. The Oklahoma PMP should be queried at least once per year for patients receiving opioid treatment for chronic pain.
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12. Health care providers treating chronic pain patients with opioids should maintain records, in accordance with state and federal law, documenting patient evaluation, treatment plan, discussion of risks and benefits, informed consent, treatments prescribed, results of treatment, and any aberrant behavior observed.
13. Health care providers should consider consultation for patients with complex pain conditions, serious co-morbidities and mental illness, a history or evidence of current drug addiction or abuse, or when the provider is not confident of his/her ability to manage the treatment.
14. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.
15. The administration of intravenous and intramuscular opioids for the relief of exacerbations of chronic pain is discouraged, except in special circumstances.
16. Long-acting opioids are associated with an increased risk of overdose death, and should only be prescribed by health care providers familiar with their indications, risks, and need for careful monitoring.
17. When opioids are prescribed for treatment of chronic pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.

**Risk assessment, as identified by use of a validated risk assessment interview or questionnaire tool, with appropriate risk stratification noted and utilized;**

- **Oklahoma Administrative Code 435:10-7-11 (6B)( 6E)**
- CDC Guideline for Prescribing Opioids for Chronic Pain, US, 2016 page 16 and 26
- CMS Local Coverage Determination, Novitas, "Controlled Substance Monitoring and Drugs of Abuse Testing", page 9
- "Prevention of Opioid Abuse in Chronic Non-Cancer Pain: An Algorithmic, Evidence Based Approach", Pain Physician 2012; pages 4-8
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, pages 1 and 2

(6) **Medical records.** Records should remain current and be maintained in an accessible manner, readily available for review. The physician should keep accurate and complete records to include:

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(7) **Compliance with controlled substances laws and regulations.** To prescribe, dispense or administer controlled substances, the physician must be licensed in Oklahoma and comply with applicable federal and state regulations. Physicians are referred to the Physicians Manual of the U.S. Drug Enforcement Administration for specific rules governing controlled substances as well as applicable state regulations.

[**Source:** Amended at 16 Ok Reg 2003, eff 6-14-99; Added at 22 Ok Reg 2096, eff 6-25-05]

**BOX 1. CDC recommendations for prescribing opioids for chronic pain outside of active cancer, palliative, and end-of-life care**

**Determining When to Initiate or Continue Opioids for Chronic Pain**

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

**Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation**

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.
7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

**Assessing Risk and Addressing Harms of Opioid Use**

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.
9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.
10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.
11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

* All recommendations are category A (apply to all patients outside of active cancer treatment, palliative care, and end-of-life care) except recommendation 10 (designated category B, with individual decision making required); see full guideline for evidence ratings.

## Considerations for Tapering Opioids

Although the clinical evidence review did not find high-quality studies comparing the effectiveness of different tapering protocols for use when opioid dosage is reduced or opioids are discontinued (KQ3), tapers reducing weekly dosage by 10%–50% of the original dosage have been recommended by other clinical guidelines (*199*), and a rapid taper over 2–3 weeks has been recommended in the case of a severe adverse event such as overdose (*30*). Experts noted that tapers slower than 10% per week (e.g., 10% per month) also might be appropriate and better tolerated than more rapid tapers, particularly when patients have been taking opioids for longer durations (e.g., for years). Opioid withdrawal during pregnancy has been associated with spontaneous abortion and premature labor.

When opioids are reduced or discontinued, a taper slow enough to minimize symptoms and signs of opioid withdrawal (e.g., drug craving, anxiety, insomnia, abdominal pain, vomiting, diarrhea, diaphoresis, mydriasis, tremor, tachycardia, or piloerection) should be used. A decrease of 10% of the original dose per week is a reasonable starting point; experts agreed that tapering plans may be individualized based on patient goals and concerns. Experts noted that at times, tapers might have to be paused and restarted again when the patient is ready and might have to be slowed once patients reach low dosages. Tapers may be considered successful as long as the patient is making progress. Once the smallest available dose is reached, the interval between doses can be extended. Opioids may be stopped when taken less frequently than once a day. More rapid tapers might be needed for patient safety under certain circumstances (e.g., for patients who have experienced overdose on their current dosage). Ultrarapid detoxification under anesthesia is associated with substantial risks, including death, and should not be used (*200*). Clinicians should access appropriate expertise if considering tapering opioids during pregnancy because of possible risk to the pregnant patient and to the fetus if the patient goes into withdrawal. Patients who are not taking opioids (including patients who are diverting all opioids they obtain) do not require tapers. Clinicians should discuss with patients undergoing tapering the increased risk for overdose on abrupt return to a previously prescribed higher dose. Primary care clinicians should collaborate with mental health providers and with other specialists as needed to optimize nonopioid pain management (see Recommendation 1), as well as psychosocial support for anxiety related to the taper. More detailed guidance on tapering, including management of withdrawal symptoms has been published previously (*30,201*). If a patient exhibits signs of opioid use disorder, clinicians should offer or arrange for treatment of opioid use disorder (see Recommendation 12) and consider offering naloxone for overdose prevention (see Recommendation 8).

## Assessing Risk and Addressing Harms of Opioid Use

8. **Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present (recommendation category: A, evidence type: 4).**

The clinical evidence review found insufficient evidence to determine how harms of opioids differ depending on patient demographics or patient comorbidities (KQ2). However, based on the contextual evidence review and expert opinion, certain risk factors are likely to increase susceptibility to opioid-associated harms and warrant incorporation of additional strategies into the management plan to mitigate risk. Clinicians should assess these risk factors periodically, with frequency varying by risk factor and patient characteristics. For example, factors that vary more frequently over time, such as alcohol use, require more frequent follow up. In addition, clinicians should consider offering naloxone, re-evaluating patients more frequently (see Recommendation 7), and referring to pain and/or behavioral health specialists when factors that increase risk for harm, such as history of overdose, history of substance use disorder, higher dosages of opioids (≥50 MME/day), and concurrent use of benzodiazepines with opioids, are present.

### Patients with Sleep-Disordered Breathing, Including Sleep Apnea

Risk factors for sleep-disordered breathing include congestive heart failure, and obesity. Experts noted that careful monitoring and cautious dose titration should be used if opioids are prescribed for patients with mild sleep-disordered breathing. Clinicians should avoid prescribing opioids to patients with moderate or severe sleep-disordered breathing whenever possible to minimize risks for opioid overdose (contextual evidence review).

### Pregnant Women

Opioids used in pregnancy might be associated with additional risks to both mother and fetus. Some studies have shown an association of opioid use in pregnancy with stillbirth, poor fetal growth, pre-term delivery, and birth defects (contextual evidence review). Importantly, in some cases, opioid use during pregnancy leads to neonatal opioid withdrawal syndrome. Clinicians and patients together should carefully weigh risks and benefits when making decisions

a. Identifies absence of prescribed medication and potential for abuse, misuse, and diversion;
b. Identifies undisclosed substances, such as alcohol, unsanctioned prescription medication, or illicit substances;
c. Identifies substances that contribute to adverse events or drug-drug interactions;
d. Provides objectivity to the treatment plan;
e. Reinforces therapeutic compliance with the patient;
f. Provides additional documentation demonstrating compliance with patient evaluation and monitoring;
g. Provides diagnostic information to help assess individual patient response to medications (e.g., metabolism, side effects, drug-drug interaction, etc.) over time for ongoing management of prescribed medications.

2. Medical Necessity Guidance:

Criteria to establish medical necessity for drug testing must be based on patient- specific elements identified during the clinical assessment, and documented by the clinician in the patient's medical record and minimally include the following elements:

- Patient history, physical examination and previous laboratory findings;
- Current treatment plan;
- Prescribed medication(s); and
- Risk assessment plan.

National pain organizations, physician societies, and the Federation of State Medical Boards recommend a practical approach to definitive UDT for COT.

Frequency of testing beyond the baseline presumptive UDT must be based on individual patient needs substantiated by documentation in the patient's medical record. Recommendations for the ordering of presumptive and definitive UDT for patients on COT are as follows:

a. COT Baseline Testing:

Initial presumptive or definitive COT patient testing may include amphetamine/methamphetamine, barbiturates, benzodiazepines, cocaine, methadone, oxycodone, tricyclic antidepressants, tetrahydrocannabinoid, opioids, opiates, heroin, and synthetic/analog or "designer" drugs.

b. COT Monitoring Testing:

Ongoing testing may be medically reasonable and necessary based on the patient history, clinical assessment, including medication side effects or inefficacy, suspicious behaviors, self -escalation of dose, doctor-shopping, indications/symptoms of illegal drug use, evidence of diversion, or other clinician documented change in affect or behavioral pattern.

The frequency of testing must be based on a complete clinical assessment of the individual's risk potential for abuse and diversion using a validated risk assessment interview or questionnaire and should include the patient's response to prescribed medications and the side effects of medications.

The clinician should perform random UDT at random intervals, in order to properly monitor a patient. UDT testing does not have to be associated with an office visit.

**Drug Testing Panels**

similar efficacy as NSAIDS, but have more side effects. Franklin et al (39) followed injured workers for one year. They found that despite a 62% increase in opioid doses over a 12 month period (from 26 mg morphine equivalent dose [MED] in the first quarter to 42 mg in the fourth quarter), improvement in pain and function was seen only in 27% and 16% of the patients. In concurrence with Franklin et al (39), multiple other authors have illustrated deleterious consequences of early or continued opioid use for chronic pain, including adverse consequences of dependence, hyperalgesia, and an association between opioid prescribing and overall health status, with increased disability, medical costs, subsequent surgery, and continued or late opioid use (1,39-56).

## Call For Responsible Prescribing

The annual US expenditures related to pain (including direct medical costs and lost wages) are higher than those for cancer, heart disease, and diabetes combined (20). The improvements in the emotional and economic impact of untreated chronic pain are often the criteria by which pain management physicians measure the success of a treatment modality. But the notion that aggressive use of opioids in trying to alleviate chronic non-cancer pain would result in improvement of function (let alone improvement in pain) has been proven erroneous. Despite a cavalier approach to the prescription of opioids in the last decade, numerous studies have shown a consistent lack of evidence that opioids decreased pain, improved function, or decreased health care costs (27,33-39). On the contrary, there is now an abundance of evidence that this aggressive approach has harmed individuals and society and has had a negative economic impact (1,14-18,23,57-87). Gomes et al's study (57) reports that the overall death rate for patients receiving opioids was 10 times higher than those not on opioids, suggesting possible harm. Eriksen et al (23) have shown that patients on opioids report higher pain scores, poor self-rated health, not being engaged in employment, higher use of the health care system, and a negative influence on quality of life. Although pharmacists, state medical boards, and other agencies and professionals play a role in curbing abuse, the primary onus is on the prescribing physician. Since the vast majority of opioid overdose deaths from opioids stem from legitimate prescriptions, calls for responsible prescribing by physicians have been made (88-94). Given that 3% of physicians accounted for 62% of the opioids prescribed in one study (61), the proliferation of high-volume prescribers can have a large impact on the use of opioids and overdose death rates (14).

For controlling acute pain and cancer pain, opioids have been shown to be quite effective. Most of the evidence for prescribing opioids comes from studies of their use in these settings. In such scenarios, other medications, namely NSAIDs, muscle relaxants, antidepressants, and anticonvulsants are not as effective and are used, if at all, in a supplementary role. However, extrapolating these results from acute pain studies to guide managing chronic non-cancer pain may not be a wise step. Opioids have a very important role in chronic pain management and their value should not be underestimated. Unlike other analgesics, opioids do not result in organ toxicity, nor is there any ceiling dose associated with their use. Opioids have, thus, become the mainstay and play a vital role but they are not a panacea for chronic pain. In order to maximize their efficacy, opioids should be used with great restraint and caution and in carefully selected patients as recommended by American Society of Interventional Pain Physicians guidelines (62). According to one study, there is evidence that opioids are being used with the wrong patients (63). We concur with Manchikanti et al (20) that the most underappreciated issue in modern medicine is the adverse consequences of appropriately prescribed opioids, with all the blame diverted to abuses and overuses.

There are 3 types of patients that we should be cautious about: the first is the abuser; the second is the one who is involved in diversion; and, the third is the patient who is a combination of the two. The cornerstones for responsible opioid use for balancing pain relief along with curbing abuse and diversion are:

- Careful patient screening to stratify patients into different risk groups for opioid abuse/diversion
- Monitoring patients to ensure compliance for the responsible use of opioids
- Establishing and adhering to dose limitations.

## Screening Patients

The need for effective screening tools was expressed as early as 2001 (64,65). A decade later we are still looking for a tool that is universally acceptable. Guidelines from AAPM and APS (27) state that risk stratification is an undeveloped skill for many physicians prescribing opioids and that these physicians should be more knowledgeable in this area. There are many screening tools that currently exist which are specifically designed for prescription opioid abuse. Solanki et al (66) reviewed all the available screening tools and con-

cluded that there was no single screening tool that can be applied universally. Chou et al (35) analyzed tools that were specific for prescription opioids and based on their criteria found that most of the studies evaluating the screening tools had methodological flaws. However, screening tools may play an important role in curbing abuse. The failure to utilize existing tools so as to find the perfect tool seems counterproductive in this environment. The question remains: Which is the best existing tool? The tools we find useful are the Screener and Opioid Assessment for Patients with Pain (SOAPP) (67), Pain Medication Questionnaire (PMQ) (68,69), Prescription Drug Use Questionnaire patient version (PDUQP) (70), Addiction Behaviors Checklist (ABC) (71), Diagnosis, Intractability, Risk, Efficacy (DIRE) score (72) and the one by Atluri and Sudarshan (73). The screening tool Current Opioid Misuse Measure (COMM) (74) and Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) (75) were not considered because many of the questions were not related to abuse/diversion and fell under the category of psychological queries. The Pain Assessment and Documentation Tool (PADT) (76) is not a screening tool as it addresses the level of analgesia, adverse events, and activities of daily living along with aberrant drug-related behavior. The section of abuse is a small component of the whole tool. The screening tool by Michna et al (77) addressed only 3 items, and is not comprehensive enough to identify abuse. The Opioid Risk Tool (ORT) (78) is a 5-item tool which is also not comprehensive. The items in this tool are not predictors of abuse. PDUQ and PDUQP tools were developed by the same group. PDUQP (70) is a modified, improved version of PDUQ (69) as all the questions are related to abuse, and questions related to psychopathology were eliminated. Among the tools selected, the first 3 tools are subjective (SOAPP, PMQ and PDUQP) and the last 3 are objective tools (DIRE score, ABC checklist and the tool by Atluri and Sudarshan). Although there has been a call for the use of these subjective tools (79-82), abusers tend not be truthful in subjective questionnaires (83-87). The screening tool developed by Wu et al (71), the DIRE Score (72), and the screening tool created by Atluri and Sudarshan (73) may have more value since they incorporate objective measures. These tools can be used singularly or in combination. Generic screening tools for drug and alcohol abuse are not as useful as those specifically designed for prescription opioid abuse. Guidelines developed for opioid use for chronic pain (27,87,88) include recommendations for using screening tools, but with the reservation that risk stratification is currently underutilized (89,90). Classifying patients into high and low risk groups helps tremendously with opioid management and might possibly be one of the cornerstones in abuse prevention. As described below, screening patients into different risk categories determines the frequency of monitoring, aggressiveness of dosage, and frequency of follow-up visits.

## Urine Drug Screens

Currently, urine drug screens (UDS) remain one of the most important tools for detecting inappropriate use of opioids. Although Starrels et al (91) concluded in their review that the evidence in support of the effectiveness of UDS for reducing opioid misuse in chronic pain is relatively weak, they have also noted that based on cross-sectional studies and case series, UDS is a valuable tool for detecting the use of unprescribed drugs and for confirming adherence to prescribed medications with a higher degree of accuracy than when identified by patient self-report or the impression of the treating physician. Starrels et al (91) also suggested that UDS might improve the provider-patient relationship and clinic morale. After a review of the literature regarding the role of UDS and opioids, Christo et al (92) concluded that, "UDS is one of the major tools of adherence monitoring in the assessment of the patient's predisposition to, and patterns of, drug misuse/abuse – a vital first step towards establishing and maintaining the safe and effective use of opioid analgesics in the treatment of chronic pain." Katz et al (93) have shown that using UDS along with monitoring aberrant behaviors enhances abuse detection. In Manchikanti et al's study (94), random UDS reduced illicit drug use in the chronic pain population. In a separate study, Manchikanti et al (95) have shown that by using UDS they could identify a combined use of illicit drugs and the misuse of prescription drugs in 24% of patients on hydrocodone and in 33% of patients receiving methadone (96). The Federation of State Medical Boards has formally included UDS in current guidelines for using opioids in the management of chronic noncancer pain (97). Since there is evidence that UDS have not been universally adopted by physicians treating chronic pain (98,99), the use of UDS must be encouraged. Random UDS may have more value in detecting abuse as patients may change their behavior when expected to be tested (27).

## Prescription Monitoring Programs

Prescription monitoring programs (PMPs) serve as a means of data collection for opioid prescriptions, providing physicians with information about who wrote the prescriptions and the pharmacies that dispensed them. Physicians have access to this data to check if patients are getting opioid prescriptions from more than one physician at the same time. This information becomes extremely useful especially if the patient signs an opioid contract agreeing to obtain the prescription from only one physician and to fill it in only one pharmacy. Currently, there are 38 states with this program (66). A national program would be invaluable in curbing abuse and doctor shopping (100). The National All Schedule Prescription Electronic Reporting Act (NASPER) was enacted by Congress in 2005 but has not yet been fully implemented (101). Calls for immediate funding and rapid implementation of NASPER have been made. This law requires states to collect prescription information for Schedule II, III, and IV medications. It also requires states to have the capability to share this information with one another. This would potentially decrease cross-border opioid trafficking and would be invaluable in curbing abuse and doctor shopping (15,102,103). Paulozzi et al's study (104) recommends using PMP to curb overuse, noting that the rate of overdose deaths is higher in those who use multiple pharmacies and doctors. This assertion is also expressed by White et al (105). In one study, 21% of overdose deaths resulted from doctor shopping (106). In response to the epidemic of prescription drug abuse, the White House Office of National Drug Control Policy issued a document in which it recommended enhanced use of prescription drug monitoring programs (106). The National Alliance for Model State Drug Laws indicates that these databases foster the legitimate medical use of controlled substances while limiting drug abuse and diversion (102). Access to PMP can help clinicians curb diversion and abuse and to decrease the number of unnecessary prescriptions while still providing analgesia to those who need it (102). Manchikanti et al (107) have recently shown that the Kentucky's PMP, KASPER (Kentucky All Schedule Prescription Electronic Reporting Program) has led to a decrease in doctor shopping from 18% in 2001 to 2.1% in 2011. Baehren et al (108) showed that in an emergency department setting, the use of PMP positively influenced the opioid prescribing pattern. Based on the PMP results, 61% of their study patients were prescribed less opioid medication than originally planned, whereas 39% received more opioid medication than previously planned. Paulozzi et al (109) reported that PMPs were not significantly associated with lower rates of drug overdose or opioid overdose mortality or lower rates of consumption of opioid drugs. An accompanying editorial (110) clarified that the lack of impact of PMPs is due to their underutilization.

## A Case for Dose Limitation

The evidence in favor of long-term opioid use for chronic pain is at best problematic. Considering the irrefutable evidence showing widespread abuse and diversion, the rationale for high dose opioids should be reexamined. Patients who do not respond to a low/medium dose of opioids generally would not find their pain alleviated by larger doses. In 2007, the state of Washington issued guidelines that in general, the daily dose should not exceed 120 mg of MED (87). The guidelines by APS and AAPM in 2009 defined high dose as 200 mg MED (27). The Canadian guidelines in 2010 identified 200 mg MED as a watchful dose (88). Until recently, however, there was only limited data verifying the safety of these recommended doses, especially in high risk patients. Five recent studies showed that the rate of overdose was directly proportional to the prescribed opioid dose (57,104,111-113). Bohnert et al's study (111) in a national sample of Veterans Health Administration patients revealed that there was a dose-response relationship between the maximum daily prescribed dose of opioid and the risk of opioid overdose death. The overdose death rate for patients receiving a dose of less than 20 mg MED was 0.11 per 1,000 compared to those getting more than 100 mg MED, for whom the death rate was 1.24/1,000. This difference was even higher in those with a history of substance abuse (0.54 versus 2.97). Since the death rates were higher in patients receiving doses of 50 mg MED versus those getting less than 50 mg MED, the authors concluded that that the risk of opioid overdose increased when the opioid dose was equivalent to 50 mg MED.

Dunn et al (112) reported that in a population from a health maintenance organization in Washington State , there was a 9-fold increase in opioid overdose in patients receiving high dose opioids (more than 100 mg MED) to those getting low dose (less than 20 mg). There was a 3.7-fold increase in overdose events in patients receiving doses between 50-99 mg MED versus those getting less than 20 mg MED. Paulozzi et al (104) found that compared to patients receiving lower opioid doses or no opioid prescriptions, the risk of overdose was greatest at daily opioid doses above 40 mg

MED. Braden et al (113) found that patients (Arkansas Medicaid and HealthCore commercially insured enrollees) receiving MEDs of more than 120 mg/d are more likely to have drug-related encounters than those getting lower doses. There were no differences between these 2 groups regarding emergency department visits. Gomes et al (57) found that patients from Ontario's public drug plan receiving "very high" doses (> 400 mg MED) and "high" doses (200-400 mg MED) had a much higher overdose death than those getting "moderate" doses (< 200 mg MED). In "very high" and "high" dose patients the opioid-related mortality rates were 9.94/1,000 for "very high" and 7.92/1,000 for "high." Comparatively, the opioid-related mortality rate was 1.63/1,000 in those with "moderate" doses. Also, the overall death rate (from any cause) was much higher in patients receiving opioids (20.05/1,000) when compared to those who were not getting any opioids (4.00/1,000).

In the above 5 studies, the doses which are related to an emergency department admission for overdoses or death are 40 mg MED (104), 50 mg MED (111,112), 120 mg MED (113), and 200 mg MED (57). We did not find any study in which a higher dose did not correlate with increased mortality and only one study where there was no correlation between higher opioid dose and emergency department visits. Moreover, Paulozzi et al (15) reported that in 80% of all patients receiving opioids, the dose was less than 100 mg MED and was obtained from one physician. This patient pool constituted 20% of the overall overdose deaths. Even though only 10% of all patients were receiving a dose of greater than 100 mg MED from a single prescriber, the overdose death rate in this population was as high as 40%. Patients receiving more than 100 mg MED from multiple physicians constituted the rest of the 10%. The percentage of overdose deaths was 40% in this segment. In other words, patients receiving more than 100 mg MED (from single or multiple prescribers), contributed to 80% of all the overdose deaths, whereas patients on doses of less than 100 mg MED contributed to only 20% of the overall overdose deaths, implying that 100 mg MED is a dangerous dose. There has been a call for establishing a maximum daily dose in order to guide physicians treating patients with chronic pain (114). Based on the current available evidence presented above, defining 50 mg MED/d as a high dose does not seem unreasonable. The dose limits recommended earlier by Washington State (120 mg MED) (109) and the Canadian guideline (200 mg MED) (110) seem excessive. Defining 200 mg MED by APS and AAPM as a high dose also appears to be harmful. We agree with Katz (114) that having dose limits will provide a guide for practicing physicians, reduce harm by eliminating high doses, assist in the negotiation process between physicians and patients pressing for higher doses and finally, impel high dose prescribers to exercise more caution. We concur with Manchikanti et al (20) that commencing long-acting opioid therapy is often the starting point for high dose opioid therapy, a practice that growing evidence suggests is harmful to patients and increases the black market availability of opioids through diversion. Many argue that chronic pain is undertreated and opioids must be used more liberally. We agree that chronic pain is undertreated, but we completely disagree, based on evidence, that aggressive opioid use is the answer to alleviating undertreated chronic pain. Given our awareness of the inadequacy and adverse effects of using opioids for the treatment of chronic pain, the failure to set dose limits is irresponsible and hazardous both to the individual and to society.

## Algorithmic Approach to Prevent Opioid Abuse

Opioids play an important but limited role in treating chronic pain. The challenge for the physician is to make opioids available for those who are truly in need, and to withhold them from those who are either abusing or diverting. Although difficult, this can be achieved in most cases. If all nonopioid measures fail in alleviating pain, and if opioids are being used, the following steps would be very helpful. The 3 cornerstones for responsible prescribing are stratifying patients by using screening tools into high, medium and low risk groups; monitoring patients by using UDS, PMPs and pill counts; and lastly, establishing dose limits (Fig. 1).

Stratification of patients into different risk categories is the first step. This requires the use of existing screening tools designed specifically to screen for opioid misuse (subjective tools like SOAPP (67), PMQ (68), PUDQP (70) or objective tools like ABC checklist (71), DIRE Score (72) and the tool by Atluri and Sudarshan (73) to classify patients as high risk, medium risk and low risk. As mentioned earlier, objective tools may be better than subjective tools. Those who are categorized as "high risk" should be monitored closely by performing UDS every 3 to 6 months and PMP every 2-4 months. Opioids should be either avoided or prescribed in low doses. Doses of more than 50 mg MED should be very rarely used and only under specialized settings in conjunction, when available, with addiction specialists. Pa-

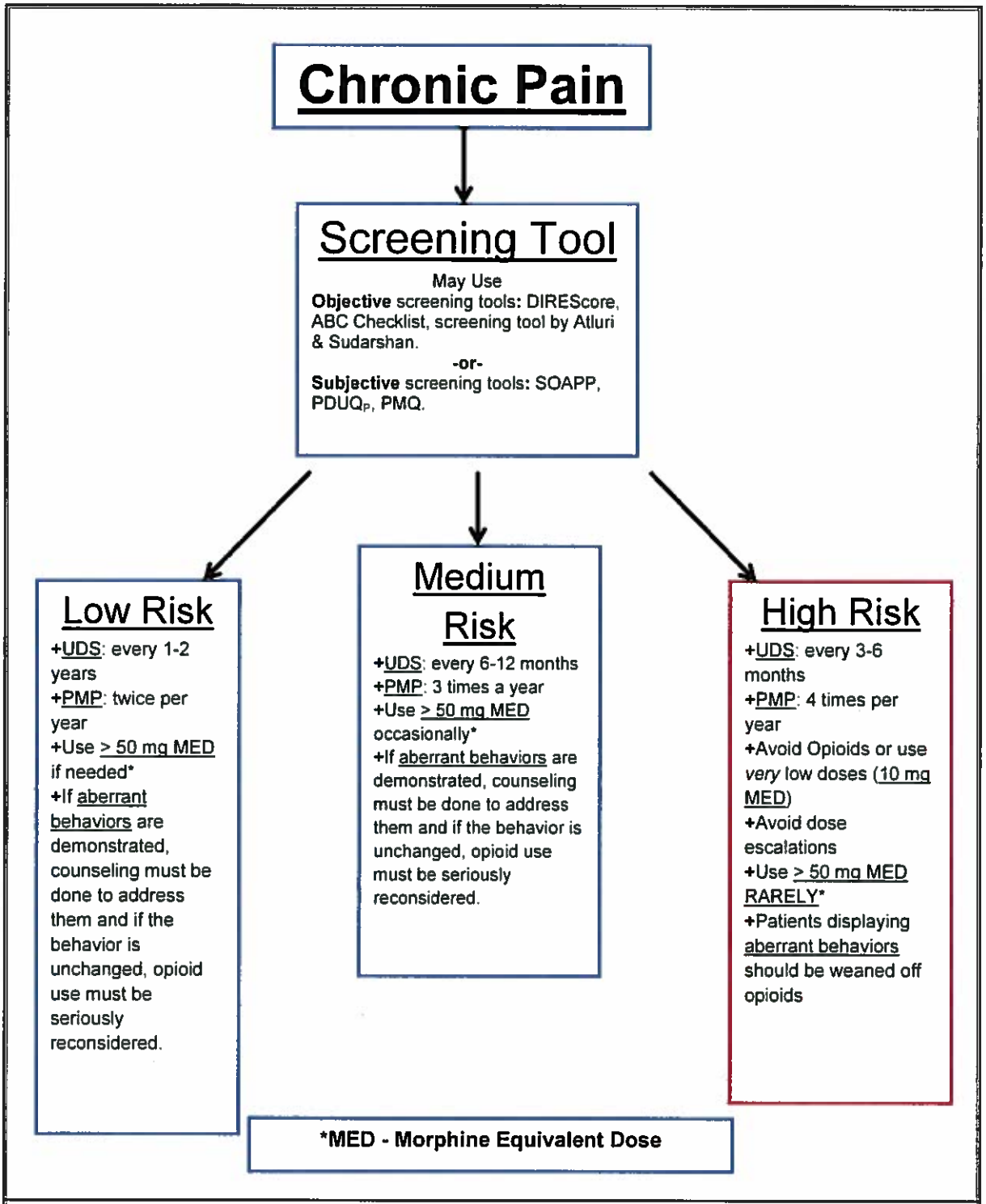


Fig. 1. *Illustration of the 3 cornerstones for responsible prescribing are stratifying patients by using screening tools into high, medium and low risk groups; monitoring patients by using UDS, PMPs and pill counts; and lastly, establishing dose limits*

tients displaying aberrant behaviors (asking for early refills, frequent visits to an emergency department for opioids, doctor shopping, taking opioids from others, etc.) should be weaned off opioids. Patients falling into the "low risk" category should be subjected to UDS every 1-2 years and PMP every 6 months to 1 year. Dose escalations can be done more liberally if required, keeping in mind that doses more than 50 mg MED/d should be an exception rather than the rule. If aberrant behaviors are present, counseling must commence. If counseling does not alter the behavior, opioid use must be seriously reconsidered. Those who are deemed as "medium risk" should be monitored with UDS every 6-12 months and PMP every 3-6 months. Opioid doses and their escalations should be guarded. Doses more than 50 mg MED/d can be used occasionally in carefully selected patients. If aberrant behaviors are present, counseling must commence, with a reconsideration of opioid use if the behavior does not change. These measures, along with an opioid agreement requiring patients to use a single prescriber and a single pharmacy, discouraging self dose escalations, giving limited refills, establishing regular office follow-ups, explaining the risks and benefits of opioids along with insisting on compliance with the opioid agreement should be useful in curbing inappropriate use of opioids.

## Conclusion

To tackle the epidemic of prescription opioid abuse, the following is suggested by Paulozzi et al (15).

1. Improving legislation and enforcement of existing laws regarding doctor shopping, diversion, and unscrupulous physicians.
2. Improving medical practice in prescribing opioids through proper education. In our opinion, and in order to encourage proper prescribing, this education should be based on evidence and not influenced by pharmaceutical companies. Currently, most of the education in this field is sponsored by pharmaceutical companies. Not surprisingly, there has been an escalation of abuse despite "voluntary" education (14). There is some evidence that the risk reduction strategies are not employed by primary care physicians, even in high risk patients (115). Mandatory education for those prescribing opioids for chronic pain may be helpful.
3. Pain organizations and societies should establish guidelines based on sound science without conflict of interest. Opioid management should be based on evidence and not on consensus of experts, no matter how learned they may be (116).

Opioids have an important but limited role in chronic pain. Their use should not be curtailed. The aim of this article is to encourage opioid use for patients who need it and at the same time deny it to those who abuse it. Unless the medical community takes an active role in curbing abuse, opioid use will be subject to excessive regulation by the government, making it difficult for us to prescribe. Responsible opioid prescribing, entails employing screening tools, monitoring patients, and establishing dose limits, and is required to prevent harm and preserve access to those who need it. Lest, we should forget, "first do no harm."

## Acknowledgments

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# Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting

*Note: These guidelines do not replace clinical judgment in the appropriate care of patients. They are not intended as standards of care or as templates for legislation, nor are they meant for patients in palliative care programs or with cancer pain. The recommendations are an educational tool based on the expert opinion of numerous physicians and other health care providers, medical/nursing boards, mental and public health officials, and law enforcement personnel in Oklahoma and throughout the United States. The guidelines are available at* http://poison.health.ok.gov.

## Opioid Treatment for Acute Pain

1. Opioids should only be used for treatment of acute pain when the severity of the pain warrants that choice and after determining that other non-opioid pain medications or therapies will not provide adequate pain relief.
2. Providers should query the Oklahoma Prescription Monitoring Program (PMP) for patients presenting with acute pain, prior to prescribing an opioid medication. In circumstances where a patient's pain is resulting from an objectively diagnosed disease process or injury, a provider may prudently opt not to review the Oklahoma PMP.
3. When opioids are prescribed for treatment of acute pain, the number of doses dispensed should be no more than the number of doses needed based on the usual duration of pain severe enough to require opioids for that condition.
4. When opioids are prescribed for treatment of acute pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.
5. Long duration-of-action opioids (e.g., methadone, buprenorphine, fentanyl, extended release oxycodone, and morphine) are rarely indicated for treatment of acute pain.
6. The use of opioids should be re-evaluated carefully, including assessing the potential for abuse, if persistent pain suggests the need to continue opioids beyond the anticipated time period of acute pain treatment for that condition. Health care providers should query the Oklahoma PMP as part of this re-evaluation process.
7. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.

## Opioid Treatment for Chronic Pain

1. Alternatives to opioid treatment should be tried, or previous attempts documented, before initiating opioid treatment.
2. A comprehensive evaluation should be performed before initiating opioid treatment for chronic pain. For chronic pain patients transferring their care to new health care providers, new opioid prescriptions should generally not be written until the previous provider's records have been reviewed or the previous health care provider has been notified of the transfer of care.
3. The health care provider should screen for risk of abuse or addiction before initiating opioid treatment.
4. Prior to the initial prescribing of opioid medications, health care providers should query the Oklahoma Prescription Monitoring Program (PMP).
5. When opioids are used for the treatment of chronic pain, a written treatment plan should be established that includes measurable goals for reduction of pain and improvement of function. One health care provider should coordinate a patient's comprehensive pain care plan and provide all opioid prescriptions required for the plan.

6. The patient should be informed of the risks, benefits, and terms for continuation of opioid treatment, ideally using a written and signed treatment agreement.
7. Opioids should be initiated as a short-term trial to assess the effects of opioid treatment on pain intensity, function, and quality of life. In most instances, the trial should begin with a short-acting opioid medication.
8. Regular visits for evaluation of progress toward goals should be scheduled during the period when the dose of opioids is being adjusted (titration period). During the titration period, and until the patient is clinically stable and judged to be compliant with therapy, it is recommended that the health care provider check the Oklahoma PMP more frequently.
9. Once a stable dose has been established (maintenance period), regular monitoring should be conducted at face-to-face visits during which treatment goals, analgesia, activity, adverse effects, and aberrant behaviors are monitored. The Oklahoma PMP should be queried at least once per year for patients receiving opioid treatment for chronic pain.
10. Continuing opioid treatment should be a deliberate decision that takes into consideration the risks and benefits of chronic opioid treatment for that patient. Patients and health care providers should periodically reassess the need for continued opioid treatment, weaning whenever possible, as part of the comprehensive pain care plan. A second opinion or consultation may be useful in making that decision.
11. Opioid treatment should be discontinued if adverse effects outweigh benefits or if aberrant, dangerous, or illegal behaviors are demonstrated.
12. Health care providers treating chronic pain patients with opioids should maintain records, in accordance with state and federal law, documenting patient evaluation, treatment plan, discussion of risks and benefits, informed consent, treatments prescribed, results of treatment, and any aberrant behavior observed.
13. Health care providers should consider consultation for patients with complex pain conditions, serious co-morbidities and mental illness, a history or evidence of current drug addiction or abuse, or when the provider is not confident of his/her ability to manage the treatment.
14. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.
15. The administration of intravenous and intramuscular opioids for the relief of exacerbations of chronic pain is discouraged, except in special circumstances.
16. Long-acting opioids are associated with an increased risk of overdose death, and should only be prescribed by health care providers familiar with their indications, risks, and need for careful monitoring.
17. When opioids are prescribed for treatment of chronic pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.

**Documentation of review of prescription drug monitoring data or pharmacy profile as warranted;**

- **63 O.S. 2011, 2-309D G**
- CDC Guideline for Prescribing Opioids for Chronic Pain, US, 2016 page 16, 29 and 32
- "Prevention of Opioid Abuse in Chronic Non-Cancer Pain: An Algorithmic, Evidence Based Approach", Pain Physician 2012; page 6
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, pages 1 and 2

# An Act

ENROLLED HOUSE
BILL NO. 1948

By: Cox, Morrissette and Ownbey of the House

and

Griffin of the Senate

An Act relating to public health and safety; amending 63 O.S. 2011, Section 2-304, which relates to denial, revocation and suspension of certain licenses; making references gender neutral; prohibiting director of Oklahoma State Bureau of Narcotics and Dangerous Drugs Control from assessing certain fee; amending 63 O.S. 2011, Section 2-309D, as last amended by Section 22, Chapter 293, O.S.L. 2014 (63 O.S. Supp. 2014, Section 2-309D), which relates to central repository information; expanding access to repository information to certain persons; permitting registrant access to certain information for certain purposes; requiring registrants or staff to access central repository prior to prescribing certain drugs; requiring notation of repository access; providing for exceptions; directing enforcement responsibility to certain state agencies; requiring Director of Oklahoma Bureau of Narcotics and Dangerous Drugs Control to provide monthly list; and providing an effective date.

SUBJECT: Controlled substances

BE IT ENACTED BY THE PEOPLE OF THE STATE OF OKLAHOMA:

SECTION 1. AMENDATORY 63 O.S. 2011, Section 2-304, is amended to read as follows:

Section 2-304. A. A registration, pursuant to Section 2-303 of this title, to manufacture, distribute, dispense, prescribe, administer or use for scientific purposes a controlled dangerous substance shall be limited, conditioned, denied, suspended or revoked by the Director upon a finding that the registrant:

1. Has materially falsified any application filed pursuant to ~~this act~~ the Uniform Controlled Dangerous Substances Act or required by ~~this act~~ the Uniform Controlled Dangerous Substances Act;

2. Has been found guilty of, entered a plea of guilty, or entered a plea of nolo contendere to a misdemeanor relating to any substance defined herein as a controlled dangerous substance or any felony under the laws of any state or the United States;

3. Has had his or her federal registration retired, suspended, or revoked by a competent federal authority and is no longer authorized by federal law to manufacture, distribute, dispense, prescribe, administer or use for scientific purposes controlled dangerous substances;

4. Has failed to maintain effective controls against the diversion of controlled dangerous substances to unauthorized persons or entities;

5. Has prescribed, dispensed or administered a controlled dangerous substance from schedules other than those specified in his or her state or federal registration;

6. Has had a restriction, suspension, revocation, limitation, condition, or probation placed on his or her professional license or certificate or practice as a result of a proceeding pursuant to the general statutes;

7. Is abusing or, within the past five (5) years, has abused or excessively used drugs or controlled dangerous substances;

8. Has prescribed, sold, administered, or ordered any controlled substance for an immediate family member, himself or herself; provided that this shall not apply to a medical emergency when no other doctor is available to respond to the emergency;

9. Has possessed, used, prescribed, dispensed or administered drugs or controlled dangerous substances for other than legitimate

medical or scientific purposes or for purposes outside the normal course of his or her professional practice;

10. Has been under the influence of alcohol or another intoxicating substance which adversely affected the central nervous system, vision, hearing or other sensory or motor functioning to such degree the person was impaired during the performance of his or her job; or

11. Has violated any federal law relating to any controlled substances, any provision of the Uniform Controlled Dangerous Substances Act~~, Section 2-101 et seq. of this title~~, or any rules of the Oklahoma State Bureau of Narcotics and Dangerous Drugs Control.

B. In the event the Director suspends or revokes a registration granted under Section 2-303 of this title, all controlled dangerous substances owned or possessed by the registrant pursuant to such registration at the time of denial or suspension or the effective date of the revocation order, as the case may be, may in the discretion of the Director be impounded and preserved. No disposition may be made of substances impounded and preserved until the time for taking an appeal has elapsed or until all appeals have been concluded unless a court, upon application therefor, orders the sale of perishable substances and the deposit of the proceeds of the sale with the court. Upon a revocation order becoming final, all such controlled dangerous substances shall be forfeited to the state.

C. The Drug Enforcement Administration shall promptly be notified of all orders suspending or revoking registration and all forfeitures of controlled dangerous substances.

D. In lieu of or in addition to any other remedies available to the Director, if a finding is made that a registrant has committed any act in violation of federal law relating to any controlled substance, any provision of the Uniform Controlled Dangerous Substances Act~~, Section 2-101 et seq. of this title~~, or any rules of the Oklahoma State Bureau of Narcotics and Dangerous Drugs Control, the Director is hereby authorized to assess an administrative penalty not to exceed Two Thousand Dollars ($2,000.00) for each such act. The provisions of this subsection shall not apply to violations of subsection G of Section 2-309D of this title. Nothing in this section shall be construed so as to permit the Director of the State Bureau of Narcotics and Dangerous Drugs Control to assess

administrative fines for violations of the provisions of subsection G of Section 2-309D of this title.

SECTION 2. AMENDATORY 63 O.S. 2011, Section 2-309D, as last amended by Section 22, Chapter 293, O.S.L. 2014 (63 O.S. Supp. 2014, Section 2-309D), is amended to read as follows:

Section 2-309D. A. The information collected at the central repository pursuant to the Anti-Drug Diversion Act shall be confidential and shall not be open to the public. Access to the information shall be limited to:

1. Peace officers certified pursuant to Section 3311 of Title 70 of the Oklahoma Statutes who are employed as investigative agents of the Oklahoma State Bureau of Narcotics and Dangerous Drugs Control;

2. The United States Drug Enforcement Administration Diversion Group Supervisor;

3. The executive director or chief investigator, as designated by each board, of the following state boards:

a. Board of Podiatric Medical Examiners,

b. Board of Dentistry,

c. State Board of Pharmacy,

d. State Board of Medical Licensure and Supervision,

e. State Board of Osteopathic Examiners,

f. State Board of Veterinary Medical Examiners,

g. Oklahoma Health Care Authority,

h. Department of Mental Health and Substance Abuse Services, ~~and~~

i. Board of Examiners in Optometry,

j. Board of Nursing,

k. Office of the Chief Medical Examiner, and

1. State Board of Health;

~~provided, however, that the executive director or chief investigator of each of these boards shall be limited to access to information relevant to licensees of the employing board of such executive director or chief investigator;~~

4. A multicounty grand jury properly convened pursuant to the Multicounty Grand Jury Act; ~~and~~

5. ~~The Department of Mental Health and Substance Abuse Services and the State Department of Health for statistical, research, substance abuse prevention or educational purposes provided that the consumer's confidentiality is not compromised~~ Medical practitioners employed by the United States Department of Veterans Affairs, the United States Military, or other federal agencies treating patients in this state; and

6. At the discretion of the Director of the Oklahoma State Bureau of Narcotics and Dangerous Drugs Control, medical practitioners and their staff, including those employed by the federal government in this state.

B. This section shall not prevent access, at the discretion of the Director of the Oklahoma State Bureau of Narcotics and Dangerous Drugs Control, to investigative information by peace officers and investigative agents of federal, state, county or municipal law enforcement agencies, district attorneys and the Attorney General in furtherance of criminal, civil or administrative investigations or prosecutions within their respective jurisdictions, and to registrants in furtherance of efforts to guard against the diversion of controlled dangerous substances.

C. This section shall not prevent the disclosure, at the discretion of the Director of the Oklahoma State Bureau of Narcotics and Dangerous Drugs Control, of statistical information gathered from the central repository to the general public which shall be limited to types and quantities of controlled substances dispensed and the county where dispensed.

D. This section shall not prevent the disclosure, at the discretion of the Director of the Oklahoma State Bureau of Narcotics and Dangerous Drugs Control, of prescription-monitoring-program

information to prescription-monitoring programs of other states provided a reciprocal data-sharing agreement is in place.

E. The Department of Mental Health and Substance Abuse Services and the State Department of Health may utilize the information in the central repository for statistical, research, substance abuse prevention, or educational purposes, provided that consumer confidentiality is not compromised.

F. Any unauthorized disclosure of any information collected at the central repository provided by the Anti-Drug Diversion Act shall be a misdemeanor. Violation of the provisions of this section shall be deemed willful neglect of duty and shall be grounds for removal from office.

~~F.~~ G. 1. Registrants shall have access to the central repository for the purposes of patient treatment and for determination in prescribing or screening new patients. The patient's history may be disclosed to the patient for the purposes of treatment of information at the discretion of the physician.

2. a. Prior to prescribing or authorizing for refill, if one hundred eighty (180) days have elapsed prior to the previous access and check, of opiates, synthetic opiates, semisynthetic opiates, benzodiazepine or carisoprodol to a patient of record, registrants or members of their medical or administrative staff shall be required until October 31, 2020, to access the information in the central repository to assess medical necessity and the possibility that the patient may be unlawfully obtaining prescription drugs in violation of the Uniform Controlled Dangerous Substances Act. The duty to access and check shall not alter or otherwise amend appropriate medical standards of care. The registrant or medical provider shall note in the patient file that the central repository has been checked and may maintain a copy of the information.

b. The requirements set forth in subparagraph a of this paragraph shall not apply:

(1) to medical practitioners who prescribe the controlled substances set forth in subparagraph a

of this paragraph for hospice or end-of-life care, or

(2) for a prescription of a controlled substance set forth in subparagraph a of this paragraph that is issued by a practitioner for a patient residing in a nursing facility as defined by Section 1-1902 of this title, provided that the prescription is issued to a resident of such facility.

3. Registrants shall not be liable to any person for any claim of damages as a result of accessing or failing to access the information in the central repository and no lawsuit may be predicated thereon.

~~G.~~ H. The State Board of Podiatric Examiners, the State Board of Dentistry, the State Board of Medical Licensure and Supervision, the State Board of Examiners in Optometry, the State Board of Nursing, the State Board of Osteopathic Examiners and the State Board of Veterinary Medical Examiners shall have the sole responsibility for enforcement of the provisions of subsection G of this section. Nothing in this section shall be construed so as to permit the Director of the State Bureau of Narcotics and Dangerous Drugs Control to assess administrative fines provided for in Section 2-304 of this title.

I. The Director of the Oklahoma State Bureau of Narcotics and Dangerous Drugs Control, or a designee thereof, shall provide a monthly list to the Directors of the State Board of Podiatric Examiners, the State Board of Dentistry, the State Board of Medical Licensure and Supervision, the State Board of Examiners in Optometry, the State Board of Nursing, the State Board of Osteopathic Examiners and the State Board of Veterinary Medical Examiners of the top twenty prescribers of controlled dangerous substances within their respective areas of jurisdiction. Upon discovering that a registrant is prescribing outside the limitations of his or her licensure or outside of drug registration rules or applicable state laws, the respective licensing board shall be notified by the Bureau in writing. Such notifications may be considered complaints for the purpose of investigations or other actions by the respective licensing board. Licensing boards shall have exclusive jurisdiction to take action against a licensee for a violation of subsection G of this section.

J. Information regarding fatal and nonfatal overdoses, other than statistical information as required by Section 2-106 of this title, shall be completely confidential. Access to this information shall be strictly limited to the Director of the Oklahoma State Bureau of Narcotics and Dangerous Drugs Control or designee, the Chief Medical Examiner, state agencies and boards provided in subsection A of this section, and the registrant that enters the information. Registrants shall not be liable to any person for a claim of damages for information reported pursuant to the provisions of Section 2-105 of this title.

~~H.~~ K. The Director of the Oklahoma State Bureau of Narcotics and Dangerous Drugs Control shall provide adequate means and procedures allowing access to central repository information for registrants lacking direct computer access.

L. Upon completion of an investigation in which it is determined that a death was caused by an overdose, either intentionally or unintentionally, of a controlled dangerous substance, the medical examiner shall be required to report the decedent's name and date of birth to the Oklahoma State Bureau of Narcotics and Dangerous Drugs Control. The Oklahoma State Bureau of Narcotics and Dangerous Drugs Control shall be required to maintain a database containing the classification of medical practitioners who prescribed or authorized controlled dangerous substances pursuant to this subsection.

SECTION 3. This act shall become effective November 1, 2015.

Passed the House of Representatives the 9th day of February, 2015.

_____
Presiding Officer of the House of Representatives

Passed the Senate the 31st day of March, 2015.

_____
Presiding Officer of the Senate

OFFICE OF THE GOVERNOR

Received by the Office of the Governor this _____ day of _____, 20_____, at _____ o'clock _____ M.

By: _____

Approved by the Governor of the State of Oklahoma this _____ day of _____, 20_____, at _____ o'clock _____ M.

_____
Governor of the State of Oklahoma

OFFICE OF THE SECRETARY OF STATE

Received by the Office of the Secretary of State this _____ day of _____, 20 _____, at _____ o'clock _____ M.

By: _____

**BOX 1. CDC recommendations for prescribing opioids for chronic pain outside of active cancer, palliative, and end-of-life care**

**Determining When to Initiate or Continue Opioids for Chronic Pain**

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

**Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation**

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.
7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

**Assessing Risk and Addressing Harms of Opioid Use**

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.
9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.
10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.
11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

* All recommendations are category A (apply to all patients outside of active cancer treatment, palliative care, and end-of-life care) except recommendation 10 (designated category B, with individual decision making required); see full guideline for evidence ratings.

(mostly due to illicit opiate use), and it is plausible that effectiveness would be observed when naloxone is provided in the clinical setting as well. Experts agreed that it is preferable not to initiate opioid treatment when factors that increase risk for opioid-related harms are present. Opinions diverged about the likelihood of naloxone being useful to patients and the circumstances under which it should be offered. However, most experts agreed that clinicians should consider offering naloxone when prescribing opioids to patients at increased risk for overdose, including patients with a history of overdose, patients with a history of substance use disorder, patients taking benzodiazepines with opioids (see Recommendation 11), patients at risk for returning to a high dose to which they are no longer tolerant (e.g., patients recently released from prison), and patients taking higher dosages of opioids (≥50 MME/day). Practices should provide education on overdose prevention and naloxone use to patients receiving naloxone prescriptions and to members of their households. Experts noted that naloxone co-prescribing can be facilitated by clinics or practices with resources to provide naloxone training and by collaborative practice models with pharmacists. Resources for prescribing naloxone in primary care settings can be found through Prescribe to Prevent at http://prescribetoprevent.org.

**9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months (recommendation category: A, evidence type: 4).**

PDMPs are state-based databases that collect information on controlled prescription drugs dispensed by pharmacies in most states and, in select states, by dispensing physicians as well. In addition, some clinicians employed by the federal government, including some clinicians in the Indian Health Care Delivery System, are not licensed in the states where they practice, and do not have access to PDMP data. Certain states require clinicians to review PDMP data prior to writing each opioid prescription (see state-level PDMP-related policies on the National Alliance for Model State Drug Laws website at http://www.namsdl.org/prescription-monitoring-programs.cfm). The clinical evidence review did not find studies evaluating the effectiveness of PDMPs on outcomes related to overdose, addiction, abuse, or misuse (KQ4). However, even though evidence is limited on the effectiveness of PDMP implementation at the state level on prescribing and mortality outcomes (*28*), the contextual evidence review found that most fatal overdoses were associated with patients receiving opioids from multiple prescribers and/or with patients receiving high total daily opioid dosages; information on both of these risk factors for overdose are available to prescribers in the PDMP. PDMP data also can be helpful when patient medication history is not otherwise available (e.g., for patients from other locales) and when patients transition care to a new clinician. The contextual evidence review also found that PDMP information could be used in a way that is harmful to patients. For example, it has been used to dismiss patients from clinician practices (*211*), which might adversely affect patient safety.

The contextual review found variation in state policies that affect timeliness of PDMP data (and therefore benefits of reviewing PDMP data) as well as time and workload for clinicians in accessing PDMP data. In states that permit delegating access to other members of the health care team, workload for prescribers can be reduced. These differences might result in a different balance of benefits to clinician workload in different states. Experts agreed that PDMPs are useful tools that should be consulted when starting a patient on opioid therapy and periodically during long-term opioid therapy. However, experts disagreed on how frequently clinicians should check the PDMP during long-term opioid therapy, given PDMP access issues and the lag time in reporting in some states. Most experts agreed that PDMP data should be reviewed every 3 months or more frequently during long-term opioid therapy. A minority of experts noted that, given the current burden of accessing PDMP data in some states and the lack of evidence surrounding the most effective interval for PDMP review to improve patient outcomes, annual review of PDMP data during long-term opioid therapy would be reasonable when factors that increase risk for opioid-related harms are not present.

Clinicians should review PDMP data for opioids and other controlled medications patients might have received from additional prescribers to determine whether a patient is receiving high total opioid dosages or dangerous combinations (e.g., opioids combined with benzodiazepines) that put him or her at high risk for overdose. Ideally, PDMP data should be reviewed before every opioid prescription. This is recommended in all states with well-functioning PDMPs and where PDMP access policies make this practicable (e.g., clinician and delegate access permitted), but it is not currently possible in states without functional PDMPs or in those that do not permit certain prescribers to access them. As vendors and practices facilitate integration of PDMP information into regular clinical workflow (e.g., data made available in electronic health records), clinicians' ease of access in reviewing PDMP data is expected to improve.

**whenever possible (recommendation category: A, evidence type: 3).**

Benzodiazepines and opioids both cause central nervous system depression and can decrease respiratory drive. Concurrent use is likely to put patients at greater risk for potentially fatal overdose. The clinical evidence review did not address risks of benzodiazepine co-prescription among patients prescribed opioids. However, the contextual evidence review found evidence in epidemiologic series of concurrent benzodiazepine use in large proportions of opioid-related overdose deaths, and a case-cohort study found concurrent benzodiazepine prescription with opioid prescription to be associated with a near quadrupling of risk for overdose death compared with opioid prescription alone (*212*). Experts agreed that although there are circumstances when it might be appropriate to prescribe opioids to a patient receiving benzodiazepines (e.g., severe acute pain in a patient taking long-term, stable low-dose benzodiazepine therapy), clinicians should avoid prescribing opioids and benzodiazepines concurrently whenever possible. In addition, given that other central nervous system depressants (e.g., muscle relaxants, hypnotics) can potentiate central nervous system depression associated with opioids, clinicians should consider whether benefits outweigh risks of concurrent use of these drugs. Clinicians should check the PDMP for concurrent controlled medications prescribed by other clinicians (see Recommendation 9) and should consider involving pharmacists and pain specialists as part of the management team when opioids are co-prescribed with other central nervous system depressants. Because of greater risks of benzodiazepine withdrawal relative to opioid withdrawal, and because tapering opioids can be associated with anxiety, when patients receiving both benzodiazepines and opioids require tapering to reduce risk for fatal respiratory depression, it might be safer and more practical to taper opioids first (see Recommendation 7). Clinicians should taper benzodiazepines gradually if discontinued because abrupt withdrawal can be associated with rebound anxiety, hallucinations, seizures, delirium tremens, and, in rare cases, death (contextual evidence review). A commonly used tapering schedule that has been used safely and with moderate success is a reduction of the benzodiazepine dose by 25% every 1–2 weeks (*213,214*). CBT increases tapering success rates and might be particularly helpful for patients struggling with a benzodiazepine taper (*213*). If benzodiazepines prescribed for anxiety are tapered or discontinued, or if patients receiving opioids require treatment for anxiety, evidence-based psychotherapies (e.g., CBT) and/or specific anti-depressants or other nonbenzodiazepine medications approved for anxiety should be offered. Experts emphasized that clinicians should communicate with mental health professionals managing the patient to discuss the patient's needs, prioritize patient goals, weigh risks of concurrent benzodiazepine and opioid exposure, and coordinate care.

**12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder (recommendation category: A, evidence type: 2).**

Opioid use disorder (previously classified as opioid abuse or opioid dependence) is defined in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) as a problematic pattern of opioid use leading to clinically significant impairment or distress, manifested by at least two defined criteria occurring within a year (http://pcssmat.org/wp-content/uploads/2014/02/5B-DSM-5-Opioid-Use-Disorder-Diagnostic-Criteria.pdf) (*20*).

The clinical evidence review found prevalence of opioid dependence (using DSM-IV diagnosis criteria) in primary care settings among patients with chronic pain on opioid therapy to be 3%–26% (KQ2). As found in the contextual evidence review and supported by moderate quality evidence, opioid agonist or partial agonist treatment with methadone maintenance therapy or buprenorphine has been shown to be more effective in preventing relapse among patients with opioid use disorder (*151–153*). Some studies suggest that using behavioral therapies in combination with these treatments can reduce opioid misuse and increase retention during maintenance therapy and improve compliance after detoxification (*154,155*); behavioral therapies are also recommended by clinical practice guidelines (*215*). The cited studies primarily evaluated patients with a history of illicit opioid use, rather than prescription opioid use for chronic pain. Recent studies among patients with prescription opioid dependence (based on DSM-IV criteria) have found maintenance therapy with buprenorphine and buprenorphine-naloxone effective in preventing relapse (*216,217*). Treatment need in a community is often not met by capacity to provide buprenorphine or methadone maintenance therapy (*218*), and patient cost can be a barrier to buprenorphine treatment because insurance coverage of buprenorphine for opioid use disorder is often limited (*219*). Oral or long-acting injectable formulations of naltrexone can also be used as medication-assisted treatment for opioid use disorder in nonpregnant adults, particularly for highly motivated persons (*220,221*). Experts agreed that clinicians prescribing opioids should identify treatment resources for opioid use disorder in the community and should work together to ensure sufficient treatment capacity for opioid use disorder at the practice level.

MED. Braden et al (113) found that patients (Arkansas Medicaid and HealthCore commercially insured enrollees) receiving MEDs of more than 120 mg/d are more likely to have drug-related encounters than those getting lower doses. There were no differences between these 2 groups regarding emergency department visits. Gomes et al (57) found that patients from Ontario's public drug plan receiving "very high" doses (> 400 mg MED) and "high" doses (200-400 mg MED) had a much higher overdose death than those getting "moderate" doses (< 200 mg MED). In "very high" and "high" dose patients the opioid-related mortality rates were 9.94/1,000 for "very high" and 7.92/1,000 for "high." Comparatively, the opioid-related mortality rate was 1.63/1,000 in those with "moderate" doses. Also, the overall death rate (from any cause) was much higher in patients receiving opioids (20.05/1,000) when compared to those who were not getting any opioids (4.00/1,000).

In the above 5 studies, the doses which are related to an emergency department admission for overdoses or death are 40 mg MED (104), 50 mg MED (111,112), 120 mg MED (113), and 200 mg MED (57). We did not find any study in which a higher dose did not correlate with increased mortality and only one study where there was no correlation between higher opioid dose and emergency department visits. Moreover, Paulozzi et al (15) reported that in 80% of all patients receiving opioids, the dose was less than 100 mg MED and was obtained from one physician. This patient pool constituted 20% of the overall overdose deaths. Even though only 10% of all patients were receiving a dose of greater than 100 mg MED from a single prescriber, the overdose death rate in this population was as high as 40%. Patients receiving more than 100 mg MED from multiple physicians constituted the rest of the 10%. The percentage of overdose deaths was 40% in this segment. In other words, patients receiving more than 100 mg MED (from single or multiple prescribers), contributed to 80% of all the overdose deaths, whereas patients on doses of less than 100 mg MED contributed to only 20% of the overall overdose deaths, implying that 100 mg MED is a dangerous dose. There has been a call for establishing a maximum daily dose in order to guide physicians treating patients with chronic pain (114). Based on the current available evidence presented above, defining 50 mg MED/d as a high dose does not seem unreasonable. The dose limits recommended earlier by Washington State (120 mg MED) (109) and the Canadian guideline (200 mg MED) (110) seem excessive. Defining 200 mg MED by APS and AAPM as a high dose also appears to be harmful. We agree with Katz (114) that having dose limits will provide a guide for practicing physicians, reduce harm by eliminating high doses, assist in the negotiation process between physicians and patients pressing for higher doses and finally, impel high dose prescribers to exercise more caution. We concur with Manchikanti et al (20) that commencing long-acting opioid therapy is often the starting point for high dose opioid therapy, a practice that growing evidence suggests is harmful to patients and increases the black market availability of opioids through diversion. Many argue that chronic pain is undertreated and opioids must be used more liberally. We agree that chronic pain is undertreated, but we completely disagree, based on evidence, that aggressive opioid use is the answer to alleviating undertreated chronic pain. Given our awareness of the inadequacy and adverse effects of using opioids for the treatment of chronic pain, the failure to set dose limits is irresponsible and hazardous both to the individual and to society.

## Algorithmic Approach to Prevent Opioid Abuse

Opioids play an important but limited role in treating chronic pain. The challenge for the physician is to make opioids available for those who are truly in need, and to withhold them from those who are either abusing or diverting. Although difficult, this can be achieved in most cases. If all nonopioid measures fail in alleviating pain, and if opioids are being used, the following steps would be very helpful. The 3 cornerstones for responsible prescribing are stratifying patients by using screening tools into high, medium and low risk groups; monitoring patients by using UDS, PMPs and pill counts; and lastly, establishing dose limits (Fig. 1).

Stratification of patients into different risk categories is the first step. This requires the use of existing screening tools designed specifically to screen for opioid misuse (subjective tools like SOAPP (67), PMQ (68), PUDQP (70) or objective tools like ABC checklist (71), DIRE Score (72) and the tool by Atluri and Sudarshan (73) to classify patients as high risk, medium risk and low risk. As mentioned earlier, objective tools may be better than subjective tools. Those who are categorized as "high risk" should be monitored closely by performing UDS every 3 to 6 months and PMP every 2-4 months. Opioids should be either avoided or prescribed in low doses. Doses of more than 50 mg MED should be very rarely used and only under specialized settings in conjunction, when available, with addiction specialists. Pa-

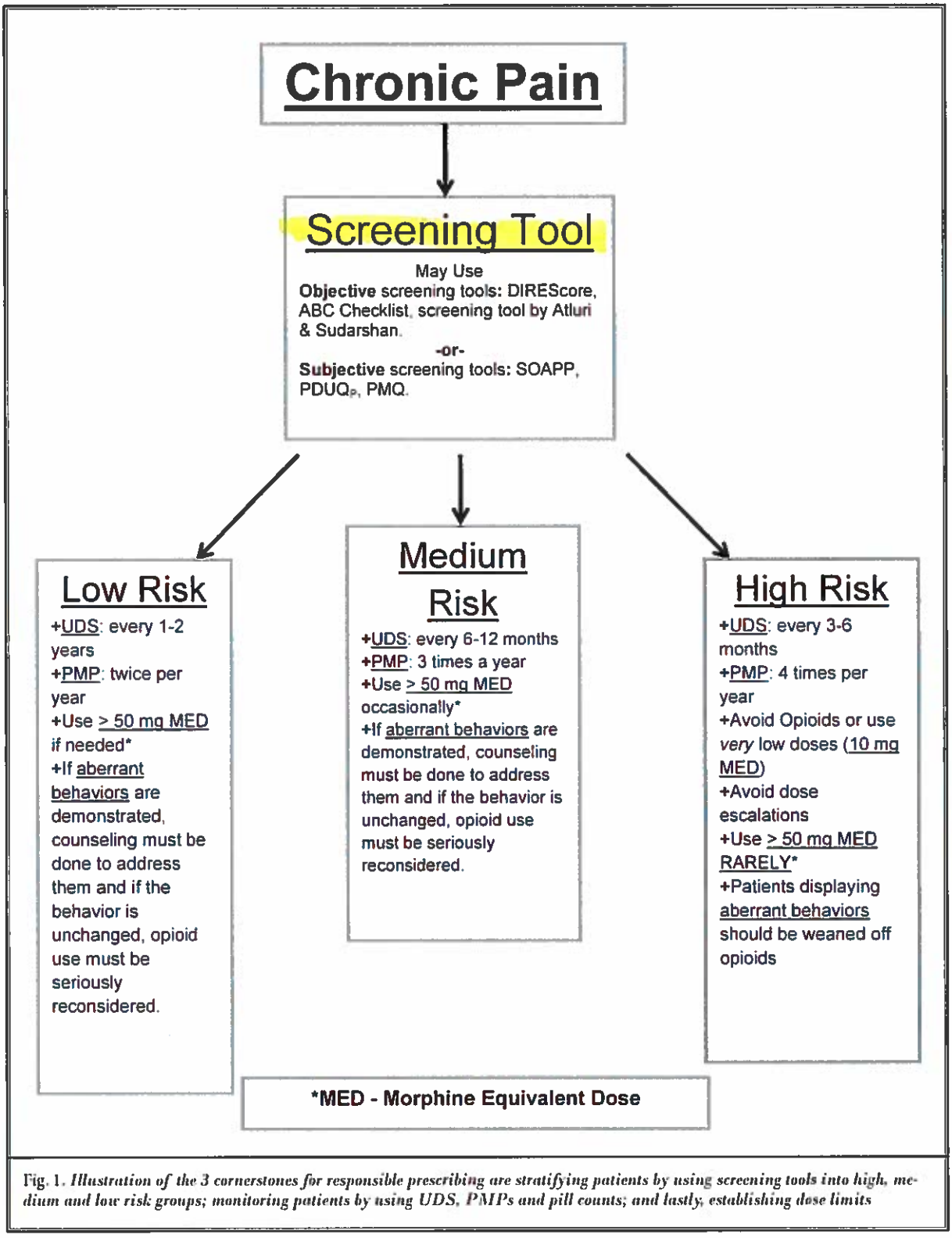


*Fig. 1. Illustration of the 3 cornerstones for responsible prescribing are stratifying patients by using screening tools into high, medium and low risk groups; monitoring patients by using UDS, PMPs and pill counts; and lastly, establishing dose limits*

## Prescription Monitoring Programs

Prescription monitoring programs (PMPs) serve as a means of data collection for opioid prescriptions, providing physicians with information about who wrote the prescriptions and the pharmacies that dispensed them. Physicians have access to this data to check if patients are getting opioid prescriptions from more than one physician at the same time. This information becomes extremely useful especially if the patient signs an opioid contract agreeing to obtain the prescription from only one physician and to fill it in only one pharmacy. Currently, there are 38 states with this program (66). A national program would be invaluable in curbing abuse and doctor shopping (100). The National All Schedule Prescription Electronic Reporting Act (NASPER) was enacted by Congress in 2005 but has not yet been fully implemented (101). Calls for immediate funding and rapid implementation of NASPER have been made. This law requires states to collect prescription information for Schedule II, III, and IV medications. It also requires states to have the capability to share this information with one another. This would potentially decrease cross-border opioid trafficking and would be invaluable in curbing abuse and doctor shopping (15,102,103). Paulozzi et al's study (104) recommends using PMP to curb overuse, noting that the rate of overdose deaths is higher in those who use multiple pharmacies and doctors. This assertion is also expressed by White et al (105). In one study, 21% of overdose deaths resulted from doctor shopping (106). In response to the epidemic of prescription drug abuse, the White House Office of National Drug Control Policy issued a document in which it recommended enhanced use of prescription drug monitoring programs (106). The National Alliance for Model State Drug Laws indicates that these databases foster the legitimate medical use of controlled substances while limiting drug abuse and diversion (102). Access to PMP can help clinicians curb diversion and abuse and to decrease the number of unnecessary prescriptions while still providing analgesia to those who need it (102). Manchikanti et al (107) have recently shown that the Kentucky's PMP, KASPER (Kentucky All Schedule Prescription Electronic Reporting Program) has led to a decrease in doctor shopping from 18% in 2001 to 2.1% in 2011. Baehren et al (108) showed that in an emergency department setting, the use of PMP positively influenced the opioid prescribing pattern. Based on the PMP results, 61% of their study patients were prescribed less opioid medication than originally planned, whereas 39% received more opioid medication than previously planned. Paulozzi et al (109) reported that PMPs were not significantly associated with lower rates of drug overdose or opioid overdose mortality or lower rates of consumption of opioid drugs. An accompanying editorial (110) clarified that the lack of impact of PMPs is due to their underutilization.

## A Case for Dose Limitation

The evidence in favor of long-term opioid use for chronic pain is at best problematic. Considering the irrefutable evidence showing widespread abuse and diversion, the rationale for high dose opioids should be reexamined. Patients who do not respond to a low/medium dose of opioids generally would not find their pain alleviated by larger doses. In 2007, the state of Washington issued guidelines that in general, the daily dose should not exceed 120 mg of MED (87). The guidelines by APS and AAPM in 2009 defined high dose as 200 mg MED (27). The Canadian guidelines in 2010 identified 200 mg MED as a watchful dose (88). Until recently, however, there was only limited data verifying the safety of these recommended doses, especially in high risk patients. Five recent studies showed that the rate of overdose was directly proportional to the prescribed opioid dose (57,104,111-113). Bohnert et al's study (111) in a national sample of Veterans Health Administration patients revealed that there was a dose-response relationship between the maximum daily prescribed dose of opioid and the risk of opioid overdose death. The overdose death rate for patients receiving a dose of less than 20 mg MED was 0.11 per 1,000 compared to those getting more than 100 mg MED, for whom the death rate was 1.24/1,000. This difference was even higher in those with a history of substance abuse (0.54 versus 2.97). Since the death rates were higher in patients receiving doses of 50 mg MED versus those getting less than 50 mg MED, the authors concluded that that the risk of opioid overdose increased when the opioid dose was equivalent to 50 mg MED.

Dunn et al (112) reported that in a population from a health maintenance organization in Washington State , there was a 9-fold increase in opioid overdose in patients receiving high dose opioids (more than 100 mg MED) to those getting low dose (less than 20 mg). There was a 3.7-fold increase in overdose events in patients receiving doses between 50-99 mg MED versus those getting less than 20 mg MED. Paulozzi et al (104) found that compared to patients receiving lower opioid doses or no opioid prescriptions, the risk of overdose was greatest at daily opioid doses above 40 mg

# Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting

*Note: These guidelines do not replace clinical judgment in the appropriate care of patients. They are not intended as standards of care or as templates for legislation, nor are they meant for patients in palliative care programs or with cancer pain. The recommendations are an educational tool based on the expert opinion of numerous physicians and other health care providers, medical/nursing boards, mental and public health officials, and law enforcement personnel in Oklahoma and throughout the United States. The guidelines are available at* http://poison.health.ok.gov.

## Opioid Treatment for Acute Pain

1. Opioids should only be used for treatment of acute pain when the severity of the pain warrants that choice and after determining that other non-opioid pain medications or therapies will not provide adequate pain relief.
2. Providers should query the Oklahoma Prescription Monitoring Program (PMP) for patients presenting with acute pain, prior to prescribing an opioid medication. In circumstances where a patient's pain is resulting from an objectively diagnosed disease process or injury, a provider may prudently opt not to review the Oklahoma PMP.
3. When opioids are prescribed for treatment of acute pain, the number of doses dispensed should be no more than the number of doses needed based on the usual duration of pain severe enough to require opioids for that condition.
4. When opioids are prescribed for treatment of acute pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.
5. Long duration-of-action opioids (e.g., methadone, buprenorphine, fentanyl, extended release oxycodone, and morphine) are rarely indicated for treatment of acute pain.
6. The use of opioids should be re-evaluated carefully, including assessing the potential for abuse, if persistent pain suggests the need to continue opioids beyond the anticipated time period of acute pain treatment for that condition. Health care providers should query the Oklahoma PMP as part of this re-evaluation process.
7. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.

## Opioid Treatment for Chronic Pain

1. Alternatives to opioid treatment should be tried, or previous attempts documented, before initiating opioid treatment.
2. A comprehensive evaluation should be performed before initiating opioid treatment for chronic pain. For chronic pain patients transferring their care to new health care providers, new opioid prescriptions should generally not be written until the previous provider's records have been reviewed or the previous health care provider has been notified of the transfer of care.
3. The health care provider should screen for risk of abuse or addiction before initiating opioid treatment.
4. Prior to the initial prescribing of opioid medications, health care providers should query the Oklahoma Prescription Monitoring Program (PMP).
5. When opioids are used for the treatment of chronic pain, a written treatment plan should be established that includes measurable goals for reduction of pain and improvement of function. One health care provider should coordinate a patient's comprehensive pain care plan and provide all opioid prescriptions required for the plan.

6. The patient should be informed of the risks, benefits, and terms for continuation of opioid treatment, ideally using a written and signed treatment agreement.
7. Opioids should be initiated as a short-term trial to assess the effects of opioid treatment on pain intensity, function, and quality of life. In most instances, the trial should begin with a short-acting opioid medication.
8. Regular visits for evaluation of progress toward goals should be scheduled during the period when the dose of opioids is being adjusted (titration period). During the titration period, and until the patient is clinically stable and judged to be compliant with therapy, it is recommended that the health care provider check the Oklahoma PMP more frequently.
9. Once a stable dose has been established (maintenance period), regular monitoring should be conducted at face-to-face visits during which treatment goals, analgesia, activity, adverse effects, and aberrant behaviors are monitored. The Oklahoma PMP should be queried at least once per year for patients receiving opioid treatment for chronic pain.
10. Continuing opioid treatment should be a deliberate decision that takes into consideration the risks and benefits of chronic opioid treatment for that patient. Patients and health care providers should periodically reassess the need for continued opioid treatment, weaning whenever possible, as part of the comprehensive pain care plan. A second opinion or consultation may be useful in making that decision.
11. Opioid treatment should be discontinued if adverse effects outweigh benefits or if aberrant, dangerous, or illegal behaviors are demonstrated.
12. Health care providers treating chronic pain patients with opioids should maintain records, in accordance with state and federal law, documenting patient evaluation, treatment plan, discussion of risks and benefits, informed consent, treatments prescribed, results of treatment, and any aberrant behavior observed.
13. Health care providers should consider consultation for patients with complex pain conditions, serious co-morbidities and mental illness, a history or evidence of current drug addiction or abuse, or when the provider is not confident of his/her ability to manage the treatment.
14. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.
15. The administration of intravenous and intramuscular opioids for the relief of exacerbations of chronic pain is discouraged, except in special circumstances.
16. Long-acting opioids are associated with an increased risk of overdose death, and should only be prescribed by health care providers familiar with their indications, risks, and need for careful monitoring.
17. When opioids are prescribed for treatment of chronic pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.

**Office/provider monitoring protocols, such as random pill counts, etc.**

- **Oklahoma Administrative Code 435:10-7-11 (6I)( 6J)**
- "Prevention of Opioid Abuse in Chronic Non-Cancer Pain: An Algorithmic, Evidence Based Approach", Pain Physician 2012; pages 7 and 8
- "Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting", Oklahoma Medical Board, October 2013, pages 10 and 16

(6) **Medical records.** Records should remain current and be maintained in an accessible manner, readily available for review. The physician should keep accurate and complete records to include:

(A) the medical history and physical examination (including vital signs),
(B) diagnostic, therapeutic and laboratory results,
(C) evaluations, consultations and follow-up evaluations,
(D) treatment objectives,
(E) discussion of risks and benefits,
(F) informed consent,
(G) treatments,
(H) medications (including date, type, dosage and quantity prescribed),
(I) instructions and agreements and
(J) periodic reviews.

(7) **Compliance with controlled substances laws and regulations.** To prescribe, dispense or administer controlled substances, the physician must be licensed in Oklahoma and comply with applicable federal and state regulations. Physicians are referred to the Physicians Manual of the U.S. Drug Enforcement Administration for specific rules governing controlled substances as well as applicable state regulations.

[Source: Amended at 16 Ok Reg 2003, eff 6-14-99; Added at 22 Ok Reg 2096, eff 6-25-05]

MED. Braden et al (113) found that patients (Arkansas Medicaid and HealthCore commercially insured enrollees) receiving MEDs of more than 120 mg/d are more likely to have drug-related encounters than those getting lower doses. There were no differences between these 2 groups regarding emergency department visits. Gomes et al (57) found that patients from Ontario's public drug plan receiving "very high" doses (> 400 mg MED) and "high" doses (200-400 mg MED) had a much higher overdose death than those getting "moderate" doses (< 200 mg MED). In "very high" and "high" dose patients the opioid-related mortality rates were 9.94/1,000 for "very high" and 7.92/1,000 for "high." Comparatively, the opioid-related mortality rate was 1.63/1,000 in those with "moderate" doses. Also, the overall death rate (from any cause) was much higher in patients receiving opioids (20.05/1,000) when compared to those who were not getting any opioids (4.00/1,000).

In the above 5 studies, the doses which are related to an emergency department admission for overdoses or death are 40 mg MED (104), 50 mg MED (111,112), 120 mg MED (113), and 200 mg MED (57). We did not find any study in which a higher dose did not correlate with increased mortality and only one study where there was no correlation between higher opioid dose and emergency department visits. Moreover, Paulozzi et al (15) reported that in 80% of all patients receiving opioids, the dose was less than 100 mg MED and was obtained from one physician. This patient pool constituted 20% of the overall overdose deaths. Even though only 10% of all patients were receiving a dose of greater than 100 mg MED from a single prescriber, the overdose death rate in this population was as high as 40%. Patients receiving more than 100 mg MED from multiple physicians constituted the rest of the 10%. The percentage of overdose deaths was 40% in this segment. In other words, patients receiving more than 100 mg MED (from single or multiple prescribers), contributed to 80% of all the overdose deaths, whereas patients on doses of less than 100 mg MED contributed to only 20% of the overall overdose deaths, implying that 100 mg MED is a dangerous dose. There has been a call for establishing a maximum daily dose in order to guide physicians treating patients with chronic pain (114). Based on the current available evidence presented above, defining 50 mg MED/d as a high dose does not seem unreasonable. The dose limits recommended earlier by Washington State (120 mg MED) (109) and the Canadian guideline (200 mg MED) (110) seem excessive. Defining 200 mg MED by APS and AAPM as a high dose also appears to be harmful. We agree with Katz (114) that having dose limits will provide a guide for practicing physicians, reduce harm by eliminating high doses, assist in the negotiation process between physicians and patients pressing for higher doses and finally, impel high dose prescribers to exercise more caution. We concur with Manchikanti et al (20) that commencing long-acting opioid therapy is often the starting point for high dose opioid therapy, a practice that growing evidence suggests is harmful to patients and increases the black market availability of opioids through diversion. Many argue that chronic pain is undertreated and opioids must be used more liberally. We agree that chronic pain is undertreated, but we completely disagree, based on evidence, that aggressive opioid use is the answer to alleviating undertreated chronic pain. Given our awareness of the inadequacy and adverse effects of using opioids for the treatment of chronic pain, the failure to set dose limits is irresponsible and hazardous both to the individual and to society.

## Algorithmic Approach to Prevent Opioid Abuse

Opioids play an important but limited role in treating chronic pain. The challenge for the physician is to make opioids available for those who are truly in need, and to withhold them from those who are either abusing or diverting. Although difficult, this can be achieved in most cases. If all nonopioid measures fail in alleviating pain, and if opioids are being used, the following steps would be very helpful. The 3 cornerstones for responsible prescribing are stratifying patients by using screening tools into high, medium and low risk groups; monitoring patients by using UDS, PMPs and pill counts; and lastly, establishing dose limits (Fig. 1).

Stratification of patients into different risk categories is the first step. This requires the use of existing screening tools designed specifically to screen for opioid misuse (subjective tools like SOAPP (67), PMQ (68), PUDQP (70) or objective tools like ABC checklist (71), DIRE Score (72) and the tool by Atluri and Sudarshan (73) to classify patients as high risk, medium risk and low risk. As mentioned earlier, objective tools may be better than subjective tools. Those who are categorized as "high risk" should be monitored closely by performing UDS every 3 to 6 months and PMP every 2-4 months. Opioids should be either avoided or prescribed in low doses. Doses of more than 50 mg MED should be very rarely used and only under specialized settings in conjunction, when available, with addiction specialists. Pa-

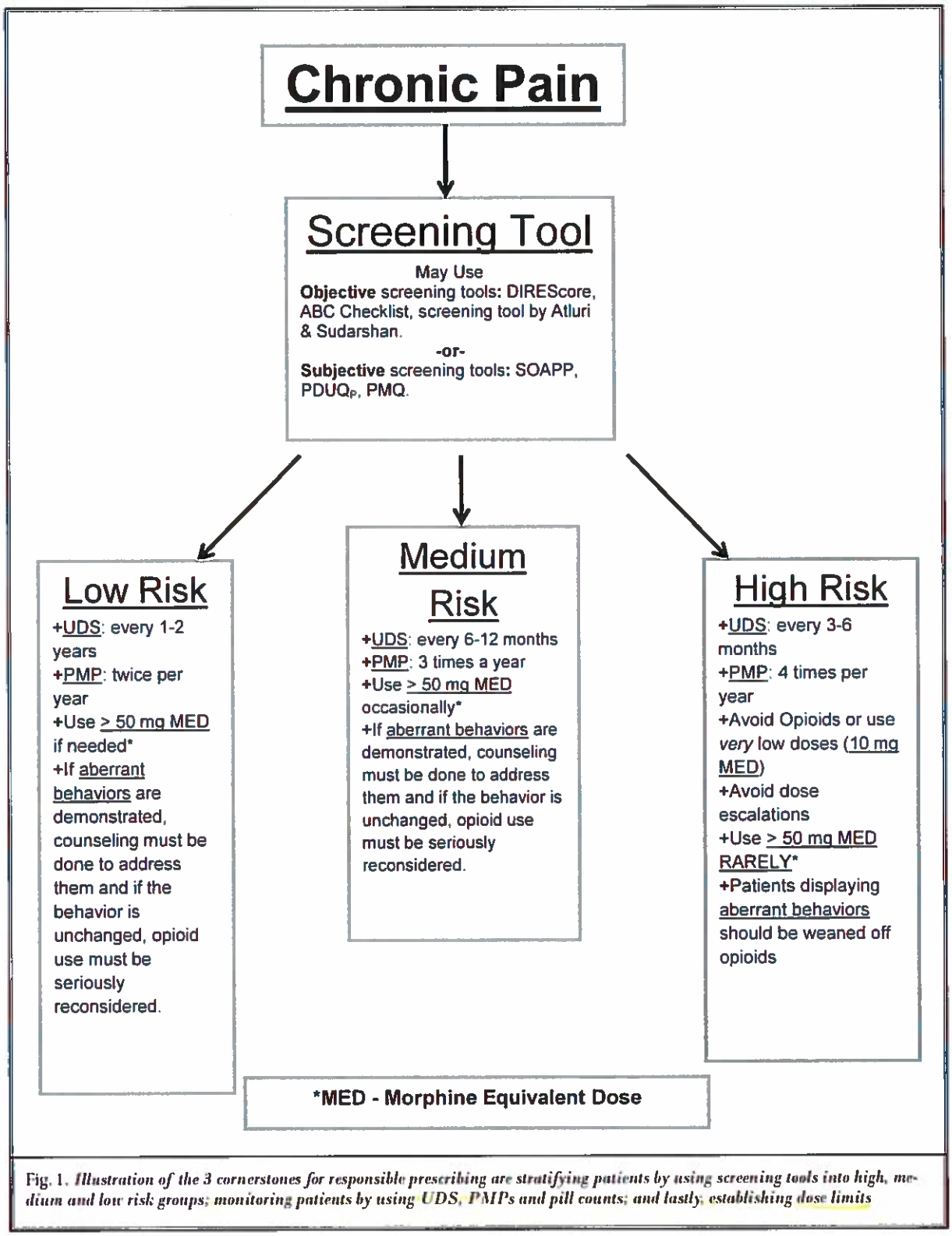


Fig. 1. *Illustration of the 3 cornerstones for responsible prescribing are stratifying patients by using screening tools into high, medium and low risk groups; monitoring patients by using UDS, PMPs and pill counts; and lastly, establishing dose limits*

present, or if other concerns arise during treatment:

- The patient has a complex pain condition and the clinician wishes verification of diagnosis;
- The patient has significant co-morbidities, including psychiatric illness;
- The patient is at high risk of aberrant behavior or addiction; or
- The clinician suspects the development of significant tolerance, particularly at higher doses.

The main goal of a consultation is for the prescribing clinician to receive recommendations for ongoing treatment.

**13.2** Patients with a history of addiction or substance use disorder or who have positive drug screens indicative of a problem should be closely monitored (e.g., more frequent random drug screens, random pill counts) or considered for referral to an addiction specialist for evaluation of recurrent risk and for assistance with treatment.[9,13,14]

Although this is a desirable approach, it is recognized that following this recommendation may not be feasible in parts of Oklahoma where there is a shortage of readily available addiction specialists.

**13.3** Pain patients addicted to medications/drugs should be referred to a pain management and/or mental health/substance use disorder specialist, if available, for recommendations on the treatment plan and assistance in management.

The health care provider may consider prescribing opioid medications for pain even if the patient has a self-reported or documented previous opioid abuse problem, as long as monitoring is performed during the titration and maintenance phase.

**13.4** Patients with a coexisting psychiatric disorder should receive ongoing mental health support and treatment while receiving an opioid medication for pain control.

Management of patients with a coexisting psychiatric condition may require extra care, monitoring, or documentation.[17,19] Consultation can be obtained to assist in formulating the treatment plan and establishing a plan for coordinated care of both the chronic pain and psychiatric condition(s).

Tools to accompany *Recommendation 13:*

- Strategies for Tapering and Weaning
  http://health.utah.gov/prescription/pdf/guidelines/Strategies_tapering_weaning.pdf

### 14. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.

Patients misusing controlled substances frequently report their opioid medications as having been lost or stolen. Pain specialists routinely stipulate in pain agreements with patients that lost or stolen controlled substances will not be replaced. Most written agreements between chronic pain patients and pain management physicians, including the Health Resources and Services Administration (HRSA) toolkit sample pain agreement, state that prescriptions for opioids will not be replaced.[10]

The diversion of prescribed opioids is common. One study looked at completed patient surveys and determined that 45% of respondents reported some form of drug diversion at least once. Stolen medication was the most prevalent method of drug diversion, and 30% of respondents reported at least one incident of stolen medication.[11] Another survey study found that among persons 12 years and older who abused opioid pain medications (2009-2010), 71.2% came from friends or relatives; 55% were given to the abuser, while 11.4% were purchased, and 4.8% were stolen.[12,13]

### 15. The administration of intravenous and intramuscular opioids for the relief of exacerbations of chronic pain is discouraged, except in special circumstances.

family members, and under what conditions discussions about the patient with others are allowed.

**6.3** The treatment plan, which defines the responsibilities of both the patient and health care provider, should be documented.[6,9,13,14,15]

Patient responsibilities include properly obtaining, filling, and using prescriptions, and adherence to the treatment plan. Patient responsibilities also include instructions to keep a pain diary, a diary or log of daily activities and accomplishments, and/or instructions on how and when to give feedback to the prescriber.[14]

The prescribing health care provider may consider requiring that the treatment plan be documented in the form of a treatment agreement signed by the patient. Patients should be encouraged to store opioid medications in a secure location to keep the medication away from others who should not have access to them.

**6.4** The treatment plan should contain goals of treatment, guidelines for prescription refills, agreement to submit to urine or serum screening upon request, and reasons for possible discontinuation of drug therapy.[9,13,14,15,17]

The treatment plan (sometimes referred to as a treatment agreement) should contain the items developed jointly by the patient and health care provider, such as follow-up appointments, the pharmacy and health care provider to be used, as well as any non-negotiable demands or limitations the health care provider wishes to make, such as the prohibition of sharing or trading the medication or getting refills early. Specific grounds for immediate termination of the agreement and cessation of prescribing may also be specified, such as forgery or selling of prescriptions or medications or obtaining them from multiple providers as documented by Oklahoma's Prescription Monitoring Program.[14,20]

Optional inclusions in the agreement:

- Pill counts may be required as a means to gauge proper medication use;[14,19]
- Prohibition of use with alcohol or certain other medications;[14]
- Documentation of counseling regarding driving or operating heavy machinery; and[6,14]
- Specific frequencies of urine testing.

Ideally, the patient should be receiving prescriptions from one prescriber only and filling those prescriptions at one pharmacy only.[14,17,19]

It is not necessary to include specific consequences for specific non-compliant behaviors, but it should be documented in the treatment agreement that continuing failure by the patient to adhere to the treatment plan will result in escalating consequences, up to and including termination of the clinician-patient relationship and of opioid prescribing by that clinician.

**6.5** Discuss involvement of family members in the patient's care and request that the patient give written permission to talk with family members about the patient's care.

This is best done before starting to treat the patient because it can be more difficult to obtain consent after an issue occurs. Prior to initiating treatment with opioids, the health care provider may want to consider a family conference to help assess the patient's integrity.[19] Consultation with others, however, must be done within the constraints of HIPAA, as noted above. (See *Recommendation 6.2.*)

Tools to accompany *Recommendation 6:*

- Absolute Contraindications to Opioid Prescribing
  http://health.utah.gov/prescription/pdf/guidelines/absolute_contraindications.pdf
- Sample Treatment Plan for Prescribing Opioids
  http://health.utah.gov/prescription/pdf/guidelines/treatment_plan.pdf
- Signs of Substance Misuse
  http://health.utah.gov/prescription/pdf/guidelines/signs_substance_misuse.pdf
- Guidance on HIPAA

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Diagnostic Accuracy Report

# Comparative Evaluation of the Accuracy of Immunoassay with Liquid Chromatography Tandem Mass Spectrometry (LC/MS/MS) of Urine Drug Testing (UDT) Opioids and Illicit Drugs in Chronic Pain Patients

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**Background:** The challenge for physicians in treating chronic pain with opioids is to eliminate or significantly curtail abuse of controlled prescription drugs while assuring proper treatment when indicated. Urine drug testing (UDT) has been shown to be a useful approach in identifying patterns of compliance, misuse, and abuse. However, significant controversy surrounds the diagnostic accuracy of UDT performed in the office (immunoassay) and the requirement for laboratory confirmation with liquid chromatography tandem mass spectrometry (LC/MS/MS).

**Study Design:** A diagnostic accuracy study of urine drug testing.

**Study Setting:** The study was performed in an interventional pain management practice, a tertiary referral center, in the United States.

**Objective:** The objective of this study was to compare the results of UDT of immunoassay in-office testing (index test) to LC/MS/MS (reference test).

**Methods:** One-thousand participants were recruited from an interventional pain management program. Urine sample was collected from all the consecutive patients with demographic information. Immunoassay testing was performed by a nurse at the location, laboratory assessment was performed with LC/MS/MS.

Results of the index test were compared to the reference test in all patients. The sensitivity, specificity, false-positive, and false-negative rates, and index test efficiency (agreement) were calculated.

**Results:** Overall, results showed that confirmation was required in 32.9% of the specimens. Agreement for prescribed opioids was high with the index test (80.4%). The reference test of opioids improved the accuracy by 8.9% from 80.4% to 89.3%. Non-prescribed opioids were used by 5.3% of patients. The index test provided false-positive results for non-opioid use in 44% or 83 of 120 patients.

For illicit drugs, the false-positive rate by index test was 0% for cocaine, whereas it was 2% for marijuana, 0.9% for amphetamines, and 1.2% for methamphetamines.

**Limitations:** The limitations include a single site study utilizing a single POC kit and a single laboratory, as well as technical sponsorship.

**Conclusion:** The UDT with immunoassay in an office setting is appropriate, convenient, and cost-effective. Compared with laboratory testing for opioids and illicit drugs, immunoassay in-office testing had high specificity and agreement, demonstrating the value of immunoassay drug testing. Because of variable sensitivity, clinicians would be well-advised to take a cautious approach when interpreting the results.

**Key words:** Controlled substances, opioids, illicit drugs, abuse, liquid chromatography tandem mass spectrometry, immunoassay, urine drug testing

**CLINICAL TRIAL:** NCT01052155

**Pain Physician 2011; 14:175-187**

The treatment of chronic pain, escalating therapeutic opioid use and abuse, and the non-medical use of prescription drugs have been topics of intense focus and debate (1-7). The present state of affairs is based on prescriptions for chronic non-cancer pain; subjective complaints of pain; recommendations from federal, state, and local governments; professional associations; massive sales promotion activities from the pharmaceutical companies; accreditation agencies; physicians promoting opioid therapy; and finally the public-at-large expecting pain relief at any cost, rather than scientific data on efficacy and safety (1,5-9). Similar states of affairs have been described in other countries including Denmark (9). However, Americans, constituting only 4.6% of the world's population, have been consuming 80% of the global opioid supply, and 99% of the global hydrocodone supply, in addition to two-thirds of the world's illegal drugs (1,2,6,7,10,11).

Retail sales of some commonly used opioid medications have increased significantly, with an increase of 866% for oxycodone and 1,293% for methadone, whereas average sales of opioids per person have increased 402% from 1997 to 2007 (1). In addition, surveys of non-prescription drug abuse (12), emergency department visits involving prescription-controlled drugs (13), unintentional deaths due to prescription controlled substances (5,14-17), therapeutic use of opioids (1,9,18-23), lack of improvement or deterioration in functional status (9,21,24-29), adverse effects (24-27,30), and opioid abuse (1-5,31-33) illustrate grave statistics. At the same time, chronic pain's prevalence and its associated disability continue to increase (34,35), while the scientific evidence for the effectiveness of opioids for chronic non-cancer pain remains unclear (5,24-27).

The challenge is to eliminate or significantly curtail abuse of controlled prescription drugs while still assuring the proper treatment of those patients with evident indications. Adherence monitoring, including urine drug testing (UDT), has been shown to be a useful approach to assist in identifying and/or predicting patterns of drug use, compliance, misuse, and abuse (36). UDT provides relatively good specificity, sensitivity, ease of administration, and cost (36). However, controversies also exist regarding the clinical value of UDT, partly because most current methods are designed for, or adapted from, forensic or occupational deterrent-based testing for illicit drug use and are not entirely optimal for application in chronic pain management settings. Further, additional issues also exist related to excessive use, misuse, abuse, and financial incentives (36-45). UDT is performed to detect the presence of prescribed medications (i.e., compliance testing) and to identify substances that are not expected to be present in the urine, such as non-prescription or illicit drugs (i.e., forensic testing). The most commonly used Current Procedural Terminology (CPT) codes for UDT, 80101 and 80102, showed 343% and 364% increases from 2004 to 2007 and an increase in allowed charges of 452% and 387%; the total allowed charges exceeded $50 million in 2007.45 The abuses related to the utilization of UDT, its value and validity, and exploding costs, led the Centers for Medicare and Medicaid (CMS) administration to impose new regulations for UDT reimbursement (37-45).

Debate surrounds the validity of in-office UDT of chronic pain patients by immunoassay methodology that has not been validated with liquid chromatography tandem mass spectrometry (LC/MS/MS). Due to multiple methodological issues, an in-office immunoassay confirmed by an independent laboratory is commonly regarded as the best and most sensitive UDT, but at the expense of escalating costs. Other issues involved are the knowledge of the physician who interprets the drug screening (including having knowledge about opioid metabolites), appropriate testing methods in an office setting, and the cost involved (37,40,41,45).

UDT manufacturers focus their marketing efforts on the value and validity of laboratory testing, and are supported by physicians who derive significant income from these tests (37,44,46,47). Others recommend in-office testing for the reasons of convenience and cost effectiveness. The absence of prescription opioids in urine specimens has ranged from 1.9% to 15% (37,44-46). Further, studies also showed an overall presence of illicit drugs in approximately 11% (37) and false-negatives of 50% for cocaine, 11% for marijuana, and 9.3% for amphetamines.

Consequently, this diagnostic accuracy study has been undertaken to evaluate the accuracy of point of care (POC) or in-office UDT (immunoassay) of chronic pain patients in a prospective analysis of LC/MS/MS.

## Methods

The study was undertaken in an interventional pain management practice, a tertiary referral center, in the United States. The protocol was approved by the Institutional Review Board (IRB) of the Ambulatory Surgery Center and it has a clinical trial registration of NCT01052155. Appropriate precautions were taken to protect the privacy and identify of patients evaluated from this study in accordance with current Health Insurance Portability and Accountability Act (HIPAA) regulations.

The protocol has been described in a previous publication (36). The study was performed utilizing the Standards for Reporting of Diagnostic Accuracy Studies (STARD) established for reporting guidelines for diagnostic accuracy studies to improve the quality of reporting (48-50).

## Objective

The objective of this study was to compare results of UDT of immunoassay in-office testing (index test) with LC/MS/MS (reference test).

## Proposed Hypothesis

It is proposed that there is no significant difference of clinical importance between POC drug testing (index test) and laboratory drug testing (reference test).

## Investigational Methodology

The investigational methodology followed the STARD checklist (48). All specimens were tested with immunoassay (index test) and LC/MS/MS (reference test).

## Participants and Recruitment

Consecutive series of patients presenting for interventional pain management were recruited in a prospective manner.

## Inclusion and Exclusion Criteria

Consecutive patients in chronic pain management were included. There were no exclusion criteria.

## Test Methods

The index test was the in-house POC office drug testing with immunoassay; the reference standard was LC/MS/MS.

The laboratory test (reference test) was performed by Millennium Laboratories, which holds certificates for moderate and high complexity testing.

## Screening Evaluation

All consecutive patients participating in the urine drug assessments diagnostic accuracy study were provided with a verbal explanation of the study. IRB-approved written informed consent to participate in the study was obtained.

Demographic details including date of birth, sex, weight, height, and drug profiles (which included a list of all prescription and over-the-counter drugs, as well as all other drugs or substances they were taking) were obtained.

## Treatment Number Assignment

Participants were consecutively assigned a number.

## Urine Sample

Urine and all other appropriate information were collected by a nurse participating in the study and provided to the study coordinator. POC testing was performed by a different nurse who was unaware of the patient's name, drug intake, etc. Drug testing was performed for opioids and illicit drugs including marijuana, cocaine, amphetamine, and methamphetamine.

## Laboratory Assessment

After immunoassay, the samples were sent to laboratory for LC/MS/MS without any identifying information or results of the index text.

## Definition and Rationale

The definition and rationale for the units, cutoffs, and categories of the results of the index test and how reference standard have been described (36).

## Personnel

A sufficient number of nurses (6) received training to conduct and read the index test. The reference test was conducted by trained certified professionals at the laboratory.

## Blinding

The personnel performing and reading the index tests and reference tests were blinded (masked) to the results of the other tests as well as patient demographics.

## Statistical Methods

### *Sample Size*

Sample size calculation was carried out for our primary outcome (accuracy of the POC drug testing in screening for opioids and illicit drugs) according to the previously published method (51), and previous results of drug abuse and illicit drug use by patients referred to clinics (31-33,52). The details are provided in the protocol (36). The sample size was calculated at 811 with a planned enrollment of 1,000 patients to be tested.

### *Analysis*

Statistical analysis was performed using SPSS 9.01 (SPSS, Inc., Chicago IL, USA). A P value below 0.05 was considered statistically significant.

Results of the index test were compared to the reference test in all patients. The sensitivity, specificity, false-positive and false-negative rates, and index test efficiency (agreement) were calculated.

## Results

### Flow Diagram

Figures 1 and 2 illustrate the patient flow diagram per STARD for opioids and illicit drugs.

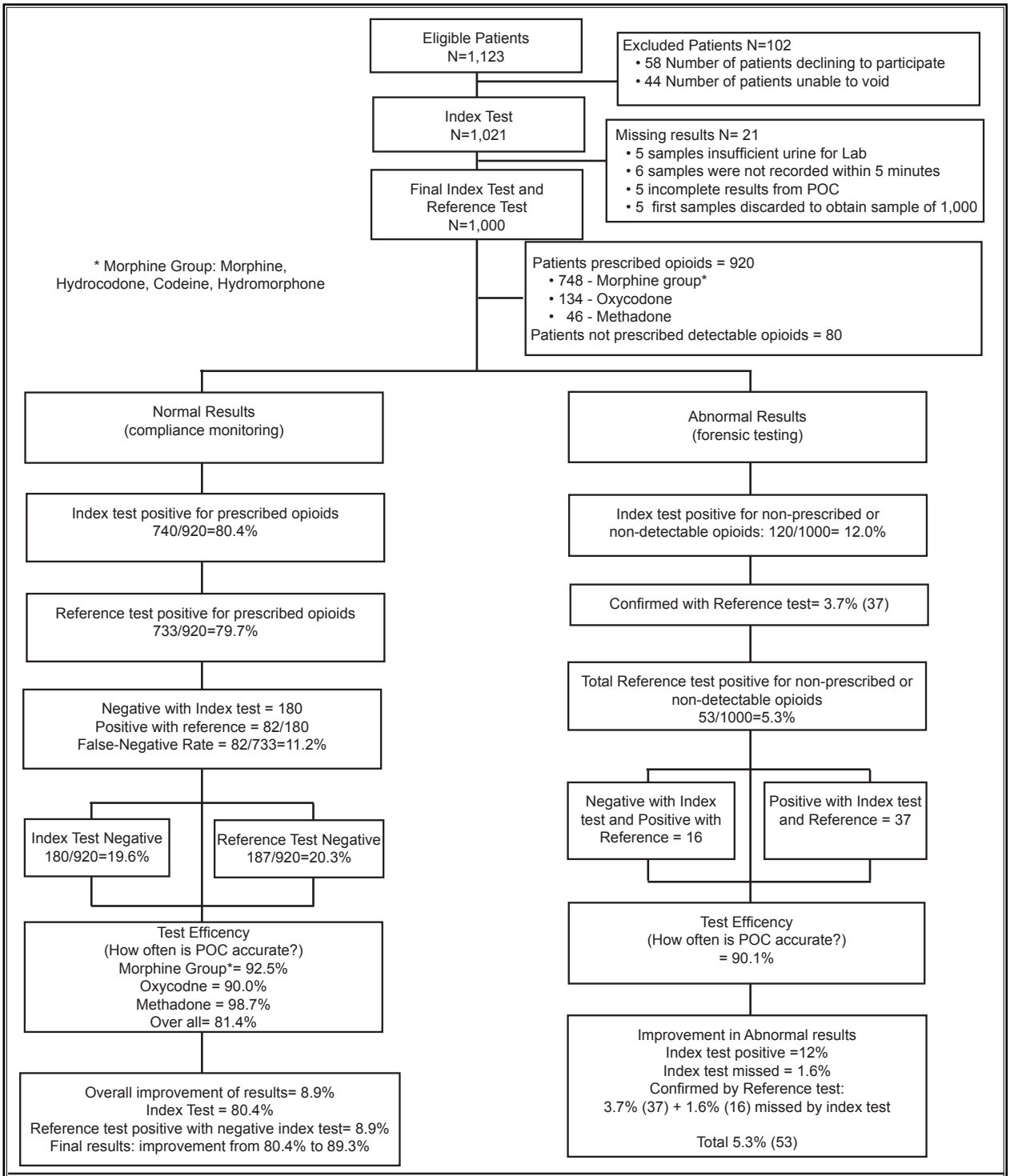


Fig. 1. *Flow diagram of diagnostic accuracy testing of opioids.*

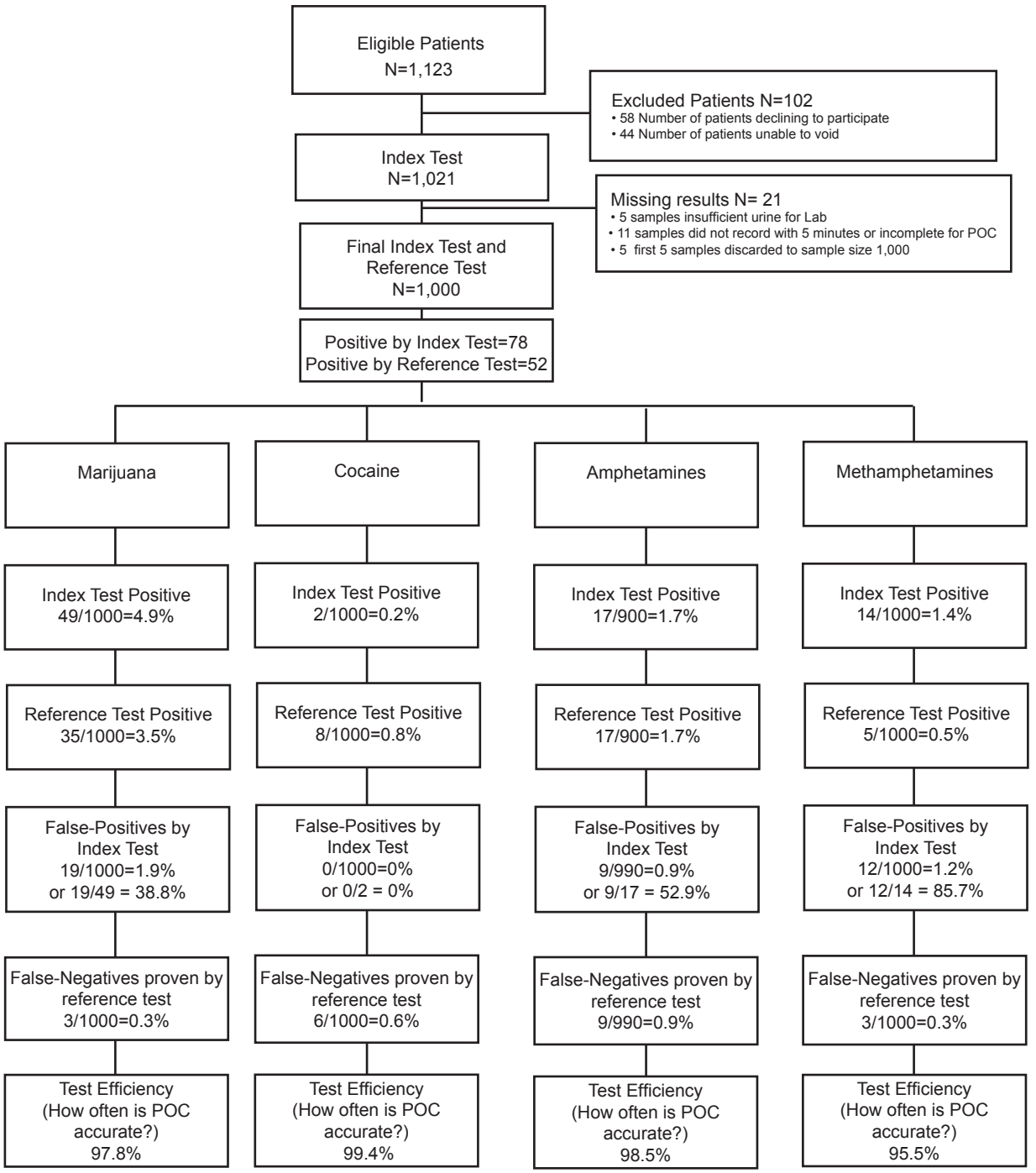


Fig. 2. *Flow diagram of diagnostic accuracy testing of illicit drugs.*

### Participants

The study lasted from March 1, 2010, through June 30, 2010, with enrollment of consecutive patients. Evaluation days were selected by computerized randomization.

### Demographic Characteristics

The demographic characteristics of the study population are illustrated in Table 1.

### Validity and Test Reproducibility

One hundred specimens without identification or demographic data were tested for validity of the reference test. This showed perfect correlation.

### Numbers Analyzed

The numbers analyzed are illustrated in Figures 1 and 2.

### Time Intervals

The index test and reference test were performed on the same sample. The time interval for transporting the sample to the lab and performance of the test is estimated to have been about 72 hours.

### Distribution Characteristics

The distribution of severity of disease is not applicable.

### Cross Tabulation of the Results

A cross tabulation of the results of the index test and the reference test were performed.

Table 1. *Demographic characteristics.*

| | | Number |
|---|---|---|
| Gender | Male | 37% (370) |
| | Female | 63% (630) |
| Age (Years) | Mean ± SD | 51 ± 12.6 |
| Height | | 66.5 ± 4.2 |
| Weight | | 184.1 ± 51.5 |
| Insurance | Medicare | 47.0% (470) |
| | Medicaid | 25.2% (252) |
| | Third Party | 27.8% (278) |
| | | |
| | | |
| State | Kentucky | 82.9% (829) |
| | Others (IL, TN, MO, IN) | 17.1% (171) |

### Adverse Events

No adverse events occurred while performing the index test or reference test.

### Estimates

The estimated diagnostic accuracy and comparison were evaluated for all patients for each opioid prescribed and for illicit drugs.

### Results of Accuracy of Opioids and Illicit Drugs

A summary of the diagnostic accuracy of the index test versus the reference test is illustrated in Table 2. This table illustrates the cut-off levels utilized along with sensitivity, specificity, and agreement. For opioids with morphine, hydrocodone, codeine, and hydromorphone, there was 92.5% agreement with sensitivity of 92.2% and specificity of 93.0%, with a false-negative rate of 7.8% and false-positive rate of 6.9%. The numbers were better for methadone with sensitivity of 96.1% and specificity of 98.8% with an agreement of 98.7%. However, for oxycodone sensitivity was 75.4% with false-negative rates of 24.6% and specificity of 92.3% with agreement of 90%. For all illicit drugs, test agreement was high (approximately 98% or over). However, for cocaine sensitivity was 25% with false-negative rates of 75% with specificity of 100%. Methamphetamines and amphetamines also had lower sensitivity with 40% and 47%. Consequently, these tests will show false-negative rates in 60% of the patients for methamphetamines and 53% for amphetamines even though specificity and agreement were high.

Table 3 illustrates a summary of the diagnostic accuracy of opioids with detailed data from the index test and the reference test. This table illustrates the same results as in Table 2 with detailed numbers.

## Discussion

The results of this prospective, diagnostic accuracy study of UDT comparing in-office testing with immunoassay (index test) confirmed with laboratory testing of LC/MS/MS (reference test) showed significant agreement for opioids as well as illicit drugs. Specificity for opioids was 93.1% for the morphine group, 92.3% for oxycodone, and 98.8% for methadone. Sensitivity for opioids was 92.2% for the morphine group, 75.4% for oxycodone, and 96.1% for methadone. The agreement or test efficiency was 92.5% for the morphine group, 90% for oxycodone, and 98.7% for methadone. Similarly, for illicit drugs, specificity was 98% for marijuana, 100% for

Table 2. *Summary of diagnostic accuracy of opioids and illicit drugs (index test vs. reference test).*

| | TP | FP | TN | FN | Cutoff levels (POC vs LC/MS/MS) | Sensitivity/ False Negative Rate | Specificity/ False Positive Rate | Test Efficiency (Agreement) |
|---|---|---|---|---|---|---|---|---|
| **Opioids** | | | | | | | | |
| Morphine, Hydrocodone, Codeine, Hydromorphone | 614 | 23 | 311 | 52 | 300 ng/mL vs 50 ng/mL | 92.2% / 7.8% | 93.1% / 6.9% | 92.5% |
| Oxycodone | 104 | 66 | 796 | 34 | 100 ng/mL vs 50 ng/mL | 75.4% / 24.6% | 92.3% / 7.7% | 90.0% |
| Methadone | 49 | 11 | 938 | 2 | 300 ng/mL vs 100 ng/mL | 96.1% / 3.9% | 98.8% / 1.2% | 98.7% |
| **Illicit Drugs** | | | | | | | | |
| Marijuana | 30 | 19 | 948 | 3 | 50 ng/mL vs 15 ng/mL | 90.9% / 9.1% | 98.0% / 2.0% | 97.8% |
| Cocaine | 2 | 0 | 992 | 6 | 300 ng/mL vs 50 ng/mL | 25.0% / 75% | 100.0% / 0% | 99.4% |
| Methamphetamines | 2 | 12 | 983 | 3 | NA 50 ng/mL | 40.0% / 60% | 98.8% / 1.2% | 98.5% |
| Amphetamines* | 8 | 9 | 964 | 9 | 1000 ng/mL vs 100 ng/mL | 47.0% / 53.0% | 99.1% / 0.9% | 98.2% |

* n=990
TP=true positive; TN=true negative; FP=false-positive; FN=false-negative; LC/MS/MS=liquid chromatography-tandem mass spectrometry; POC=point of care; NA=not applicable

Table 3. *Illustration of summary of diagnostic accuracy of opioids (index test vs. reference test).*

| | | Patients Prescribed Morphine, Hydrocodone, Codeine, Hydromorphone group (748) | | | Patients Prescribed Oxycodone (134) | | | Patients Prescribed Methadone (46) | | | Patients with non-prescribed opioids or no prescribed opioids (1000) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Reference Test (LC/MS/MS) | | | Reference Test (LC/MS/MS) | | | Reference Test (LC/MS/MS) | | | Reference Test (LC/MS/MS) | | |
| | | Positive | Negative | Totals | Positive | Negative | Totals | Positive | Negative | Totals | Positive | Negative | Totals |
| Index Test (POC) | Positive | 594 | 11 | 605 | 92 | 3 | 95 | 44 | 0 | 44 | 37 | 83 | 120 |
| | Negative | 48 | 95 | 143 | 23 | 16 | 39 | 1 | 1 | 2 | 16 | 864 | 880 |
| | Totals | 642 | 106 | 748 | 115 | 19 | 134 | 45 | 1 | 46 | 53 | 947 | 1000 |
| Test Efficiency (Agreement) | | 92.1% | | | 80.6% | | | 97.8% | | | 90.1% | | |
| Sensitivity | | 92.5% (90% - 94%) | | | 80.0% (71% - 87%) | | | 97.8% (88% - 99%) | | | 69.8% (55% - 82%) | | |
| Specificity | | 89.6% (82% - 95%) | | | 84.2% (60% - 96%) | | | 100 (2% - 100%) | | | 93% (89% - 93%) | | |

LC/MS/MS=liquid chromatography-tandem mass spectrometry; POC=point of care

cocaine, 98.8% for methamphetamine, and 99.1% for amphetamine. However, the sensitivity was only 25% for cocaine, 40% for methamphetamine, 47% for amphetamine, and 90.9% for marijuana. One reason for such low sensitivity for illicit drugs is low prevalence rates. Thus, a larger sample size is needed to detect sensitivity. The agreement, or test specificity, for all illicit drugs was 95%, with 97.8% for marijuana, 99.4% for cocaine, 98.5% for methamphetamine, and 98.2% for amphetamine.

Multiple methodological issues are present in UDT, with immunoassays being based on the principle of competitive binding, detecting a particular drug group in a urine sample. In contrast, laboratory-based specific drug identification is sophisticated, but also more expensive. Thus, laboratory-based specific drug identification is needed to confirm the presence of a given drug and/or to identify drugs that cannot be isolated by a screening test. In addition, the cutoff levels for various drugs detected by urine analysis are also different between immunoassay testing and LC/MS/MS. Consequently, the capability of a particular immunoassay to detect drugs can vary according to both the drug concentration in the urine and the assessed cutoff concentration – with drug levels above cutoff being deemed to be positive. However, almost all immunoassays are subject to cross-reactivity. Some tests are highly predictive (i.e., cocaine, morphine, codeine), whereas others are very poorly predictive (i.e., amphetamine, methamphetamines, oxycodone) based on various other substances being ingested.

Previous studies performed in a prospective manner (31-33) showed the prevalence of illicit drug use to vary from 4.8% to 6.25% for cocaine, 11% to 18% for marijuana, and 2% to 3% for amphetamines and/or methamphetamine. Other studies, though not prospective and not diagnostic accuracy studies (37,44,46,47), showed false-negative rates for oxycodone, hydrocodone, methadone, and other opioids variable from 1.9% to 15% (37,44,46) and false-negative rates for illicit drugs which were not detected in 9% to 50% of patients. Further, Gilbert et al (41), in attempting to reverse CMS regulation, showed that urine drug testing represented only approximately 18.2% of professional medical services rendered in 2007, a figure considered extremely high by others (38,39). POC testing results examined in the present evaluation show an overall positive rate of 7.8%; 0.2% for cocaine, 4.9% for marijuana, 1.7% for amphetamines, and 1.4% for methamphetamines. These results differ with previous studies. Further, false-negatives were observed in 75% for cocaine, 9.1%, for marijuana, 53% for amphetamines, and 60% for methamphetamines.

The results of the present study illustrated similar results for patients with prescribed opioids, with a false-negative rate of 19.6% for the index test and 20.3% for the reference test. The improved diagnostic accuracy with the reference test is 8.9%, rising from 80.4% to 89.3%; all the samples which were tested to be negative by immunoassay were confirmed by LC/MS/MS, with 82 of 180 patients testing positive. In reference to non-prescribed opioids, 12% tested positive with the index test, with that test missing in 1.6% of the patients. However, only 37 of 120 were confirmed with the reference test, with 83 of 120 patients or 44% with false-positive results for non-opioid use with the index test performed in the office. Thus, a total of 53 patients, or 5.3%, were using non-prescribed opioids.

Multiple authors have described the utility and application of UDT in chronic pain management with opioids (31-33,36,52-54). Nafziger and Bertino (53) described that UDT, when used with an understanding of the principles of pharmacokinetics, pharmacodynamics, and pharmacogenetics of opioids, can be a useful tool in chronic pain management. Thus, clinicians must keep in mind the limitations, purpose, and value of UDT, and the inability to predict patient compliance with the drug dosages used in commercial algorithms. Pergolizzi et al (52), in a compliance survey, discussed various aspects of UDT for patients in opioid therapy including the validity of UDT with reference to index and reference tests and the implications for reimbursement. With reference to cost issues, Gilbert et al (41) discussed the cost-benefit considerations of UDT, and that testing of chronic pain patients is analogous to the federal work place drug testing program, methadone clinics, and other areas, which have shown a definite cost benefit for UDT in this complex population. It has been estimated that each UDT in the past has cost Medicare up to $220 per physician office payment, and up to an additional $600 for laboratory testing. Some physicians have stated that any patient treated with controlled substances, including stable patients, should be seen in an office every 4 weeks and be required to have a UDT (40,41,55,56). This increased frequency obviously has had a negative impact on patients and payers, as seen by new CMS guidance on this testing (45). Gilbert et al's (41) illustration of 18.2% income, the Ameritox indictment, and change of CMS coding patterns, illustrates the economic incentives for UDT (43).

The question which needs to be answered is: How many POC testing samples need to be sent to the lab? Based on our evaluation, it appears that it should be all samples testing negative for prescribed (detectable) opioids (184 patients), positive for non-prescribed opioids (123 patients), and positive for illicit drugs (68 patients), totaling 329 patients after eliminating positive duplications. However, these can be reduced based on a patient's admission of abnormal use, and the clinic's policy for controlled substances and illicit drugs. The re-

ductions could range from 20% to 60%, with a repeat of the immunoassay test during the patient's next appointment or at random. A repeat test should be much less expensive compared to sending the test to a lab; generally $25 versus as much as $600. Thus, careful analysis can save substantial amounts of health care dollars, specifically when performed judiciously without repeating during each visit in patients who do test normally, and repeating their tests only once a year and then only repeating in patients who present with abnormal results. One UDT might be more expensive than providing 2 to 3 epidural injections. Routine excessive UDT could result in annual charges as high as $10,000, which is more expensive than managing patients with common opioids or appropriately performed therapeutic interventional techniques. However, multiple interventional techniques also have been criticized for escalating use, abuse, and lack of effectiveness (38,39,57-66). Based on cost-effectiveness, numerous guidelines have been developed, which are curbing chronic pain management therapy in the era of increasing pain, including interventional techniques and surgery based on evidence-based medicine and comparative effectiveness research (34,38,39,67-99). Thus, appropriate use of immunoassay will be cost-effective with provision of appropriate care.

The present study can be criticized for limitations, which include a single site study utilizing a single POC kit and a single laboratory, as well as technical sponsorship. A multicenter study could be performed utilizing various manufacturers and different kits, etc.; however, this might provide irregular results. Consequently, as an initial diagnostic accuracy study, the present study is appropriate. Millennium Laboratories provided urine drug kits, laboratory evaluation at no cost, and expenses for employees for collecting the samples, transporting them, data entry, and analysis. However, They had no influence or interference after the protocol was designed. Further, the authors of the manuscript received no remuneration. Thus, we believe the results are valid.

Further, the results of this study illustrate practice patterns in an interventional pain management practice, rather than results generalizable to either all interventional pain medicine settings or primary care settings.

## Conclusion

UDT with immunoassay in an office setting is an appropriate, convenient, and cost-effective test providing rapid results for evaluating opioid compliance. Compared with laboratory testing (LC/MS/MS) for opioids and illicit drugs, immunoassay in-office testing had high specificity and agreement, but variable sensitivity, demonstrating the value of immunoassay drug testing.

However, in patients with abnormal results, either by detection of non-prescribed opioid or illicit drugs, the results are not dependable and might have to be confirmed either by a repeat test, proper history, or confirmation by LC/MS/MS. Based on this evaluation, it appears that overall, as many as 32.9% or as few as 20% of patients could require their samples be sent for LC/MS/MS confirmation and subsequent patient management.

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**Author Contributions:** Dr. Manchikanti had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs. Manchikanti, Malla, and Wargo designed the study protocol. Dr. Manchikanti managed the literature searches and summaries of previous related work and wrote the first draft of the manuscript. All other authors provided revision for intellectual content and final approval of the manuscript.

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Physicians, a state organization, has no relevance to the study and none of the Florida members were involved in conduct of the study.

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Diagnostic Accuracy Report

# Comparative Evaluation of the Accuracy of Benzodiazepine Testing in Chronic Pain Patients Utilizing Immunoassay with Liquid Chromatography Tandem Mass Spectrometry (LC/MS/MS) of Urine Drug Testing

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**Background:** Eradicating or appreciably limiting controlled prescription drug abuse, such as opioids and benzodiazepines, continues to be a challenge for clinicians, while providing needed, proper treatment. Detection of misuse and abuse is facilitated with urine drug testing (UDT). However, there are those who dispute UDT's diagnostic accuracy when done in the office (immunoassay) and claim that laboratory confirmation using liquid chromatography tandem mass spectrometry (LC/MS/MS) is required in each and every examination.

**Study Design:** A diagnostic accuracy study of UDT.

**Study Setting:** The study was conducted in a tertiary referral center and interventional pain management practice in the United States.

**Objective:** Comparing UDT results of in-office immunoassay testing (the index test) with LC/MS/MS (the reference test).

**Methods:** A total of 1,000 consecutive patients were recruited to be participants. Along with demographic information, a urine sample was obtained from them. A nurse conducted the immunoassay testing at the interventional pain management practice location; a laboratory conducted the LC/MS/MS.

All index test results were compared with the reference test results. The index test's efficiency (agreement) was calculated as were calculations for sensitivity, specificity, false-positive, and false-negative rates.

**Results:** Approximately 36% of the specimens required confirmation. The index test's efficiency for prescribed benzodiazepines was 78.4%. Reference testing improved accuracy to 83.2%, a 19.6% increase, and 8.9% of participants were found to be taking non-prescribed benzodiazepines. The index test's false-positive rate for benzodiazepines use was 10.5% in patients receiving benzodiazepines.

**Limitations:** This study was limited by its single-site location, its use of a single type of point of care (POC) kit, and reference testing being conducted by a single laboratory, as well as technical sponsorship.

**Conclusion:** Clinicians should feel comfortable conducting in-office UDT immunoassay testing. The present study shows that it is reliable, expedient, and fiscally sound for all involved. In-office immunoassay testing compares favorably with laboratory testing for benzodiazepines, offering both high specificity and agreement. However, clinicians should be vigilant and wary when interpreting results, weighing all factors involved in their decision.

**Key words:** Controlled substances, benzodiazepines, opioids, illicit drugs, abuse, liquid chromatography tandem mass spectrometry, immunoassay, urine drug testing

**CLINICAL TRIAL:** NCT01052155

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The treatment of chronic pain with escalating controlled substance use and abuse, and the nonmedical use of prescription drugs have been topics of intense focus and debate (1). The controlled substances often prescribed for chronic noncancer pain include not only opioids, but also various other drugs including benzodiazepines. Benzodiazepines have been shown to be as abused as opioids; they have also resulted in similar emergency department visits (2-15). The present state of affairs is based on prescriptions for chronic noncancer pain; subjective complaints of pain; prevalence of psychologically-specific anxiety and sleep disorders in chronic pain patients; recommendations from federal, state, and local governments; professional associations; massive sales promotion activities from the pharmaceutical companies; physicians promoting opioid therapy with comorbid disorders; accreditation agencies promoting pain management in conjunction with a biopsychosocial approach, which involves psychological management including psychotherapeutic drug therapy; and finally the public-at-large expecting pain relief and relief of all symptoms at any cost, rather than on scientific data on efficacy and safety (1,7-18). The results from the 2009 National Survey on Drug Use and Health illustrated increasing use of benzodiazepines (1,7). Further, national estimates of drug-related emergency department visits (8) also showed increasing visits related to benzodiazepines at a rate similar to opioids. Consequently, benzodiazepines are considered the most frequently prescribed sedatives and hypnotic drugs with increasing evidence of overuse, abuse, and dependence (19,20). Benzodiazepine abuse is associated with the abuse of alcohol and other psychoactive substances, along with widespread use among heroin addicts treated with methadone (21-23). Benzodiazepines have been described as part of the methadone program to alleviate some of the withdrawal symptoms of treated heroin addicts such as insomnia, nausea, anxiety, and depression.

The prevalence of chronic pain and its associated disability continue to increase (24-26). Similar to the extensive therapeutic use of opioids and benzodiazepines, along with associated abuse and dependence, a multitude of other techniques, including interventional pain management techniques, also have been escalating (27-30). Further, the psychological issues associated with chronic pain, specifically, generalized anxiety disorder, have also been shown to be present in greater than 50% of patients (31-35). Following a biopsychosocial perspective in management, instead of utilizing behavioral therapy, practitioners are increasingly utilizing benzodiazepines to manage anxiety, and even occasionally depression, as well as all other types of symptoms, including muscle spasm.

The challenge is to eliminate or significantly curtail abuse of controlled prescription drugs while still assuring the proper treatment of those patients with evident indications. Adherence monitoring, including urine drug testing (UDT), has been shown to be a useful approach to assist in identifying and/or predicting patterns of drug use, compliance, misuse, and abuse (36-38). UDT provides relatively good specificity, sensitivity, ease of administration, and cost for various drugs including benzodiazepines (6,19,36-49). However, controversies also exist regarding the clinical value of UDT, partly because most current methods are designed for, or adapted from, forensic or occupational deterrent-based testing for illicit drug use and are not entirely optimal for application in chronic pain management settings. Further, additional issues also exist related to excessive use, misuse, abuse, and financial incentives (36-38,47-57). UDT is performed to detect the presence of prescribed medications (i.e., compliance testing) and to identify substances that are not expected to be present in the urine, such as non-prescription or illicit drugs (i.e., forensic testing). The most commonly used Current Procedural Terminology (CPT) codes for UDT, 80101 and 80102, showed 343% and 364% increases from 2004 to 2007 and an increase in allowed charges of 452% and 387%; the total allowed charges exceeded $50 million in 2007 (57). The abuses related to the utilization of UDT, its value and validity, and exploding costs, has led the Centers for Medicare and Medicaid (CMS) administration to impose new regulations for UDT reimbursement (47-57).

Consequently, the pain physician is confused by the available options, indications, and medical necessity of UDT. Recently, Christo et al (37) illustrated an algorithmic approach to UDT. Even so, debate continues regarding the validity of in-office UDT of chronic pain patients by immunoassay methodology that has not been validated with liquid chromatography tandem mass spectrometry (LC/MS/MS). Recently, Manchikanti et al (38) published a comparative evaluation of the accuracy of immunoassay with LC/MS/MS of UDT of opioids and the use of drugs in chronic pain patients. Overall results showed that confirmation was required in 32.9% of the specimens, without taking into consideration a history and evaluation for opioids and illicit drugs. Agreement for prescribed opioids was high

with the index test (80.4%), whereas the reference test for opioids improved accuracy by 8.9% from 80.4% to 89.3%. However, positive results with the reference test were also the same as the index test with a positive rate of 79.7%. This evaluation also showed that non-prescribed opioids were used by 5.3% of patients. The index test provided false-positive results for non-opioid use in 44%, or 83 of 120 patients. Test efficiency or agreement was present in over 90% for all opioids and for illicit drugs, approaching 99.4%; ranging from a low of 90% for oxycodone, to 98.7% for methadone, and an even higher agreement of over 97% for all illicit drugs tested (marijuana, cocaine, methamphetamines, and amphetamines). The authors concluded that UDT with immunoassay in an office setting is appropriate, convenient, and cost-effective. However, they caution that due to variable sensitivity, clinicians would be well-advised to take a cautious approach when interpreting the results, in conjunction with other compliance monitoring measures.

Thus, despite the recent report, due to multiple methodological issues, an in-office immunoassay confirmed by an independent laboratory is commonly regarded as the best and most sensitive UDT, even at the expense of escalating costs. Other issues involved are the knowledge of the physician who interprets the drug screening, including knowledge about opioid and benzodiazepines metabolites, appropriate testing methods in an office setting, and the cost involved (37,38,50,53,54,56,57).

At present, the marketing efforts of UDT manufacturers and physicians who receive substantial income from UDT continue to market the value and validity of laboratory testing and describe it as the only way to monitor compliance consistently despite escalating costs (37,38,47,50-56). However, others recommend in-office testing for the reasons of convenience and cost effectiveness (37,38). While the issues have been well studied for prescription opioids, there is a paucity of literature concerning prescription benzodiazepines.

Benzodiazepines are structurally similar to one another, and it has been described that the most convenient screening methods for UDT for benzodiazepines are based on immunoassay, and only inappropriate results need to be confirmed, usually using gas chromatography, or liquid chromatography coupled with mass spectometry (58-60). However, these methods are not suitable for quantification in some biological samples due to the presence of their different metabolites and/or other substances in the matrix with similar properties (19,58-60). Thus, multiple techniques have been developed to assess levels of benzodiazepines (19,61-64).

This diagnostic accuracy study has been undertaken to evaluate the accuracy of immunoassay compared to LC/MS/MS of UDT. The results of opioid and benzodiazepine testing, as well as illicit drug use in chronic pain patients and their correlations, have been published in a previous report (38). This report describes comparative evaluation of the accuracy of benzodiazepines.

## Methods

The study was undertaken in an interventional pain management practice, a tertiary referral center, in the United States. The protocol was approved by the Institutional Review Board (IRB) of the Ambulatory Surgery Center and it has a clinical trial registration of NCT01052155. Appropriate precautions were taken to protect the privacy and identity of patients evaluated from this study in accordance with current Health Insurance Portability and Accountability Act (HIPAA) regulations.

The protocol has been described in a previous publication (36). The study was performed utilizing the Standards for Reporting of Diagnostic Accuracy Studies (STARD) established for reporting guidelines for diagnostic accuracy studies to improve the quality of reporting (65-67). The results of opioid and illicit drug use have been published (38).

## Objective

The objective of this study was to compare results of UDT of immunoassay in-office testing (index test) with LC/MS/MS (reference test).

### Proposed Hypothesis

It is proposed that there is no significant difference of clinical importance between point of care (POC) drug testing (index test) and laboratory drug testing (reference test).

### Investigational Methodology

The investigational methodology followed the STARD checklist (65). All specimens were tested with immunoassay (index test) and LC/MS/MS (reference test).

#### *Participants and Recruitment*

Consecutive series of patients presenting for interventional pain management were recruited in a prospective manner.

*Inclusion and Exclusion Criteria*

Consecutive patients in chronic pain management were included. There were no exclusion criteria.

### Test Methods

The index test was in-house POC office drug testing with immunoassay; the reference standard was LC/MS/MS.

The laboratory test (reference test) was performed by Millennium Laboratories, which holds certificates for moderate and high complexity testing.

### Screening Evaluation

All consecutive patients participating in the urine drug assessments diagnostic accuracy study were provided with a verbal explanation of the study. IRB-approved written informed consent to participate in the study was obtained.

Demographic details including date of birth, sex, weight, height, and drug profiles (which included a list of all prescription and over-the-counter drugs, as well as all other drugs or substances they were taking) were obtained.

### Treatment Number Assignment

Participants were consecutively assigned a number.

### Urine Sample

Urine and all other appropriate information were collected by a nurse participating in the study and provided to the study coordinator. POC testing was performed by a different nurse who was unaware of the patient's name, drug intake, etc. Drug testing was performed for opioids, benzodiazepines, and illicit drugs.

### Laboratory Assessment

After immunoassay, the samples were sent to a laboratory for LC/MS/MS without any identifying information or results of the index text.

### Definition and Rationale

The definition and rationale for the units, cutoffs, and categories of the results of the index test and the reference standard have been described (36,38).

### Personnel

Six nurses, determined to be a sufficient number, received training to conduct and read the index test. The reference test was conducted by trained, certified professionals at the laboratory.

### Blinding

The personnel performing and reading the index tests and reference tests were blinded (masked) to the results of the other tests as well as patient demographics.

### Statistical Methods

*Sample Size*

Sample size calculation was carried out for our primary outcome (accuracy of the POC drug test in screening for opioids, benzodiazepines, and illicit drugs) according to the previously published method (68), and previous results of drug abuse and illicit drug use by patients referred to clinics (2,9-11). The details are provided in previous publications (36,38). The sample size was calculated at 811 with a planned enrollment of 1,000 patients to be tested.

*Analysis*

Statistical analysis was performed using SPSS 9.01 (SPSS, Inc., Chicago IL, USA). A *P* value below 0.05 was considered statistically significant.

Results of the index test were compared to the reference test in all patients. The sensitivity, specificity, false-positive and false-negative rates, and index test efficiency (agreement) were calculated.

## Results

### Flow Diagram

Figure 1 illustrates the patient flow diagram per STARD for benzodiazepines.

### Participants

The study lasted from March 1, 2010, through June 30, 2010, with enrollment of consecutive patients.

### Demographic Characteristics

The demographic characteristics of the study population are illustrated in Table 1.

### Validity and Test Reproducibility

One hundred specimens without identification or demographic data were tested for validity of the reference test. This showed perfect correlation.

### Numbers Analyzed

The numbers analyzed are illustrated in Fig. 1.

### Time Intervals

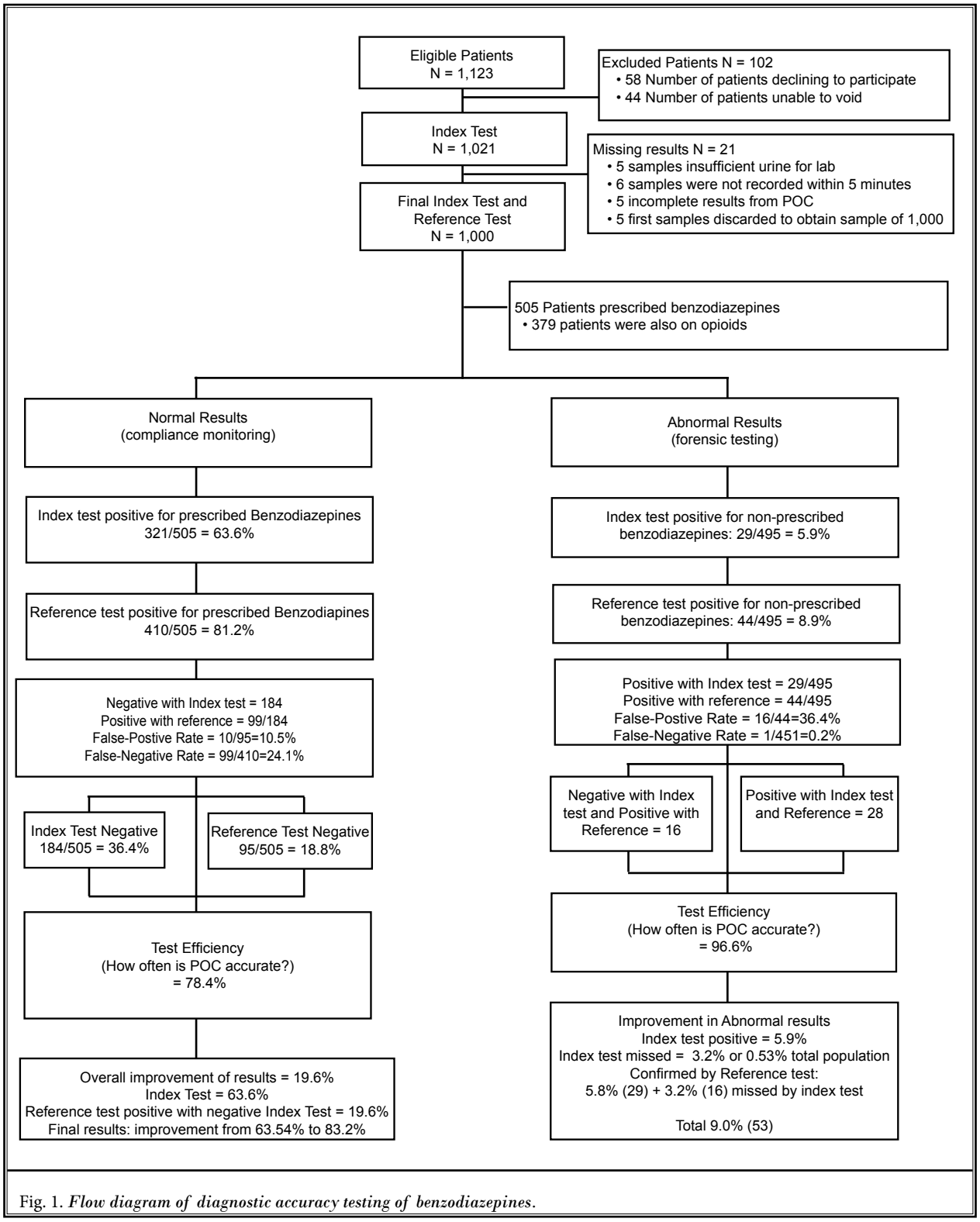


Fig. 1. *Flow diagram of diagnostic accuracy testing of benzodiazepines.*

Table 1. *Demographic characteristics of patients undergoing urine drug testing.*

| | | Number |
|---|---|---|
| Gender | Male | 37% (370) |
| | Female | 63% (630) |
| Age (Years) | Mean ± SD | 51 ± 12.6 |
| Height | | 66.5 ± 4.2 |
| Weight | | 184.1 ± 51.5 |
| Insurance | Medicare | 20.7% (207) |
| | Medicaid & Medicare | 15.3% (153%) |
| | Medicare & Third Party | 11.0% (110) |
| | Medicaid | 25.2% (252) |
| | Self Pay | 1.9 (19) |
| | Third Party | 22.5% (225) |
| | Workers' Compensation | 3.4 (34) |
| State | Kentucky | 82.9% (829) |
| | Other States (IL, TN, MO, IN) | 17.1% (171) |

The index test and reference test were performed on the same sample. The time interval for transporting the sample to the lab and performance of the test is estimated to have been 72 hours.

### Distribution Characteristics

The distribution of severity of disease is not applicable.

### Cross Tabulation of the Results

A cross tabulation of the results of the index test and the reference test was performed.

### Adverse Events

No adverse events occurred while performing the index test or reference test.

### Estimates

The estimated diagnostic accuracy and comparison were evaluated for all patients for each benzodiazepine prescribed and for illicit drugs.

### Results of Accuracy of Benzodiazepine Testing

Table 2 illustrates a summary of the diagnostic accuracy of benzodiazepines with detailed data from the index test and the reference test.

## Discussion

The comparative evaluation of the accuracy of UDT for benzodiazepine detection in chronic pain patients utilizing both immunoassay and LC/MS/MS showed significant agreement for benzodiazepines similar to opioids and illicit drugs. This assessment showed test efficiency of 87.4% when all patients were assessed compared to 78.4% in patients with prescribed benzodiazepines, and 96.6% in patients without prescribed benzodiazepines. Positive predictive value, which shows how often a positive office test is correct, was 96.9%. Specificity was high, being 98% when all patients were assessed, 89.5% when only patients with prescribed benzodiazepines were considered, and 99.8% for patients without prescribed benzodiazepines. However, sensitivity was lower compared to specificity with 75.9% of the patients with prescribed benzodiazepines and 63.6% of the patients without prescribed benzodiazepines. The false-positive rates varied from 0.2% in patients without prescribed benzodiazepines to 2% when all patients were assessed, and 10.5% in patients with prescribed benzodiazepines. However, false-negative rates with patients being misdiagnosed as negative, when in fact they were positive, was relatively high, 24.1% in patients with prescribed benzodiazepines and 36.4% in patients without prescribed benzodiazepines. Consequently, one can miss a significant proportion of patients without prescribed benzodiazepines; however, to obtain this result all 1,000 specimens had to be sent for confirmation. In contrast, only 29 of 495 patients not on benzodiazepines tested positive for benzodiazepines with POC testing. Thus, when 29 of these specimens were confirmed by LC/MS/MS, only 16 were positive, thus improving the diagnostic accuracy only slightly.

In patients taking benzodiazepines, the index test was positive in 63.6% of the patients, whereas the reference test was positive for prescribed benzodiazepines in 81.2%, a wider difference than opioids, where it was shown to be equal at approximately 80%. It appears that the reference test is equally accurate for opioids and benzodiazepines; however, the index test is positive in a lower proportion of patients. When all the index test negative specimens (184 of 505, or 36.4%) were confirmed by the reference test, the overall results improved by 19.6%, thus improving the final results from 63.6% to 83.2%, a number which is 2 percentage points higher than straightforward reference test results. Thus, confirming only the negative specimens will improve diagnostic accuracy bet-

Table 2. *Summary of diagnostic accuracy of POC vs LC/MS/MS – benzodiazepines.*

| | | All patients (1000) | | | Patients with Prescribed Benzodiazepines (505) | | | Patients without Prescribed Benzodiazepines (495) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Reference Test (LC/MS/MS) | | | Reference Test (LC/MS/MS) | | | Reference Test (LC/MS/MS) | | |
| | | Positive | Negative | Totals | Positive | Negative | Totals | Positive | Negative | Totals |
| Index Test (POC) | Positive | 339 | 11 | 350 | 311 | 10 | 321 | 28 | 1 | 29 |
| | Negative | 115 | 535 | 650 | 99 | 85 | 184 | 16 | 450 | 466 |
| | Totals | 454 | 546 | 1000 | 410 | 95 | 505 | 44 | 451 | 495 |
| Test Efficiency (How often does the POCT get the right answer?) | | 87.4% | | | 78.4% | | | 96.6% | | |
| Sensitivity (TP/(TP+FN) | | 74.7% (70 – 78) | | | 75.9% (71 – 80) | | | 63.6% (47 – 78) | | |
| Specificity (TN/(TN+FP) | | 98.0% (96 – 98) | | | 89.5% (81 – 94 | | | 99.8% (98 – 99) | | |
| False Negative Rate (% of positives that misdiagnosed as negative on POCT) | | 25.3% | | | 24.1% | | | 36.4% | | |
| False Positive Rate (% of negatives misdiagnosed as positive on POCT) | | 2% | | | 10.5% | | | 0.2% | | |
| Positive Predictive Value (how often is a positive POCT correct?) | | 96.9% | | | 96.9% | | | NA | | |
| Negative Predictive Value (how often is a negative POCT correct?) | | 82.3% | | | NA | | | 96.6% | | |

POCT = point of care testing; TP = true-positive; FN = false-negative; TN = true negative; FP = false-positive

ter than sending all specimens to a lab and depending only on LC/MS/MS results.

Multiple methodological issues are present in UDT, with immunoassays being based on the principle of competitive binding for detecting a particular drug group in a urine sample. In contrast, laboratory-based specific drug identification is sophisticated, but also much more expensive. Thus, laboratory-based specific drug identification is needed to confirm the presence of a given drug and/or to identify drugs that cannot be isolated by a screening test. In addition, the cutoff levels for various drugs detected by urinalysis are also different between immunoassay testing and LC/MS/MS. Consequently, the capability of a particular immunoassay to detect drugs can vary according to both the drug concentration in the urine and the assessed cutoff concentration – with drug levels above cutoff being deemed to be positive. However, almost all immunoassays are subject to cross-reactivity.

POC testing results examined in the present evaluation for benzodiazepines showed overall inappropriate findings in 36.4% of the patients on benzodiazepines (184 of 505), whereas benzodiazepines were present in 29 of the 495 patients, with overall inappropriate results in 213 of 21.3% of the patients. However, false-negative rates were observed in 24.1% of the patients taking prescribed benzodiazepines. The false-positive rate for patients taking prescribed benzodiazepines was 10.5% compared to almost 0% (0.2%) for patients not taking prescribed benzodiazepines. Thus, if all the questionable specimens were sent to the lab, 184 + 29 = 213, the accuracy would be improved for patients who are on benzodiazepines by 19.6%, whereas there was no significant improvement in patients who were not on benzodiazepines.

The present study illustrates results for patients taking prescribed benzodiazepines, with a false-negative rate of 36.4% for the index test and 18.8% for the reference test. The improved diagnostic accuracy with the reference test was 19.6%, rising from 63.6% to 89.2%; all the samples which were tested to be negative by immunoassay were confirmed by LC/MS/MS, with 95 of 184 patients testing positive. In reference to non-prescribed benzodiazepines, 5.9% (29 of 495) tested positive with the index test, with that test missing 8.9% or 44 of 495 patients.

Multiple authors have described the utility and application of UDT for opioids in chronic pain management (9-11,19,36-50,69,70). Nafziger and Bertino (70) described that UDT, when used with an understanding of the principles of pharmacokinetics, pharmacodynamics, and pharmacogenetics of opioids, can be a useful tool in chronic pain management. Thus, clinicians must keep in mind the limitations, purpose, and value of UDT, and the inability to predict patient compliance with the drug dosages used in commercial algorithms. The question which needs to be answered is: How many POC testing samples need to be sent to the lab? Based on our evaluation, it appears that it should be all samples testing negative for prescribed benzodiazepines (184 patients) and positive for non-prescribed benzodiazepines (29 patients), totaling 213. Thus, without consideration of history, these can be reduced based on a patient's admission of abnormal use, and the clinic's policy for controlled substances and illicit drugs. The reductions could range to 2% to 10%, with a repeat of the immunoassay test during the patient's next appointment or at random. A repeat test should be much less expensive compared to sending the test to a lab; generally $25 versus as much as $600. Thus, careful analysis can save substantial amounts of health care dollars, specifically when performed judiciously without repeating during each visit in patients who do test normally, and repeating their tests only once a year and then only repeating in patients who present with abnormal results. One UDT might be more expensive than providing 2 to 3 epidural injections. Routine excessive UDT could result in annual charges as high as $10,000, which is more expensive than managing patients with common opioids and benzodiazepines or appropriately performed therapeutic interventional techniques. However, multiple interventional techniques also have been criticized for escalating use, abuse, and lack of effectiveness (28-31,51,52,71-76). Based on cost-effectiveness, numerous guidelines have been developed, which are curbing chronic pain management therapy in the era of increasing pain, including interventional techniques and surgery based on evidence-based medicine and comparative effectiveness research (26,51,52,77-100). Thus, appropriate use of immunoassay will be cost-effective with provision of appropriate care.

The present study can be criticized for limitations, which include a single site study utilizing a single POC kit and a single laboratory, as well as technical sponsorship. A multicenter study could be performed utilizing various manufacturers and different kits, etc.; however, this might provide irregular results. Consequently, as an initial diagnostic accuracy study, the present study is appropriate. Millennium Laboratories provided urine drug kits, laboratory evaluation at no cost, and expenses for employees for collecting the samples, transporting them, data entry, and analysis. However, they had no influence or interference after the protocol was designed. Further, the authors of the manuscript received no remuneration. Thus, we believe the results are valid.

Further, the results of this study illustrate practice patterns in an interventional pain management practice, rather than results generalizable to either all interventional pain medicine settings or primary care settings.

## Conclusion

UDT with immunoassay in an office setting is an appropriate, convenient, and cost-effective test providing rapid results for evaluating opioid compliance. Compared with laboratory testing LC/MS/MS for opioids and illicit drugs, benzodiazepine immunoassay in-office testing had high specificity and agreement, but variable sensitivity.

However, in patients with abnormal results, results are not dependable and might have to be confirmed either by a repeat test, proper history, or confirmation by LC/MS/MS.

## Disclosures

**Author Contributions:** Dr. Manchikanti had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs. Manchikanti, Malla, and Wargo designed the study protocol. Vidyasagar Pampati, MSc, was in charge of data entry, storage, and analysis. Dr. Manchikanti managed the literature searches and summaries of previous related work and wrote the first draft of the manuscript. All other authors provided revision for intellectual content and final approval of the manuscript.

**Conflict of Interest Disclosures:** All authors have no conflicts of interest to report. None of the authors of the manuscript received any remuneration. Further, the authors have not received any reimbursement or honorarium in any other manner. The authors are not affiliated in any manner with Millennium Laboratories. However, all the authors are members of the American Society of Interventional Pain Physicians (ASIPP) and practicing interventional pain physicians except for Bert Fellows, who is a retired psychologist. Dr. Manchikanti is

the Chairman of the Board and founder of ASIPP, which was responsible for the National All Schedules Prescription Electronic Reporting Act (NASPER) legislation and its implementation. Vidyasagar Pampati, MSc, statistician, is an employee of Ambulatory Surgery Center.

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**Role of Sponsor:** The financial sponsor of this work had no role in the design and conduct of the study or the collection, management, analysis, and interpretation of the data. The sponsor also did not have a role in the preparation or review of the manuscript or the decision to submit.

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## 435:30-7-11. Use of controlled substances for the management of chronic pain

The Board has recognized that principles of quality medical practice dictate that the people of the State of Oklahoma have access to appropriate and effective pain relief and has adopted the following criteria when evaluating the physician's treatment of pain, including the use of controlled substances:

(1) **Evaluation of the patient.** A medical history and physical examination must be obtained, evaluated and documented in the medical record. The medical record should document the nature and intensity of the pain, current and past treatments for pain, underlying or coexisting diseases or conditions, the effect of the pain on physical and psychological function and history of substance abuse. The medical record also should document the presence of one or more recognized medical indications for the use of a controlled substance.

(2) **Treatment plan.** The written treatment plan should state objectives that will be used to determine treatment success, such as pain relief and improved physical and psychosocial function, and should indicate if any further diagnostic evaluations or other treatments are planned. After treatment begins, the physician should adjust drug therapy to the individual medical needs of each patient. Other treatment modalities or a rehabilitation program may be necessary depending on the etiology of the pain and the extent to which the pain is associated with physical and psychosocial impairment.

(3) **Informed consent and agreement for treatment.** The physician should discuss the risks and benefits of the use of controlled substances with the patient, persons designated by the patient or with the patient's surrogate or guardian if the patient is without medical decision-making capacity. The patient should receive prescriptions from one physician and one pharmacy whenever possible. If the patient is at high risk for medication abuse or has a history of substance abuse, the physician should consider the use of a written agreement between physician and patient outlining patient responsibilities, including:

(A) urine/serum medication levels screening when requested;
(B) number and frequency of all prescription refills; and
(C) reasons for which drug therapy may be discontinued (e.g. violation of agreement)

(4) **Periodic review.** The physician should periodically review the course of pain treatment and any new information about the etiology of the pain or the patient's state of health. Continuation or modification of controlled substances for pain management therapy depends on the physician's evaluation of progress toward treatment objectives. Satisfactory response to treatment may be indicated by the patient's decreased pain, increased level of function or improved quality of life. Objective evidence of improved or diminished function should be monitored and information from family members or other caregivers should be considered in determining the patient's response to treatment. If the patient's progress is unsatisfactory, the physician should assess the appropriateness of continued use of the current treatment plan and consider the use of other therapeutic modalities.

(5) **Consultation.** The physician should be willing to refer the patient, as necessary, for additional evaluation and treatment in order to achieve treatment objectives. Special attention should be given to those patients with pain who are at risk for medication misuse, abuse or diversion. The management of pain in patients with a history of substance abuse or with a comorbid psychiatric disorder may require extra care, monitoring, documentation and consultation with or referral to an expert in the management of such patients.

(6) **Medical records.** Records should remain current and be maintained in an accessible manner, readily available for review. The physician should keep accurate and complete records to include:

(A) the medical history and physical examination (including vital signs),
(B) diagnostic, therapeutic and laboratory results,
(C) evaluations, consultations and follow-up evaluations,
(D) treatment objectives,
(E) discussion of risks and benefits,
(F) informed consent,
(G) treatments,
(H) medications (including date, type, dosage and quantity prescribed),
(I) instructions and agreements and
(J) periodic reviews.

(7) **Compliance with controlled substances laws and regulations.** To prescribe, dispense or administer controlled substances, the physician must be licensed in Oklahoma and comply with applicable federal and state regulations. Physicians are referred to the Physicians Manual of the U.S. Drug Enforcement Administration for specific rules governing controlled substances as well as applicable state regulations.

[**Source:** Amended at 16 Ok Reg 2003, eff 6-14-99; Added at 22 Ok Reg 2096, eff 6-25-05]

## 510:5-9-2 Guidelines and requirements

This rule requires that diagnosis be documented, it requires that certain records be maintained, and it requires that the physician must discuss the risks and benefits with the patient or the patient's guardian.

(1) To treat a patient's intractable pain, as long as the benefit of the expected relief outweighs the risk, even if the use of the drug increases the risk of death, so long as it is not furnished for the purpose of causing, or the purpose of assisting in causing death, the physician may prescribe or administer Schedule II, III, IV or V controlled dangerous substances or other pain relieving drugs in higher than normal dosages when, in that physician's judgment, the higher dosages are necessary to produce the desired therapeutic effect.

(2) The determination of intractable pain must include a complete medical history and physical examination which includes an assessment of the patient's pain, physical and psychological function, substance abuse history, underlying or co-existing diseases or conditions and the presence of a recognized medical indication for the use of an analgesic.

(3) The treatment plan must state objectives by which treatment success can be evaluated, such as pain relief and or improved physical and psychological function, and must indicate what further diagnostic evaluations or other treatments are planned. The drug therapy must be tailored to the individual needs of each patient.

(4) The course of treatment and any new information about the etiology of the intractable pain must be reviewed periodically, at least annually, with consideration given to referral for a current second opinion. The continuation or modification of treatment will depend on the results of this review and the evaluation of the patient's progress toward the treatment objectives. If the patient has not improved, the physician must assess the appropriateness of continuing the current therapy and the trial of other modalities.

(5) The management of intractable pain in patients with a history of substance abuse requires extra care, monitoring, documentation and consultation with addiction medicine specialists, and may include the use of agreements between the physician and patient specifying rules for medication use and consequences for its misuse.

(6) The physician must discuss the risks and benefits of the use of controlled substances with the patient or the patient's guardian and obtain informed consent prior to proceeding if it substantially increases the risk of death.

(7) Accurate and complete records documenting these requirements must be kept.

(8) To prescribe controlled substances, the physician must be licensed in Oklahoma, have a valid controlled substances registration and comply with federal and state regulations for issuing controlled substances prescriptions.

(9) Expert clinical testimony may be used to prove a violation of this rule. As used herein, a "clinical expert" is a physician who, by reason of specialized education or substantial relevant experience in pain management, has knowledge regarding current standards, practices and guidelines.

(10) Nothing in this rule shall limit a physician's authority to prescribe or administer prescription drug products beyond the customary indications as noted in the manufacturer's package insert for use in treating intractable pain, provided the drug is recognized for treatment of intractable pain in standard reference compendia or medical literature.

[Source: Added at 16 Ok Reg 2539, eff 6-25-99]

Centers for Disease Control and Prevention
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# CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016


Continuing Education Examination available at http://www.cdc.gov/mmwr/cme/conted.html.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

## CONTENTS



### Disclosure of Relationship

The Core Expert Group (CEG) members disclose that they have no financial conflicts of interest. Experts disclose the following activities related to the content of this guideline: Pam Archer discloses authorship of the Oklahoma Emergency Department and Urgent Care Clinic Opioid Prescribing Guidelines and the Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office Based Setting; Bonnie Burman discloses authorship of the Ohio Guidelines for Prescribing Opioids for the Treatment of Chronic, Non-Terminal Pain; Jane Ballantyne discloses that she has served as a paid consultant to Cohen Milstein Sellers & Toll, PLLC, and has special advisory committee responsibilities on the Food and Drug Administration (FDA) Risk Evaluation and Mitigation Strategies committee; Phillip Coffin discloses that in 2012 he provided expert testimony to the California State Assembly regarding a bill to expand naloxone access and reports that he is the principal investigator on a research study of methamphetamine dependence that receives donated injectable naltrexone from Alkermes, Inc.; Gary Franklin discloses authorship of the AMDG Interagency Guideline on Prescribing Opioids for Pain; Erin Krebs discloses that she represented the American College of Physicians at a 2014 Food and Drug Administration meeting on Abuse Deterrent Opioid Formulations; Lewis Nelson discloses his ad-hoc membership on the FDA Drug Safety and Risk Management Advisory Committee; Trupti Patel discloses authorship of the Arizona Opioid Prescribing Guidelines; Robert "Chuck" Rich discloses that he was an author of the 2013 American Academy of Family Physicians position paper on opioids and pain management; Joanna Starrels discloses that she received honoraria from the Betty Ford Institute; Thomas Tape discloses that he was an author of the 2013 American College of Physicians policy position paper on prescription drug abuse. CDC provided 100% of the funding for the supplemental evidence review tasks and meeting support. No foundation or industry support was accepted.

The Opioid Guideline Workgroup (OGW) members disclose that they have no financial conflicts of interest. Experts disclose the following activities related to the content of this guideline: Anne Burns discloses that she participated in a congressional briefing sponsored by Reps. Carter and DeSaulnier on the pharmacist's role of furnishing Naloxone and that she participates on the National Advisory Board for the Prescription Drug Abuse and Heroin Summit. Chinazo Cunningham discloses that her husband is employed by Quest Diagnostics and Dr. Cunningham was recused from any discussion related to urine drug testing. Traci Green discloses that she was previously employed by Inflexxion, a small business that conducts Small Business Innovation Research on behavioral interventions for behavioral health and chronic pain and created several psychometric tools for conducting risk assessment for prescription opioid abuse potential. Dr. Green also discloses that while at the hospital where she is employed, she provided consultation to Purdue Pharma Ltd to design overdose prevention brochures for persons who use diverted prescription opioids non-medically with an emphasis on persons who inject prescription drugs, and not for patients using opioid therapy for pain. Dr. Green was recused from any discussion related to risk assessment tools and patient education materials. Erin Krebs discloses that she served on the CDC Opioid Prescribing Guideline CEG. Christina Porucznik discloses that she served on the CDC Opioid Prescribing Guideline CEG. Greg Terman discloses that he serves as the President of the American Pain Society. Mark Wallace discloses that he served on a Kempharma advisory panel for an abuse-deterrent hydrocodone formulation to treat acute postoperative pain and Dr. Wallace was recused form any discussion related to abuse-deterrent drugs.

The NCIPC Board of Scientific Counselors (BSC) members disclose that they have no financial conflicts of interest. Two BSC members, Traci Green and Christina Porucznik, served on the Opioid Guideline Workgroup. Traci Green discloses that she was previously employed by Inflexxion, a small business that conducts Small Business Innovation Research on behavioral interventions for behavioral health and chronic pain and created several psychometric tools for conducting risk assessment for prescription opioid abuse potential. Dr. Green also discloses that while at the hospital where she is employed, she provided consultation to Purdue Pharma Ltd to design overdose prevention brochures for persons who use diverted prescription opioids non-medically with an emphasis on persons who inject prescription drugs, and not for patients using opioid therapy for pain. Dr. Green was recused from any discussion related to risk assessment tools and patient education materials. Christina Porucznik discloses that she served on the CDC Opioid Prescribing Guideline CEG.

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# CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

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## Summary

*This guideline provides recommendations for primary care clinicians who are prescribing opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care. The guideline addresses 1) when to initiate or continue opioids for chronic pain; 2) opioid selection, dosage, duration, follow-up, and discontinuation; and 3) assessing risk and addressing harms of opioid use. CDC developed the guideline using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework, and recommendations are made on the basis of a systematic review of the scientific evidence while considering benefits and harms, values and preferences, and resource allocation. CDC obtained input from experts, stakeholders, the public, peer reviewers, and a federally chartered advisory committee. It is important that patients receive appropriate pain treatment with careful consideration of the benefits and risks of treatment options. This guideline is intended to improve communication between clinicians and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death. CDC has provided a checklist for prescribing opioids for chronic pain (http://stacks.cdc.gov/view/cdc/38025) as well as a website (http://www.cdc.gov/drugoverdose/prescribingresources.html) with additional tools to guide clinicians in implementing the recommendations.*

## Introduction

### Background

Opioids are commonly prescribed for pain. An estimated 20% of patients presenting to physician offices with noncancer pain symptoms or pain-related diagnoses (including acute and chronic pain) receive an opioid prescription (*1*). In 2012, health care providers wrote 259 million prescriptions for opioid pain medication, enough for every adult in the United States to have a bottle of pills (*2*). Opioid prescriptions per capita increased 7.3% from 2007 to 2012, with opioid prescribing rates increasing more for family practice, general practice, and internal medicine compared with other specialties (*3*). Rates of opioid prescribing vary greatly across states in ways that cannot be explained by the underlying health status of the population, highlighting the lack of consensus among clinicians on how to use opioid pain medication (*2*).

Prevention, assessment, and treatment of chronic pain are challenges for health providers and systems. Pain might go unrecognized, and patients, particularly members of racial and ethnic minority groups, women, the elderly, persons with cognitive impairment, and those with cancer and at the end of life, can be at risk for inadequate pain treatment (*4*). Patients can experience persistent pain that is not well controlled. There are clinical, psychological, and social consequences associated with chronic pain including limitations in complex activities, lost work productivity, reduced quality of life, and stigma, emphasizing the importance of appropriate and compassionate patient care (*4*). Patients should receive appropriate pain treatment based on a careful consideration of the benefits and risks of treatment options.

Chronic pain has been variably defined but is defined within this guideline as pain that typically lasts >3 months or past the time of normal tissue healing (*5*). Chronic pain can be the result of an underlying medical disease or condition, injury, medical treatment, inflammation, or an unknown cause (*4*). Estimates of the prevalence of chronic pain vary, but it is clear that the number of persons experiencing chronic pain in the United States is substantial. The 1999–2002 National Health and Nutrition Examination Survey estimated that 14.6% of adults have current widespread or localized pain lasting at least 3 months (*6*). Based on a survey conducted during 2001–2003 (*7*), the overall prevalence of common, predominantly musculoskeletal pain conditions (e.g., arthritis, rheumatism, chronic back or neck problems, and frequent severe headaches) was estimated at 43% among adults in the

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United States, although minimum duration of symptoms was not specified. Most recently, analysis of data from the 2012 National Health Interview Study showed that 11.2% of adults report having daily pain (*8*). Clinicians should consider the full range of therapeutic options for the treatment of chronic pain. However, it is hard to estimate the number of persons who could potentially benefit from opioid pain medication long term. Evidence supports short-term efficacy of opioids for reducing pain and improving function in noncancer nociceptive and neuropathic pain in randomized clinical trials lasting primarily ≤12 weeks (*9*,*10*), and patients receiving opioid therapy for chronic pain report some pain relief when surveyed (*11*–*13*). However, few studies have been conducted to rigorously assess the long-term benefits of opioids for chronic pain (pain lasting >3 months) with outcomes examined at least 1 year later (*14*). On the basis of data available from health systems, researchers estimate that 9.6–11.5 million adults, or approximately 3%–4% of the adult U.S. population, were prescribed long-term opioid therapy in 2005 (*15*).

Opioid pain medication use presents serious risks, including overdose and opioid use disorder. From 1999 to 2014, more than 165,000 persons died from overdose related to opioid pain medication in the United States (*16*). In the past decade, while the death rates for the top leading causes of death such as heart disease and cancer have decreased substantially, the death rate associated with opioid pain medication has increased markedly (*17*). Sales of opioid pain medication have increased in parallel with opioid-related overdose deaths (*18*). The Drug Abuse Warning Network estimated that >420,000 emergency department visits were related to the misuse or abuse of narcotic pain relievers in 2011, the most recent year for which data are available (*19*). Although clinical criteria have varied over time, opioid use disorder is a problematic pattern of opioid use leading to clinically significant impairment or distress. This disorder is manifested by specific criteria such as unsuccessful efforts to cut down or control use and use resulting in social problems and a failure to fulfill major role obligations at work, school, or home (*20*). This diagnosis has also been referred to as "abuse or dependence" and "addiction" in the literature, and is different from tolerance (diminished response to a drug with repeated use) and physical dependence (adaptation to a drug that produces symptoms of withdrawal when the drug is stopped), both of which can exist without a diagnosed disorder. In 2013, on the basis of DSM-IV diagnosis criteria, an estimated 1.9 million persons abused or were dependent on prescription opioid pain medication (*21*). Having a history of a prescription for an opioid pain medication increases the risk for overdose and opioid use disorder (*22*–*24*), highlighting the value of guidance on safer prescribing practices for clinicians. For example, a recent study of patients aged 15–64 years receiving opioids for chronic noncancer pain and followed for up to 13 years revealed that one in 550 patients died from opioid-related overdose at a median of 2.6 years from their first opioid prescription, and one in 32 patients who escalated to opioid dosages >200 morphine milligram equivalents (MME) died from opioid-related overdose (*25*).

This guideline provides recommendations for the prescribing of opioid pain medication by primary care clinicians for chronic pain (i.e., pain conditions that typically last >3 months or past the time of normal tissue healing) in outpatient settings outside of active cancer treatment, palliative care, and end-of-life care. Although the guideline does not focus broadly on pain management, appropriate use of long-term opioid therapy must be considered within the context of all pain management strategies (including nonopioid pain medications and nonpharmacologic treatments). CDC's recommendations are made on the basis of a systematic review of the best available evidence, along with input from experts, and further review and deliberation by a federally chartered advisory committee. The guideline is intended to ensure that clinicians and patients consider safer and more effective treatment, improve patient outcomes such as reduced pain and improved function, and reduce the number of persons who develop opioid use disorder, overdose, or experience other adverse events related to these drugs. Clinical decision making should be based on a relationship between the clinician and patient, and an understanding of the patient's clinical situation, functioning, and life context. The recommendations in the guideline are voluntary, rather than prescriptive standards. They are based on emerging evidence, including observational studies or randomized clinical trials with notable limitations. Clinicians should consider the circumstances and unique needs of each patient when providing care.

## Rationale

Primary care clinicians report having concerns about opioid pain medication misuse, find managing patients with chronic pain stressful, express concern about patient addiction, and report insufficient training in prescribing opioids (*26*). Across specialties, physicians believe that opioid pain medication can be effective in controlling pain, that addiction is a common consequence of prolonged use, and that long-term opioid therapy often is overprescribed for patients with chronic noncancer pain (*27*). These attitudes and beliefs, combined with increasing trends in opioid-related overdose, underscore the need for better clinician guidance on opioid prescribing. Clinical practice guidelines focused on prescribing can improve clinician knowledge, change prescribing practices (*28*), and ultimately benefit patient health.

Professional organizations, states, and federal agencies (e.g., the American Pain Society/American Academy of Pain Medicine, 2009; the Washington Agency Medical Directors Group, 2015; and the U.S. Department of Veterans Affairs/Department of Defense, 2010) have developed guidelines for opioid prescribing (*29–31*). Existing guidelines share some common elements, including dosing thresholds, cautious titration, and risk mitigation strategies such as using risk assessment tools, treatment agreements, and urine drug testing. However, there is considerable variability in the specific recommendations (e.g., range of dosing thresholds of 90 MME/day to 200 MME/day), audience (e.g., primary care clinicians versus specialists), use of evidence (e.g., systematic review, grading of evidence and recommendations, and role of expert opinion), and rigor of methods for addressing conflict of interest (*32*). Most guidelines, especially those that are not based on evidence from scientific studies published in 2010 or later, also do not reflect the most recent scientific evidence about risks related to opioid dosage.

This CDC guideline offers clarity on recommendations based on the most recent scientific evidence, informed by expert opinion and stakeholder and public input. Scientific research has identified high-risk prescribing practices that have contributed to the overdose epidemic (e.g., high-dose prescribing, overlapping opioid and benzodiazepine prescriptions, and extended-release/long-acting [ER/LA] opioids for acute pain) (*24*,*33*,*34*). Using guidelines to address problematic prescribing has the potential to optimize care and improve patient safety based on evidence-based practice (*28*), as well as reverse the cycle of opioid pain medication misuse that contributes to the opioid overdose epidemic.

## Scope and Audience

This guideline is intended for primary care clinicians (e.g., family physicians and internists) who are treating patients with chronic pain (i.e., pain lasting >3 months or past the time of normal tissue healing) in outpatient settings. Prescriptions by primary care clinicians account for nearly half of all dispensed opioid prescriptions, and the growth in prescribing rates among these clinicians has been above average (*3*). Primary care clinicians include physicians as well as nurse practitioners and physician assistants. Although the focus is on primary care clinicians, because clinicians work within team-based care, the recommendations refer to and promote integrated pain management and collaborative working relationships with other providers (e.g., behavioral health providers, pharmacists, and pain management specialists). Although the transition from use of opioid therapy for acute pain to use for chronic pain is hard to predict and identify, the guideline is intended to inform clinicians who are considering prescribing opioid pain medication for painful conditions that can or have become chronic.

This guideline is intended to apply to patients aged ≥18 years with chronic pain outside of palliative and end-of-life care. For this guideline, palliative care is defined in a manner consistent with that of the Institute of Medicine as care that provides relief from pain and other symptoms, supports quality of life, and is focused on patients with serious advanced illness. Palliative care can begin early in the course of treatment for any serious illness that requires excellent management of pain or other distressing symptoms (*35*). End-of-life care is defined as care for persons with a terminal illness or at high risk for dying in the near future in hospice care, hospitals, long-term care settings, or at home. Patients within the scope of this guideline include cancer survivors with chronic pain who have completed cancer treatment, are in clinical remission, and are under cancer surveillance only. The guideline is not intended for patients undergoing active cancer treatment, palliative care, or end-of-life care because of the unique therapeutic goals, ethical considerations, opportunities for medical supervision, and balance of risks and benefits with opioid therapy in such care.

The recommendations address the use of opioid pain medication in certain special populations (e.g., older adults and pregnant women) and in populations with conditions posing special risks (e.g., a history of substance use disorder). The recommendations do not address the use of opioid pain medication in children or adolescents aged <18 years. The available evidence concerning the benefits and harms of long-term opioid therapy in children and adolescents is limited, and few opioid medications provide information on the label regarding safety and effectiveness in pediatric patients. However, observational research shows significant increases in opioid prescriptions for pediatric populations from 2001 to 2010 (*36*), and a large proportion of adolescents are commonly prescribed opioid pain medications for conditions such as headache and sports injuries (e.g., in one study, 50% of adolescents presenting with headache received a prescription for an opioid pain medication [*37*,*38*]). Adolescents who misuse opioid pain medication often misuse medications from their own previous prescriptions (*39*), with an estimated 20% of adolescents with currently prescribed opioid medications reporting using them intentionally to get high or increase the effects of alcohol or other drugs (*40*). Use of prescribed opioid pain medication before high school graduation is associated with a 33% increase in the risk of later opioid misuse (*41*). Misuse of opioid pain medications in adolescence strongly predicts later onset of heroin use (*42*). Thus, risk of opioid medication use in pediatric populations is of great concern. Additional clinical trial and observational research is needed,

and encouraged, to inform development of future guidelines for this critical population.

The recommendations are not intended to provide guidance on use of opioids as part of medication-assisted treatment for opioid use disorder. Some of the recommendations might be relevant for acute care settings or other specialists, such as emergency physicians or dentists, but use in these settings or by other specialists is not the focus of this guideline. Readers are referred to other sources for prescribing recommendations within acute care settings and in dental practice, such as the American College of Emergency Physicians' guideline for prescribing of opioids in the emergency department (*43*); the American Society of Anesthesiologists' guideline for acute pain management in the perioperative setting (*44*); the Washington Agency Medical Directors' Group Interagency Guideline on Prescribing Opioids for Pain, Part II: Prescribing Opioids in the Acute and Subacute Phase (*30*); and the Pennsylvania Guidelines on the Use of Opioids in Dental Practice (*45*). In addition, given the challenges of managing the painful complications of sickle cell disease, readers are referred to the NIH National Heart, Lung, and Blood Institute's Evidence Based Management of Sickle Cell Disease Expert Panel Report for management of sickle cell disease (*46*).

# Guideline Development Methods

## Guideline Development Using the Grading of Recommendations Assessment, Development, and Evaluation Method

CDC developed this guideline using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method (http://www.gradeworkinggroup.org). This method specifies the systematic review of scientific evidence and offers a transparent approach to grading quality of evidence and strength of recommendations. The method has been adapted by the CDC Advisory Committee on Immunization Practices (ACIP) (*47*). CDC has applied the ACIP translation of the GRADE framework in this guideline. Within the ACIP GRADE framework, the body of evidence is categorized in a hierarchy. This hierarchy reflects degree of confidence in the effect of a clinical action on health outcomes. The categories include type 1 evidence (randomized clinical trials or overwhelming evidence from observational studies), type 2 evidence (randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies), type 3 evidence (observational studies or randomized clinical trials with notable limitations), and type 4 evidence (clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations). Type of evidence is categorized by study design as well as limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and a constellation of plausible biases that could change observations of effects. Type 1 evidence indicates that one can be very confident that the true effect lies close to that of the estimate of the effect; type 2 evidence means that the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; type 3 evidence means that confidence in the effect estimate is limited and the true effect might be substantially different from the estimate of the effect; and type 4 evidence indicates that one has very little confidence in the effect estimate, and the true effect is likely to be substantially different from the estimate of the effect (*47*,*48*). When no studies are present, evidence is considered to be insufficient. The ACIP GRADE framework places recommendations in two categories, Category A and Category B. Four major factors determine the category of the recommendation: the quality of evidence, the balance between desirable and undesirable effects, values and preferences, and resource allocation (cost). Category A recommendations apply to all persons in a specified group and indicate that most patients should receive the recommended course of action. Category B recommendations indicate that there should be individual decision making; different choices will be appropriate for different patients, so clinicians must help patients arrive at a decision consistent with patient values and preferences, and specific clinical situations (*47*). According to the GRADE methodology, a particular quality of evidence does not necessarily imply a particular strength of recommendation (*48*–*50*). Category A recommendations can be made based on type 3 or type 4 evidence when the advantages of a clinical action greatly outweigh the disadvantages based on a consideration of benefits and harms, values and preferences, and costs. Category B recommendations are made when the advantages and disadvantages of a clinical action are more balanced. GRADE methodology is discussed extensively elsewhere (*47*,*51*). The U.S. Preventive Services Task Force (USPSTF) follows different methods for developing and categorizing recommendations (http://www.uspreventiveservicestaskforce.org). USPSTF recommendations focus on preventive services and are categorized as A, B, C, D, and I. Under the Affordable Care Act, all "nongrandfathered" health plans (that is, those health plans not in existence prior to March 23, 2010 or those with significant changes to their coverage) and expanded Medicaid plans are required to cover

preventive services recommended by USPSTF with a category A or B rating with no cost sharing. The coverage requirements went into effect September 23, 2010. Similar requirements are in place for vaccinations recommended by ACIP, but do not exist for other recommendations made by CDC, including recommendations within this guideline.

A previously published systematic review sponsored by the Agency for Healthcare Research and Quality (AHRQ) on the effectiveness and risks of long-term opioid treatment of chronic pain (*14*,*52*) initially served to directly inform the recommendation statements. This systematic clinical evidence review addressed the effectiveness of long-term opioid therapy for outcomes related to pain, function, and quality of life; the comparative effectiveness of different methods for initiating and titrating opioids; the harms and adverse events associated with opioids; and the accuracy of risk-prediction instruments and effectiveness of risk mitigation strategies on outcomes related to overdose, addiction, abuse, or misuse. For the current guideline development, CDC conducted additional literature searches to update the evidence review to include more recently available publications and to answer an additional clinical question about the effect of opioid therapy for acute pain on long-term use. More details about the literature search strategies and GRADE methods applied are provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026). CDC developed GRADE evidence tables to illustrate the quality of the evidence for each clinical question.

As identified in the AHRQ-sponsored clinical evidence review, the overall evidence base for the effectiveness and risks of long-term opioid therapy is low in quality per the GRADE criteria. Thus, contextual evidence is needed to provide information about the benefits and harms of nonpharmacologic and nonopioid pharmacologic therapy and the epidemiology of opioid pain medication overdose and inform the recommendations. Further, as elucidated by the GRADE Working Group, supplemental information on clinician and patient values and preferences and resource allocation can inform judgments of benefits and harms and be helpful for translating the evidence into recommendations. CDC conducted a contextual evidence review to supplement the clinical evidence review based on systematic searches of the literature. The review focused on the following four areas: effectiveness of nonpharmacologic and nonopioid pharmacologic treatments; benefits and harms related to opioid therapy (including additional studies not included in the clinical evidence review such as studies that evaluated outcomes at any duration or used observational study designs related to specific opioid pain medications, high-dose opioid therapy, co-prescription of opioids with other controlled substances, duration of opioid use, special populations, risk stratification/mitigation approaches, and effectiveness of treatments for addressing potential harms of opioid therapy); clinician and patient values and preferences; and resource allocation. CDC constructed narrative summaries of this contextual evidence and used the information to support the clinical recommendations. More details on methods for the contextual evidence review are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027).

On the basis of a review of the clinical and contextual evidence (review methods are described in more detail in subsequent sections of this report), CDC drafted recommendation statements focused on determining when to initiate or continue opioids for chronic pain; opioid selection, dosage, duration, follow-up, and discontinuation; and assessing risk and addressing harms of opioid use. To help assure the draft guideline's integrity and credibility, CDC then began a multistep review process to obtain input from experts, stakeholders, and the public to help refine the recommendations.

## Solicitation of Expert Opinion

CDC sought the input of experts to assist in reviewing the evidence and providing perspective on how CDC used the evidence to develop the draft recommendations. These experts, referred to as the "Core Expert Group" (CEG) included subject matter experts, representatives of primary care professional societies and state agencies, and an expert in guideline development methodology.* CDC identified subject matter experts with high scientific standing; appropriate academic and clinical training and relevant clinical experience; and proven scientific excellence in opioid prescribing, substance use disorder treatment, and pain management. CDC identified representatives from leading primary care professional organizations to represent the audience for this guideline. Finally, CDC identified state agency officials and representatives based on their experience with state guidelines for opioid prescribing that were developed with multiple agency stakeholders and informed by scientific literature and existing evidence-based guidelines.

Prior to their participation, CDC asked potential experts to reveal possible conflicts of interest such as financial relationships with industry, intellectual preconceptions, or previously stated public positions. Experts could not serve if they had conflicts that might have a direct and predictable effect on the recommendations. CDC excluded experts who had a financial or promotional relationship with a company

* A list of the members appears at the end of this report. The recommendations and all statements included in this guideline are those of CDC and do not necessarily represent the official position of any persons or organizations providing comments on the draft guideline.

that makes a product that might be affected by the guideline. CDC reviewed potential nonfinancial conflicts carefully (e.g., intellectual property, travel, public statements or positions such as congressional testimony) to determine if the activities would have a direct and predictable effect on the recommendations. CDC determined the risk of these types of activities to be minimal for the identified experts. All experts completed a statement certifying that there was no potential or actual conflict of interest. Activities that did not pose a conflict (e.g., participation in Food and Drug Administration [FDA] activities or other guideline efforts) are disclosed.

CDC provided to each expert written summaries of the scientific evidence (both the clinical and contextual evidence reviews conducted for this guideline) and CDC's draft recommendation statements. Experts provided individual ratings for each draft recommendation statement based on the balance of benefits and harms, evidence strength, certainty of values and preferences, cost, recommendation strength, rationale, importance, clarity, and ease of implementation. CDC hosted an in-person meeting of the experts that was held on June 23–24, 2015, in Atlanta, Georgia, to seek their views on the evidence and draft recommendations and to better understand their premeeting ratings. CDC sought the experts' individual opinions at the meeting. Although there was widespread agreement on some of the recommendations, there was disagreement on others. Experts did not vote on the recommendations or seek to come to a consensus. Decisions about recommendations to be included in the guideline, and their rationale, were made by CDC. After revising the guideline, CDC sent written copies of it to each of the experts for review and asked for any additional comments; CDC reviewed these written comments and considered them when making further revisions to the draft guideline. The experts have not reviewed the final version of the guideline.

## Federal Partner Engagement

Given the scope of this guideline and the interest of agencies across the federal government in appropriate pain management, opioid prescribing, and related outcomes, CDC invited its National Institute of Occupational Safety and Health and CDC's federal partners to observe the expert meeting, provide written comments on the full draft guideline after the meeting, and review the guideline through an agency clearance process; CDC reviewed comments and incorporated changes. Interagency collaboration will be critical for translating these recommendations into clinical practice. Federal partners included representatives from the Substance Abuse and Mental Health Services Administration, the National Institute on Drug Abuse, FDA, the U.S. Department of Veterans Affairs, the U.S. Department of Defense, the Office of the National Coordinator for Health Information Technology, the Centers for Medicare and Medicaid Services, the Health Resources and Services Administration, AHRQ, and the Office of National Drug Control Policy.

## Stakeholder Comment

Given the importance of the guideline for a wide variety of stakeholders, CDC also invited review from a Stakeholder Review Group (SRG) to provide comment so that CDC could consider modifications that would improve the recommendations' specificity, applicability, and ease of implementation. The SRG included representatives from professional organizations that represent specialties that commonly prescribe opioids (e.g., pain medicine, physical medicine and rehabilitation), delivery systems within which opioid prescribing occurs (e.g., hospitals), and representation from community organizations with interests in pain management and opioid prescribing.* Representatives from each of the SRG organizations were provided a copy of the guideline for comment. Each of these representatives provided written comments. Once input was received from the full SRG, CDC reviewed all comments and carefully considered them when revising the draft guideline.

## Constituent Engagement

To obtain initial perspectives from constituents on the recommendation statements, including clinicians and prospective patients, CDC convened a constituent engagement webinar and circulated information about the webinar in advance through announcements to partners. CDC hosted the webinar on September 16 and 17, 2015, provided information about the methodology for developing the guideline, and presented the key recommendations. A fact sheet was posted on the CDC Injury Center website (http://www.cdc.gov/injury) summarizing the guideline development process and clinical practice areas addressed in the guideline; instructions were included on how to submit comments via email. CDC received comments during and for 2 days following the first webinar. Over 1,200 constituent comments were received. Comments were reviewed and carefully considered when revising the draft guideline.

## Peer Review

Per the final information quality bulletin for peer review (https://www.whitehouse.gov/sites/default/files/omb/memoranda/fy2005/m05-03.pdf), peer review requirements applied to this guideline because it provides influential

scientific information that could have a clear and substantial impact on public- and private-sector decisions. Three experts independently reviewed the guideline to determine the reasonableness and strength of recommendations; the clarity with which scientific uncertainties were clearly identified; and the rationale, importance, clarity, and ease of implementation of the recommendations.* CDC selected peer reviewers based on expertise, diversity of scientific viewpoints, and independence from the guideline development process. CDC assessed and managed potential conflicts of interest using a process similar to the one as described for solicitation of expert opinion. No financial interests were identified in the disclosure and review process, and nonfinancial activities were determined to be of minimal risk; thus, no significant conflict of interest concerns were identified. CDC placed the names of peer reviewers on the CDC and the National Center for Injury Prevention and Control Peer Review Agenda websites that are used to provide information about the peer review of influential documents. CDC reviewed peer review comments and revised the draft guideline accordingly.

## Public Comment

To obtain comments from the public on the full guideline, CDC published a notice in the *Federal Register* (80 FR 77351) announcing the availability of the guideline and the supporting clinical and contextual evidence reviews for public comment. The comment period closed January 13, 2016. CDC received more than 4,350 comments from the general public, including patients with chronic pain, clinicians, families who have lost loved ones to overdose, medical associations, professional organizations, academic institutions, state and local governments, and industry. CDC reviewed each of the comments and carefully considered them when revising the draft guideline.

## Federal Advisory Committee Review and Recommendation

The National Center for Injury Prevention and Control (NCIPC) Board of Scientific Counselors (BSC) is a federal advisory committee that advises and makes recommendations to the Secretary of the Department of Health and Human Services, the Director of CDC, and the Director of NCIPC.* The BSC makes recommendations regarding policies, strategies, objectives, and priorities, and reviews progress toward injury and violence prevention. CDC sought the BSC's advice on the draft guideline. BSC members are special government employees appointed as CDC advisory committee members; as such, all members completed an OGE Form 450 to disclose relevant interests. BSC members also reported on their disclosures during meetings. Disclosures for the BSC are reported in the guideline.

To assist in guideline review, on December 14, 2015, via Federal Register notice, CDC announced the intent to form an Opioid Guideline Workgroup (OGW) to provide observations on the draft guideline to the BSC. CDC provided the BSC with the draft guideline as well as summaries of comments provided to CDC by stakeholders, constituents, and peer reviewers, and edits made to the draft guideline in response. During an open meeting held on January 7, 2016, the BSC recommended the formation of the OGW. The OGW included a balance of perspectives from audiences directly affected by the guideline, audiences that would be directly involved with implementing the recommendations, and audiences qualified to provide representation. The OGW comprised clinicians, subject matter experts, and a patient representative, with the following perspectives represented: primary care, pain medicine, public health, behavioral health, substance abuse treatment, pharmacy, patients, and research.* Additional sought-after attributes were appropriate academic and clinical training and relevant clinical experience; high scientific standing; and knowledge of the patient, clinician, and caregiver perspectives. In accordance with CDC policy, two BSC committee members also served as OGW members, with one serving as the OGW Chair. The professional credentials and interests of OGW members were carefully reviewed to identify possible conflicts of interest such as financial relationships with industry, intellectual preconceptions, or previously stated public positions. Only OGW members whose interests were determined to be minimal were selected. When an activity was perceived as having the potential to affect a specific aspect of the recommendations, the activity was disclosed, and the OGW member was recused from discussions related to that specific aspect of the recommendations (e.g., urine drug testing and abuse-deterrent formulations). Disclosures for the OGW are reported. CDC and the OGW identified ad-hoc consultants to supplement the workgroup expertise, when needed, in the areas of pediatrics, occupational medicine, obstetrics and gynecology, medical ethics, addiction psychiatry, physical medicine and rehabilitation, guideline development methodology, and the perspective of a family member who lost a loved one to opioid use disorder or overdose.

The BSC charged the OGW with reviewing the quality of the clinical and contextual evidence reviews and reviewing each of the recommendation statements and accompanying rationales. For each recommendation statement, the OGW considered the quality of the evidence, the balance of benefits and risks, the values and preferences of clinicians and patients, the cost feasibility, and the category designation

of the recommendation (A or B). The OGW also reviewed supplementary documents, including input provided by the CEG, SRG, peer reviewers, and the public. OGW members discussed the guideline accordingly during virtual meetings and drafted a summary report of members' observations, including points of agreement and disagreement, and delivered the report to the BSC.

NCIPC announced an open meeting of the NCIPC BSC in the Federal Register on January 11, 2015. The BSC met on January 28, 2016, to discuss the OGW report and deliberate on the draft guideline itself. Members of the public provided comments at this meeting. After discussing the OGW report, deliberating on specific issues about the draft guideline identified at the meeting, and hearing public comment, the BSC voted unanimously: to support the observations made by the OGW; that CDC adopt the guideline recommendations that, according to the workgroup's report, had unanimous or majority support; and that CDC further consider the guideline recommendations for which the group had mixed opinions. CDC carefully considered the OGW observations, public comments, and BSC recommendations, and revised the guideline in response.

# Summary of the Clinical Evidence Review

## Primary Clinical Questions

CDC conducted a clinical systematic review of the scientific evidence to identify the effectiveness, benefits, and harms of long-term opioid therapy for chronic pain, consistent with the GRADE approach (*47*,*48*). Long-term opioid therapy is defined as use of opioids on most days for >3 months. A previously published AHRQ-funded systematic review on the effectiveness and risks of long-term opioid therapy for chronic pain comprehensively addressed four clinical questions (*14*,*52*). CDC, with the assistance of a methodology expert, searched the literature to identify newly published studies on these four original questions. Because long-term opioid use might be affected by use of opioids for acute pain, CDC subsequently developed a fifth clinical question (last in the series below), and in collaboration with a methodologist conducted a systematic review of the scientific evidence to address it. In brief, five clinical questions were addressed:

- The effectiveness of long-term opioid therapy versus placebo, no opioid therapy, or nonopioid therapy for long term (≥1 year) outcomes related to pain, function, and quality of life, and how effectiveness varies according to the type/cause of pain, patient demographics, and patient comorbidities (Key Question [KQ] 1).
- The risks of opioids versus placebo or no opioids on abuse, addiction, overdose, and other harms, and how harms vary according to the type/cause of pain, patient demographics, patient comorbidities, and dose (KQ2).
- The comparative effectiveness of opioid dosing strategies (different methods for initiating and titrating opioids; immediate-release versus ER/LA opioids; different ER/LA opioids; immediate-release plus ER/LA opioids versus ER/LA opioids alone; scheduled, continuous versus as-needed dosing; dose escalation versus dose maintenance; opioid rotation versus maintenance; different strategies for treating acute exacerbations of chronic pain; decreasing opioid doses or tapering off versus continuation; and different tapering protocols and strategies) (KQ3).
- The accuracy of instruments for predicting risk for opioid overdose, addiction, abuse, or misuse; the effectiveness of risk mitigation strategies (use of risk prediction instruments); effectiveness of risk mitigation strategies including opioid management plans, patient education, urine drug testing, prescription drug monitoring program (PDMP) data, monitoring instruments, monitoring intervals, pill counts, and abuse-deterrent formulations for reducing risk for opioid overdose, addiction, abuse, or misuse; and the comparative effectiveness of treatment strategies for managing patients with addiction (KQ4).
- The effects of prescribing opioid therapy versus not prescribing opioid therapy for acute pain on long-term use (KQ5).

The review was focused on the effectiveness of long-term opioid therapy on long-term (>1 year) outcomes related to pain, function, and quality of life to ensure that findings are relevant to patients with chronic pain and long-term opioid prescribing. The effectiveness of short-term opioid therapy has already been established (*10*). However, opioids have unique effects such as tolerance and physical dependence that might influence assessments of benefit over time. These effects raise questions about whether findings on short-term effectiveness of opioid therapy can be extrapolated to estimate benefits of long-term therapy for chronic pain. Thus, it is important to consider studies that provide data on long-term benefit. For certain opioid-related harms (overdose, fractures, falls, motor vehicle crashes), observational studies were included with outcomes measured at shorter intervals because such outcomes can occur early during opioid therapy, and such harms are not captured well in short-term clinical trials. A detailed listing of the key questions is provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026).

## Clinical Evidence Systematic Review Methods

Complete methods and data for the 2014 AHRQ report, upon which this updated systematic review is based, have been published previously (*14*,*52*). Study authors developed the protocol using a standardized process (*53*) with input from experts and the public and registered the protocol in the PROSPERO database (*54*). For the 2014 AHRQ report, a research librarian searched MEDLINE, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, PsycINFO, and CINAHL for English-language articles published January 2008 through August 2014, using search terms for opioid therapy, specific opioids, chronic pain, and comparative study designs. Also included were relevant studies from an earlier review (*10*) in which searches were conducted without a date restriction, reference lists were reviewed, and ClinicalTrials.gov was searched. CDC updated the AHRQ literature search using the same search strategies as in the original review including studies published before April, 2015. Seven additional studies met inclusion criteria and were added to the review. CDC used the GRADE approach outlined in the ACIP Handbook for Developing Evidence-Based Recommendations (*47*) to rate the quality of evidence for the full body of evidence (evidence from the 2014 AHRQ review plus the update) for each clinical question. Evidence was categorized into the following types: type 1 (randomized clinical trials or overwhelming evidence from observational studies), type 2 (randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies), type 3 (observational studies, or randomized clinical trials with notable limitations), or type 4 (clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations). When no studies were present, evidence was considered to be insufficient. Per GRADE methods, type of evidence was categorized by study design as well as a function of limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and constellation of plausible biases that could change effects. Results were synthesized qualitatively, highlighting new evidence identified during the update process. Meta-analysis was not attempted due to the small numbers of studies, variability in study designs and clinical heterogeneity, and methodological shortcomings of the studies. More detailed information about data sources and searches, study selection, data extraction and quality assessment, data synthesis, and update search yield and new evidence for the current review is provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026).

## Summary of Findings for Clinical Questions

The main findings of this updated review are consistent with the findings of the 2014 AHRQ report (*14*). In summary, evidence on long-term opioid therapy for chronic pain outside of end-of-life care remains limited, with insufficient evidence to determine long-term benefits versus no opioid therapy, though evidence suggests risk for serious harms that appears to be dose-dependent. These findings supplement findings from a previous review of the effectiveness of opioids for adults with chronic noncancer pain. In this previous review, based on randomized trials predominantly ≤12 weeks in duration, opioids were found to be moderately effective for pain relief, with small benefits for functional outcomes; although estimates vary, based on uncontrolled studies, a high percentage of patients discontinued long-term opioid use because of lack of efficacy and because of adverse events (*10*).

The GRADE evidence summary with type of evidence ratings for the five clinical questions for the current evidence review are outlined (Table 1). This summary is based on studies included in the AHRQ 2014 review (35 studies) plus additional studies identified in the updated search (seven studies). Additional details on findings from the original review are provided in the full 2014 AHRQ report (*14*,*52*). Full details on the clinical evidence review findings supporting this guideline are provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026).

### Effectiveness

For KQ1, no study of opioid therapy versus placebo, no opioid therapy, or nonopioid therapy for chronic pain evaluated long-term (≥1 year) outcomes related to pain, function, or quality of life. Most placebo-controlled randomized clinical trials were ≤6 weeks in duration. Thus, the body of evidence for KQ1 is rated as insufficient (0 studies contributing) (*14*).

### Harms

For KQ2, the body of evidence is rated as type 3 (12 studies contributing; 11 from the original review plus one new study). One fair-quality cohort study found that long-term opioid therapy is associated with increased risk for an opioid abuse or dependence diagnosis (as defined by ICD-9-CM codes) versus no opioid prescription (*22*). Rates of opioid abuse or dependence diagnosis ranged from 0.7% with lower-dose (≤36 MME) chronic therapy to 6.1% with higher-dose (≥120 MME) chronic therapy, versus 0.004% with no opioids prescribed. Ten fair-quality uncontrolled studies reported estimates of opioid abuse, addiction, and related outcomes (*55*–*65*). In primary care settings, prevalence of opioid dependence

(using DSM-IV criteria) ranged from 3% to 26% (*55*,*56*,*59*). In pain clinic settings, prevalence of addiction ranged from 2% to 14% (*57*,*58*,*60*,*61*,*63–65*).

Factors associated with increased risk for misuse included history of substance use disorder, younger age, major depression, and use of psychotropic medications (*55*,*62*). Two studies reported on the association between opioid use and risk for overdose (*66*,*67*). One large fair-quality retrospective cohort study found that recent opioid use was associated with increased risk for any overdose events and serious overdose events versus nonuse (*66*). It also found higher doses associated with increased risk. Relative to 1–19 MME/day, the adjusted hazard ratio (HR) for any overdose event (consisting of mostly nonfatal overdose) was 1.44 for 20 to 49 MME/day, 3.73 for 50–99 MME/day, and 8.87 for ≥100 MME/day. A similar pattern was observed for serious overdose. A good-quality population-based, nested case-control study also found a dose-dependent association with risk for overdose death (*67*). Relative to 1–19 MME/day, the adjusted odds ratio (OR) was 1.32 for 20–49 MME/day, 1.92 for 50–99 MME/day, 2.04 for 100–199 MME/day, and 2.88 for ≥200 MME/day.

Findings of increased fracture risk for current opioid use, versus nonuse, were mixed in two studies (*68*,*69*). Two studies found an association between opioid use and increased risk for cardiovascular events (*70*,*71*). Indirect evidence was found for endocrinologic harms (increased use of medications for erectile dysfunction or testosterone from one previously included study; laboratory-defined androgen deficiency from one newly reviewed study) (*72*,*73*). One study found that opioid dosages ≥20 MME/day were associated with increased odds of road trauma among drivers (*74*).

## Opioid Dosing Strategies

For KQ3, the body of evidence is rated as type 4 (14 studies contributing; 12 from the original review plus two new studies). For initiation and titration of opioids, the 2014 AHRQ report found insufficient evidence from three fair-quality, open-label trials to determine comparative effectiveness of ER/LA versus immediate-release opioids for titrating patients to stable pain control (*75*,*76*). One new fair-quality cohort study of Veterans Affairs patients found initiation of therapy with an ER/LA opioid associated with greater risk for nonfatal overdose than initiation with an immediate-release opioid, with risk greatest in the first 2 weeks after initiation of treatment (*77*).

For comparative effectiveness and harms of ER/LA opioids, the 2014 AHRQ report included three randomized, head-to-head trials of various ER/LA opioids that found no clear differences in 1-year outcomes related to pain or function (*78–80*) but had methodological shortcomings. A fair-quality retrospective cohort study based on national Veterans Health Administration system pharmacy data found that methadone was associated with lower overall risk for all-cause mortality versus morphine (*81*), and a fair-quality retrospective cohort study based on Oregon Medicaid data found no statistically significant differences between methadone and long-acting morphine in risk for death or overdose symptoms (*82*). However, a new observational study (*83*) found methadone associated with increased risk for overdose versus sustained-release morphine among Tennessee Medicaid patients. The observed inconsistency in study findings suggests that risks of methadone might vary in different settings as a function of different monitoring and management protocols, though more research is needed to understand factors associated with safer methadone prescribing.

For dose escalation, the 2014 AHRQ report included one fair-quality randomized trial that found no differences between more liberal dose escalation and maintenance of current doses after 12 months in pain, function, all-cause withdrawals, or withdrawals due to opioid misuse (*84*). However, the difference in opioid dosages prescribed at the end of the trial was relatively small (mean 52 MME/day with more liberal dosing versus 40 MME/day). Evidence on other comparisons related to opioid dosing strategies (ER/LA versus immediate-release opioids; immediate-release plus ER/LA opioids versus ER/LA opioids alone; scheduled continuous dosing versus as-needed dosing; or opioid rotation versus maintenance of current therapy; long-term effects of strategies for treating acute exacerbations of chronic pain) was not available or too limited to determine effects on long-term clinical outcomes. For example, evidence on the comparative effectiveness of opioid tapering or discontinuation versus maintenance, and of different opioid tapering strategies, was limited to small, poor-quality studies (*85–87*).

## Risk Assessment and Mitigation

For KQ4, the body of evidence is rated as type 3 for the accuracy of risk assessment tools and insufficient for the effectiveness of use of risk assessment tools and mitigation strategies in reducing harms (six studies contributing; four from the original review plus two new studies). The 2014 AHRQ report included four studies (*88–91*) on the accuracy of risk assessment instruments, administered prior to opioid therapy initiation, for predicting opioid abuse or misuse. Results for the Opioid Risk Tool (ORT) (*89–91*) were extremely inconsistent; evidence for other risk assessment instruments was very sparse, and studies had serious methodological shortcomings. One additional fair-quality (*92*) and one poor-quality (*93*) study identified for this update compared the predictive accuracy of the ORT, the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R), and the Brief Risk Interview.

For the ORT, sensitivity was 0.58 and 0.75 and specificity 0.54 and 0.86; for the SOAPP-R, sensitivity was 0.53 and 0.25 and specificity 0.62 and 0.73; and for the Brief Risk Interview, sensitivity was 0.73 and 0.83 and specificity 0.43 and 0.88. For the ORT, positive likelihood ratios ranged from noninformative (positive likelihood ratio close to 1) to moderately useful (positive likelihood ratio >5). The SOAPP-R was associated with noninformative likelihood ratios (estimates close to 1) in both studies.

No study evaluated the effectiveness of risk mitigation strategies (use of risk assessment instruments, opioid management plans, patient education, urine drug testing, use of PDMP data, use of monitoring instruments, more frequent monitoring intervals, pill counts, or use of abuse-deterrent formulations) for improving outcomes related to overdose, addiction, abuse, or misuse.

### Effects of Opioid Therapy for Acute Pain on Long-Term Use

For KQ5, the body of evidence is rated as type 3 (two new studies contributing). Two fair-quality retrospective cohort studies found opioid therapy prescribed for acute pain associated with greater likelihood of long-term use. One study evaluated opioid-naïve patients who had undergone low-risk surgery, such as cataract surgery and varicose vein stripping (*94*). Use of opioids within 7 days of surgery was associated with increased risk for use at 1 year. The other study found that among patients with a workers' compensation claim for acute low back pain, compared to patients who did not receive opioids early after injury (defined as use within 15 days following onset of pain), patients who did receive early opioids had an increased likelihood of receiving five or more opioid prescriptions 30–730 days following onset that increased with greater early exposure. Versus no early opioid use, the adjusted OR was 2.08 (95% CI = 1.55–2.78) for 1–140 MME/day and increased to 6.14 (95% confidence interval [CI] = 4.92–7.66) for ≥450 MME/day (*95*).

## Summary of the Contextual Evidence Review

### Primary Areas of Focus

Contextual evidence is complementary information that assists in translating the clinical research findings into recommendations. CDC conducted contextual evidence reviews on four topics to supplement the clinical evidence review findings:

- Effectiveness of nonpharmacologic (e.g., cognitive behavioral therapy [CBT], exercise therapy, interventional treatments, and multimodal pain treatment) and nonopioid pharmacologic treatments (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], antidepressants, and anticonvulsants), including studies of any duration.
- Benefits and harms of opioid therapy (including additional studies not included in the clinical evidence review, such as studies that were not restricted to patients with chronic pain, evaluated outcomes at any duration, performed ecological analyses, or used observational study designs other than cohort and case-cohort control studies) related to specific opioids, high-dose therapy, co-prescription with other controlled substances, duration of use, special populations, and potential usefulness of risk stratification/mitigation approaches, in addition to effectiveness of treatments associated with addressing potential harms of opioid therapy (opioid use disorder).
- Clinician and patient values and preferences related to opioids and medication risks, benefits, and use.
- Resource allocation including costs and economic efficiency of opioid therapy and risk mitigation strategies.

CDC also reviewed clinical guidelines that were relevant to opioid prescribing and could inform or complement the CDC recommendations under development (e.g., guidelines on nonpharmacologic and nonopioid pharmacologic treatments and guidelines with recommendations related to specific clinician actions such as urine drug testing or opioid tapering protocols).

## Contextual Evidence Review Methods

CDC conducted a contextual evidence review to assist in developing the recommendations by providing an assessment of the balance of benefits and harms, values and preferences, and cost, consistent with the GRADE approach. Given the public health urgency for developing opioid prescribing recommendations, a rapid review was required for the contextual evidence review for the current guideline. Rapid reviews are used when there is a need to streamline the systematic review process to obtain evidence quickly (*96*). Methods used to streamline the process include limiting searches by databases, years, and languages considered, and truncating quality assessment and data abstraction protocols. CDC conducted "rapid reviews" of the contextual evidence on nonpharmacologic and nonopioid pharmacologic treatments, benefits and harms, values and preferences, and resource allocation.

Detailed information about contextual evidence data sources and searches, inclusion criteria, study selection, and

data extraction and synthesis are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027). In brief, CDC conducted systematic literature searches to identify original studies, systematic reviews, and clinical guidelines, depending on the topic being searched. CDC also solicited publication referrals from subject matter experts. Given the need for a rapid review process, grey literature (e.g., literature by academia, organizations, or government in the forms of reports, documents, or proceedings not published by commercial publishers) was not systematically searched. Database sources, including MEDLINE, PsycINFO, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews, varied by topic. Multiple reviewers scanned study abstracts identified through the database searches and extracted relevant studies for review. CDC constructed narrative summaries and tables based on relevant articles that met inclusion criteria, which are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027).

Findings from the contextual reviews provide indirect evidence and should be interpreted accordingly. CDC did not formally rate the quality of evidence for the studies included in the contextual evidence review using the GRADE method. The studies that addressed benefits and harms, values and preferences, and resource allocation most often employed observational methods, used short follow-up periods, and evaluated selected samples. Therefore the strength of the evidence from these contextual review areas was considered to be low, comparable to type 3 or type 4 evidence. The quality of evidence for nonopioid pharmacologic and nonpharmacologic pain treatments was generally rated as moderate, comparable to type 2 evidence, in systematic reviews and clinical guidelines (e.g., for treatment of chronic neuropathic pain, low back pain, osteoarthritis, and fibromyalgia). Similarly, the quality of evidence on pharmacologic and psychosocial opioid use disorder treatment was generally rated as moderate, comparable to type 2 evidence, in systematic reviews and clinical guidelines.

## Summary of Findings for Contextual Areas

Full narrative reviews and tables that summarize key findings from the contextual evidence review are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027).

### Effectiveness of Nonpharmacologic and Nonopioid Pharmacologic Treatments

Several nonpharmacologic and nonopioid pharmacologic treatments have been shown to be effective in managing chronic pain in studies ranging in duration from 2 weeks to 6 months. For example, CBT that trains patients in behavioral techniques and helps patients modify situational factors and cognitive processes that exacerbate pain has small positive effects on disability and catastrophic thinking (*97*). Exercise therapy can help reduce pain and improve function in chronic low back pain (*98*), improve function and reduce pain in osteoarthritis of the knee (*99*) and hip (*100*), and improve well-being, fibromyalgia symptoms, and physical function in fibromyalgia (*101*). Multimodal and multidisciplinary therapies (e.g., therapies that combine exercise and related therapies with psychologically based approaches) can help reduce pain and improve function more effectively than single modalities (*102*,*103*). Nonopioid pharmacologic approaches used for pain include analgesics such as acetaminophen, NSAIDs, and cyclooxygenase 2 (COX-2) inhibitors; selected anticonvulsants; and selected antidepressants (particularly tricyclics and serotonin and norepinephrine reuptake inhibitors [SNRIs]). Multiple guidelines recommend acetaminophen as first-line pharmacotherapy for osteoarthritis (*104*–*109*) or for low back pain (*110*) but note that it should be avoided in liver failure and that dosage should be reduced in patients with hepatic insufficiency or a history of alcohol abuse (*109*). Although guidelines also recommend NSAIDs as first-line treatment for osteoarthritis or low back pain (*106*,*110*), NSAIDs and COX-2 inhibitors do have risks, including gastrointestinal bleeding or perforation as well as renal and cardiovascular risks (*111*). FDA has recently strengthened existing label warnings that NSAIDs increase risks for heart attack and stroke, including that these risks might increase with longer use or at higher doses (*112*). Several guidelines agree that first- and second-line drugs for neuropathic pain include anticonvulsants (gabapentin or pregabalin), tricyclic antidepressants, and SNRIs (*113*–*116*). Interventional approaches such as epidural injection for certain conditions (e.g., lumbar radiculopathy) can provide short-term improvement in pain (*117*–*119*). Epidural injection has been associated with rare but serious adverse events, including loss of vision, stroke, paralysis, and death (*120*).

### Benefits and Harms of Opioid Therapy

Balance between benefits and harms is a critical factor influencing the strength of clinical recommendations. In particular, CDC considered what is known from the epidemiology research about benefits and harms related to specific opioids and formulations, high dose therapy, co-prescription with other controlled substances, duration of use, special populations, and risk stratification and mitigation approaches. Additional information on benefits and harms of long-term opioid therapy from studies meeting rigorous selection criteria is provided in the clinical evidence review (e.g., see KQ2). CDC also considered the number of persons experiencing chronic pain, numbers potentially benefiting

from opioids, and numbers affected by opioid-related harms. A review of these data is presented in the background section of this document, with detailed information provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027). Finally, CDC considered the effectiveness of treatments that addressed potential harms of opioid therapy (opioid use disorder).

Regarding specific opioids and formulations, as noted by FDA, there are serious risks of ER/LA opioids, and the indication for this class of medications is for management of pain severe enough to require daily, around-the-clock, long-term opioid treatment in patients for whom other treatment options (e.g., nonopioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain (*121*). Time-scheduled opioid use was associated with substantially higher average daily opioid dosage than as-needed opioid use in one study (*122*). Methadone has been associated with disproportionate numbers of overdose deaths relative to the frequency with which it is prescribed for pain. Methadone has been found to account for as much as a third of opioid-related overdose deaths involving single or multiple drugs in states that participated in the Drug Abuse Warning Network, which was more than any opioid other than oxycodone, despite representing <2% of opioid prescriptions outside of opioid treatment programs in the United States; further, methadone was involved in twice as many single-drug deaths as any other prescription opioid (*123*).

Regarding high-dose therapy, several epidemiologic studies that were excluded from the clinical evidence review because patient samples were not restricted to patients with chronic pain also examined the association between opioid dosage and overdose risk (*23*,*24*,*124*–*126*). Consistent with the clinical evidence review, the contextual review found that opioid-related overdose risk is dose-dependent, with higher opioid dosages associated with increased overdose risk. Two of these studies (*23*,*24*), as well as the two studies in the clinical evidence review (*66*,*67*), evaluated similar MME/day dose ranges for association with overdose risk. In these four studies, compared with opioids prescribed at <20 MME/day, the odds of overdose among patients prescribed opioids for chronic nonmalignant pain were between 1.3 (*67*) and 1.9 (*24*) for dosages of 20 to <50 MME/day, between 1.9 (*67*) and 4.6 (*24*) for dosages of 50 to <100 MME/day, and between 2.0 (*67*) and 8.9 (*66*) for dosages of ≥100 MME/day. Compared with dosages of 1–<20 MME/day, absolute risk difference approximation for 50–<100 MME/day was 0.15% for fatal overdose (*24*) and 1.40% for any overdose (*66*), and for ≥100 MME/day was 0.25% for fatal overdose (*24*) and 4.04% for any overdose (*66*). A recent study of Veterans Health Administration patients with chronic pain found that patients who died of overdoses related to opioids were prescribed higher opioid dosages (mean: 98 MME/day; median: 60 MME/day) than controls (mean: 48 MME/day, median: 25 MME/day) (*127*). Finally, another recent study of overdose deaths among state residents with and without opioid prescriptions revealed that prescription opioid-related overdose mortality rates rose rapidly up to prescribed doses of 200 MME/day, after which the mortality rates continued to increase but grew more gradually (*128*). A listing of common opioid medications and their MME equivalents is provided (Table 2).

Regarding coprescription of opioids with benzodiazepines, epidemiologic studies suggest that concurrent use of benzodiazepines and opioids might put patients at greater risk for potentially fatal overdose. Three studies of fatal overdose deaths found evidence of concurrent benzodiazepine use in 31%–61% of decedents (*67*,*128*,*129*). In one of these studies (*67*), among decedents who received an opioid prescription, those whose deaths were related to opioids were more likely to have obtained opioids from multiple physicians and pharmacies than decedents whose deaths were not related to opioids.

Regarding duration of use, patients can experience tolerance and loss of effectiveness of opioids over time (*130*). Patients who do not experience clinically meaningful pain relief early in treatment (i.e., within 1 month) are unlikely to experience pain relief with longer-term use (*131*).

Regarding populations potentially at greater risk for harm, risk is greater for patients with sleep apnea or other causes of sleep-disordered breathing, patients with renal or hepatic insufficiency, older adults, pregnant women, patients with depression or other mental health conditions, and patients with alcohol or other substance use disorders. Interpretation of clinical data on the effects of opioids on sleep-disordered breathing is difficult because of the types of study designs and methods employed, and there is no clear consensus regarding association with risk for developing obstructive sleep apnea syndrome (*132*). However, opioid therapy can decrease respiratory drive, a high percentage of patients on long-term opioid therapy have been reported to have an abnormal apnea-hypopnea index (*133*), opioid therapy can worsen central sleep apnea in obstructive sleep apnea patients, and it can cause further desaturation in obstructive sleep apnea patients not on continuous positive airway pressure (CPAP) (*31*). Reduced renal or hepatic function can result in greater peak effect and longer duration of action and reduce the dose at which respiratory depression and overdose occurs (*134*). Age-related changes in patients aged ≥65 years, such as reduced renal function and medication clearance, even in the absence of renal disease (*135*), result in a smaller therapeutic window between safe dosages and dosages associated with respiratory depression and overdose. Older adults might also be at increased risk for falls and fractures related to opioids (*136*–*138*). Opioids used

in pregnancy can be associated with additional risks to both mother and fetus. Some studies have shown an association of opioid use in pregnancy with birth defects, including neural tube defects (*139*,*140*), congenital heart defects (*140*), and gastroschisis (*140*); preterm delivery (*141*), poor fetal growth (*141*), and stillbirth (*141*). Importantly, in some cases, opioid use during pregnancy leads to neonatal opioid withdrawal syndrome (*142*). Patients with mental health comorbidities and patients with histories of substance use disorders might be at higher risk than other patients for opioid use disorder (*62*,*143*,*144*). Recent analyses found that depressed patients were at higher risk for drug overdose than patients without depression, particularly at higher opioid dosages, although investigators were unable to distinguish unintentional overdose from suicide attempts (*145*). In case-control and case-cohort studies, substance abuse/dependence was more prevalent among patients experiencing overdose than among patients not experiencing overdose (12% versus 6% [*66*], 40% versus 10% [*24*], and 26% versus 9% [*23*]).

Regarding risk stratification approaches, limited evidence was found regarding benefits and harms. Potential benefits of PDMPs and urine drug testing include the ability to identify patients who might be at higher risk for opioid overdose or opioid use disorder, and help determine which patients will benefit from greater caution and increased monitoring or interventions when risk factors are present. For example, one study found that most fatal overdoses could be identified retrospectively on the basis of two pieces of information, multiple prescribers and high total daily opioid dosage, both important risk factors for overdose (*124*,*146*) that are available to prescribers in the PDMP (*124*). However, limited evaluation of PDMPs at the state level has revealed mixed effects on changes in prescribing and mortality outcomes (*28*). Potential harms of risk stratification include underestimation of risks of opioid therapy when screening tools are not adequately sensitive, as well as potential overestimation of risk, which could lead to inappropriate clinical decisions.

Regarding risk mitigation approaches, limited evidence was found regarding benefits and harms. Although no studies were found to examine prescribing of naloxone with opioid pain medication in primary care settings, naloxone distribution through community-based programs providing prevention services for substance users has been demonstrated to be associated with decreased risk for opioid overdose death at the community level (*147*).

Concerns have been raised that prescribing changes such as dose reduction might be associated with unintended negative consequences, such as patients seeking heroin or other illicitly obtained opioids (*148*) or interference with appropriate pain treatment (*149*). With the exception of a study noting an association between an abuse-deterrent formulation of OxyContin and heroin use, showing that some patients in qualitative interviews reported switching to another opioid, including heroin, for many reasons, including cost and availability as well as ease of use (*150*), CDC did not identify studies evaluating these potential outcomes.

Finally, regarding the effectiveness of opioid use disorder treatments, methadone and buprenorphine for opioid use disorder have been found to increase retention in treatment and to decrease illicit opioid use among patients with opioid use disorder involving heroin (*151*–*153*). Although findings are mixed, some studies suggest that effectiveness is enhanced when psychosocial treatments (e.g., contingency management, community reinforcement, psychotherapeutic counseling, and family therapy) are used in conjunction with medication-assisted therapy; for example, by reducing opioid misuse and increasing retention during maintenance therapy, and improving compliance after detoxification (*154*,*155*).

## Clinician and Patient Values and Preferences

Clinician and patient values and preferences can inform how benefits and harms of long-term opioid therapy are weighted and estimate the effort and resources required to effectively provide implementation support. Many physicians lack confidence in their ability to prescribe opioids safely (*156*), to predict (*157*) or detect (*158*) prescription drug abuse, and to discuss abuse with their patients (*158*). Although clinicians have reported favorable beliefs and attitudes about improvements in pain and quality of life attributed to opioids (*159*), most consider prescription drug abuse to be a "moderate" or "big" problem in their community, and large proportions are "very" concerned about opioid addiction (55%) and death (48%) (*160*). Clinicians do not consistently use practices intended to decrease the risk for misuse, such as PDMPs (*161*,*162*), urine drug testing (*163*), and opioid treatment agreements (*164*). This is likely due in part to challenges related to registering for PDMP access and logging into the PDMP (which can interrupt normal clinical workflow if data are not integrated into electronic health record systems) (*165*), competing clinical demands, perceived inadequate time to discuss the rationale for urine drug testing and to order confirmatory testing, and feeling unprepared to interpret and address results (*166*).

Many patients do not have an opinion about "opioids" or know what this term means (*167*). Most are familiar with the term "narcotics." About a third associated "narcotics" with addiction or abuse, and about half feared "addiction" from long-term "narcotic" use (*168*). Most patients taking opioids experience side effects (73% of patients taking hydrocodone for noncancer pain [*11*], 96% of patients taking opioids for chronic pain [*12*]), and side effects, rather than pain relief,

have been found to explain most of the variation in patients' preferences related to taking opioids (*12*). For example, patients taking hydrocodone for noncancer pain commonly reported side effects including dizziness, headache, fatigue, drowsiness, nausea, vomiting, and constipation (*11*). Patients with chronic pain in focus groups emphasized effectiveness of goal setting for increasing motivation and functioning (*168*). Patients taking high dosages report reliance on opioids despite ambivalence about their benefits (*169*) and regardless of pain reduction, reported problems, concerns, side effects, or perceived helpfulness (*13*).

### Resource Allocation

Resource allocation (cost) is an important consideration in understanding the feasibility of clinical recommendations. CDC searched for evidence on opioid therapy compared with other treatments; costs of misuse, abuse, and overdose from prescription opioids; and costs of specific risk mitigation strategies (e.g., urine drug testing). Yearly direct and indirect costs related to prescription opioids have been estimated (based on studies published since 2010) to be $53.4 billion for nonmedical use of prescription opioids (*170*); $55.7 billion for abuse, dependence (i.e., opioid use disorder), and misuse of prescription opioids (*171*); and $20.4 billion for direct and indirect costs related to opioid-related overdose alone (*172*). In 2012, total expenses for outpatient prescription opioids were estimated at $9.0 billion, an increase of 120% from 2002 (*173*). Although there are perceptions that opioid therapy for chronic pain is less expensive than more time-intensive nonpharmacologic management approaches, many pain treatments, including acetaminophen, NSAIDs, tricyclic antidepressants, and massage therapy, are associated with lower mean and median annual costs compared with opioid therapy (*174*). COX-2 inhibitors, SNRIs, anticonvulsants, topical analgesics, physical therapy, and CBT are also associated with lower median annual costs compared with opioid therapy (*174*). Limited information was found on costs of strategies to decrease risks associated with opioid therapy; however, urine drug testing, including screening and confirmatory tests, has been estimated to cost $211–$363 per test (*175*).

## Recommendations

The recommendations are grouped into three areas for consideration:

- Determining when to initiate or continue opioids for chronic pain.
- Opioid selection, dosage, duration, follow-up, and discontinuation.
- Assessing risk and addressing harms of opioid use.

There are 12 recommendations (Box 1). Each recommendation is followed by a rationale for the recommendation, with considerations for implementation noted. In accordance with the ACIP GRADE process, CDC based the recommendations on consideration of the clinical evidence, contextual evidence (including benefits and harms, values and preferences, resource allocation), and expert opinion. For each recommendation statement, CDC notes the recommendation category (A or B) and the type of the evidence (1, 2, 3, or 4) supporting the statement (Box 2). Expert opinion is reflected within each of the recommendation rationales. While there was not an attempt to reach consensus among experts, experts from the Core Expert Group and from the Opioid Guideline Workgroup ("experts") expressed overall, general support for all recommendations. Where differences in expert opinion emerged for detailed actions within the clinical recommendations or for implementation considerations, CDC notes the differences of opinion in the supporting rationale statements.

Category A recommendations indicate that most patients should receive the recommended course of action; category B recommendations indicate that different choices will be appropriate for different patients, requiring clinicians to help patients arrive at a decision consistent with patient values and preferences and specific clinical situations. Consistent with the ACIP (*47*) and GRADE process (*48*), category A recommendations were made, even with type 3 and 4 evidence, when there was broad agreement that the advantages of a clinical action greatly outweighed the disadvantages based on a consideration of benefits and harms, values and preferences, and resource allocation. Category B recommendations were made when there was broad agreement that the advantages and disadvantages of a clinical action were more balanced, but advantages were significant enough to warrant a recommendation. All recommendations are category A recommendations, with the exception of recommendation 10, which is rated as category B. Recommendations were associated with a range of evidence types, from type 2 to type 4.

In summary, the categorization of recommendations was based on the following assessment:

- No evidence shows a long-term benefit of opioids in pain and function versus no opioids for chronic pain with outcomes examined at least 1 year later (with most placebo-controlled randomized trials ≤6 weeks in duration).
- Extensive evidence shows the possible harms of opioids (including opioid use disorder, overdose, and motor vehicle injury).
- Extensive evidence suggests some benefits of nonpharmacologic and nonopioid pharmacologic treatments compared with long-term opioid therapy, with less harm.

**BOX 1. CDC recommendations for prescribing opioids for chronic pain outside of active cancer, palliative, and end-of-life care**

**Determining When to Initiate or Continue Opioids for Chronic Pain**

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

**Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation**

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.
7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

**Assessing Risk and Addressing Harms of Opioid Use**

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.
9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.
10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.
11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

* All recommendations are category A (apply to all patients outside of active cancer treatment, palliative care, and end-of-life care) except recommendation 10 (designated category B, with individual decision making required); see full guideline for evidence ratings.

**BOX 2. Interpretation of recommendation categories and evidence type**

**Recommendation Categories**

Based on evidence type, balance between desirable and undesirable effects, values and preferences, and resource allocation (cost).

**Category A recommendation**: Applies to all persons; most patients should receive the recommended course of action.

**Category B recommendation**: Individual decision making needed; different choices will be appropriate for different patients. Clinicians help patients arrive at a decision consistent with patient values and preferences and specific clinical situations.

**Evidence Type**

Based on study design as well as a function of limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and constellation of plausible biases that could change effects.

**Type 1 evidence**: Randomized clinical trials or overwhelming evidence from observational studies.

**Type 2 evidence**: Randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies.

**Type 3 evidence**: Observational studies or randomized clinical trials with notable limitations.

**Type 4 evidence**: Clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations.

## Determining When to Initiate or Continue Opioids for Chronic Pain

1. **Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate (recommendation category: A, evidence type: 3).**

Patients with pain should receive treatment that provides the greatest benefits relative to risks. The contextual evidence review found that many nonpharmacologic therapies, including physical therapy, weight loss for knee osteoarthritis, psychological therapies such as CBT, and certain interventional procedures can ameliorate chronic pain. There is high-quality evidence that exercise therapy (a prominent modality in physical therapy) for hip (*100*) or knee (*99*) osteoarthritis reduces pain and improves function immediately after treatment and that the improvements are sustained for at least 2–6 months. Previous guidelines have strongly recommended aerobic, aquatic, and/or resistance exercises for patients with osteoarthritis of the knee or hip (*176*). Exercise therapy also can help reduce pain and improve function in low back pain and can improve global well-being and physical function in fibromyalgia (*98*,*101*). Multimodal therapies and multidisciplinary biopsychosocial rehabilitation-combining approaches (e.g., psychological therapies with exercise) can reduce long-term pain and disability compared with usual care and compared with physical treatments (e.g., exercise) alone. Multimodal therapies are not always available or reimbursed by insurance and can be time-consuming and costly for patients. Interventional approaches such as arthrocentesis and intraarticular glucocorticoid injection for pain associated with rheumatoid arthritis (*117*) or osteoarthritis (*118*) and subacromial corticosteroid injection for rotator cuff disease (*119*) can provide short-term improvement in pain and function. Evidence is insufficient to determine the extent to which repeated glucocorticoid injection increases potential risks such as articular cartilage changes (in osteoarthritis) and sepsis (*118*). Serious adverse events are rare but have been reported with epidural injection (*120*).

Several nonopioid pharmacologic therapies (including acetaminophen, NSAIDs, and selected antidepressants and anticonvulsants) are effective for chronic pain. In particular, acetaminophen and NSAIDs can be useful for arthritis and low back pain. Selected anticonvulsants such as pregabalin and gabapentin can improve pain in diabetic neuropathy and post-herpetic neuralgia (contextual evidence review). Pregabalin, gabapentin, and carbamazepine are FDA-approved for treatment of certain neuropathic pain conditions, and pregabalin is FDA approved for fibromyalgia management. In patients with or without depression, tricyclic antidepressants and SNRIs provide effective analgesia for neuropathic pain conditions including diabetic neuropathy and post-herpetic neuralgia, often at lower dosages and with a shorter time to onset of effect than for treatment of depression (see contextual evidence review). Tricyclics and SNRIs can also relieve fibromyalgia symptoms. The SNRI duloxetine is FDA-approved for the treatment of diabetic neuropathy and fibromyalgia. Because patients with chronic pain often suffer from concurrent depression (*144*), and depression can exacerbate physical symptoms including pain (*177*), patients with co-occurring pain and depression are especially likely to benefit from antidepressant medication (see Recommendation 8). Nonopioid pharmacologic therapies

are not generally associated with substance use disorder, and the numbers of fatal overdoses associated with nonopioid medications are a fraction of those associated with opioid medications (contextual evidence review). For example, acetaminophen, NSAIDs, and opioid pain medication were involved in 881, 228, and 16,651 pharmaceutical overdose deaths in the United States in 2010 (*178*). However, nonopioid pharmacologic therapies are associated with certain risks, particularly in older patients, pregnant patients, and patients with certain co-morbidities such as cardiovascular, renal, gastrointestinal, and liver disease (see contextual evidence review). For example, acetaminophen can be hepatotoxic at dosages of >3–4 grams/day and at lower dosages in patients with chronic alcohol use or liver disease (*109*). NSAID use has been associated with gastritis, peptic ulcer disease, cardiovascular events (*111*,*112*), and fluid retention, and most NSAIDs (choline magnesium trilisate and selective COX-2 inhibitors are exceptions) interfere with platelet aggregation (*179*). Clinicians should review FDA-approved labeling including boxed warnings before initiating treatment with any pharmacologic therapy.

Although opioids can reduce pain during short-term use, the clinical evidence review found insufficient evidence to determine whether pain relief is sustained and whether function or quality of life improves with long-term opioid therapy (KQ1). While benefits for pain relief, function, and quality of life with long-term opioid use for chronic pain are uncertain, risks associated with long-term opioid use are clearer and significant. Based on the clinical evidence review, long-term opioid use for chronic pain is associated with serious risks including increased risk for opioid use disorder, overdose, myocardial infarction, and motor vehicle injury (KQ2). At a population level, more than 165,000 persons in the United States have died from opioid pain-medication-related overdoses since 1999 (see Contextual Evidence Review).

Integrated pain management requires coordination of medical, psychological, and social aspects of health care and includes primary care, mental health care, and specialist services when needed (*180*). Nonpharmacologic physical and psychological treatments such as exercise and CBT are approaches that encourage active patient participation in the care plan, address the effects of pain in the patient's life, and can result in sustained improvements in pain and function without apparent risks. Despite this, these therapies are not always or fully covered by insurance, and access and cost can be barriers for patients. For many patients, aspects of these approaches can be used even when there is limited access to specialty care. For example, previous guidelines have strongly recommended aerobic, aquatic, and/or resistance exercises for patients with osteoarthritis of the knee or hip (*176*) and maintenance of activity for patients with low back pain (*110*). A randomized trial found no difference in reduced chronic low back pain intensity, frequency or disability between patients assigned to relatively low-cost group aerobics and individual physiotherapy or muscle reconditioning sessions (*181*). Low-cost options to integrate exercise include brisk walking in public spaces or use of public recreation facilities for group exercise. CBT addresses psychosocial contributors to pain and improves function (*97*). Primary care clinicians can integrate elements of a cognitive behavioral approach into their practice by encouraging patients to take an active role in the care plan, by supporting patients in engaging in beneficial but potentially anxiety-provoking activities, such as exercise (*179*), or by providing education in relaxation techniques and coping strategies. In many locations, there are free or low-cost patient support, self-help, and educational community-based programs that can provide stress reduction and other mental health benefits. Patients with more entrenched anxiety or fear related to pain, or other significant psychological distress, can be referred for formal therapy with a mental health specialist (e.g., psychologist, psychiatrist, clinical social worker). Multimodal therapies should be considered for patients not responding to single-modality therapy, and combinations should be tailored depending on patient needs, cost, and convenience.

To guide patient-specific selection of therapy, clinicians should evaluate patients and establish or confirm the diagnosis. Detailed recommendations on diagnosis are provided in other guidelines (*110*,*179*), but evaluation should generally include a focused history, including history and characteristics of pain and potentially contributing factors (e.g., function, psychosocial stressors, sleep) and physical exam, with imaging or other diagnostic testing only if indicated (e.g., if severe or progressive neurologic deficits are present or if serious underlying conditions are suspected) (*110*,*179*). For complex pain syndromes, pain specialty consultation can be considered to assist with diagnosis as well as management. Diagnosis can help identify disease-specific interventions to reverse or ameliorate pain; for example, improving glucose control to prevent progression of diabetic neuropathy; immune-modulating agents for rheumatoid arthritis; physical or occupational therapy to address posture, muscle weakness, or repetitive occupational motions that contribute to musculoskeletal pain; or surgical intervention to relieve mechanical/compressive pain (*179*). The underlying mechanism for most pain syndromes can be categorized as neuropathic (e.g., diabetic neuropathy, postherpetic neuralgia, fibromyalgia), or nociceptive (e.g., osteoarthritis, muscular back pain). The diagnosis and pathophysiologic mechanism of pain have implications for symptomatic pain treatment with medication. For example, evidence is limited or insufficient

for improved pain or function with long-term use of opioids for several chronic pain conditions for which opioids are commonly prescribed, such as low back pain (*182*), headache (*183*), and fibromyalgia (*184*). Although NSAIDs can be used for exacerbations of nociceptive pain, other medications (e.g., tricyclics, selected anticonvulsants, or transdermal lidocaine) generally are recommended for neuropathic pain. In addition, improvement of neuropathic pain can begin weeks or longer after symptomatic treatment is initiated (*179*). Medications should be used only after assessment and determination that expected benefits outweigh risks given patient-specific factors. For example, clinicians should consider falls risk when selecting and dosing potentially sedating medications such as tricyclics, anticonvulsants, or opioids, and should weigh risks and benefits of use, dose, and duration of NSAIDs when treating older adults as well as patients with hypertension, renal insufficiency, or heart failure, or those with risk for peptic ulcer disease or cardiovascular disease. Some guidelines recommend topical NSAIDs for localized osteoarthritis (e.g., knee osteoarthritis) over oral NSAIDs in patients aged ≥75 years to minimize systemic effects (*176*).

Experts agreed that opioids should not be considered first-line or routine therapy for chronic pain (i.e., pain continuing or expected to continue >3 months or past the time of normal tissue healing) outside of active cancer, palliative, and end-of-life care, given small to moderate short-term benefits, uncertain long-term benefits, and potential for serious harms; although evidence on long-term benefits of nonopioid therapies is also limited, these therapies are also associated with short-term benefits, and risks are much lower. This does not mean that patients should be required to sequentially "fail" nonpharmacologic and nonopioid pharmacologic therapy before proceeding to opioid therapy. Rather, expected benefits specific to the clinical context should be weighed against risks before initiating therapy. In some clinical contexts (e.g., headache or fibromyalgia), expected benefits of initiating opioids are unlikely to outweigh risks regardless of previous nonpharmacologic and nonopioid pharmacologic therapies used. In other situations (e.g., serious illness in a patient with poor prognosis for return to previous level of function, contraindications to other therapies, and clinician and patient agreement that the overriding goal is patient comfort), opioids might be appropriate regardless of previous therapies used. In addition, when opioid pain medication is used, it is more likely to be effective if integrated with nonpharmacologic therapy. Nonpharmacologic approaches such as exercise and CBT should be used to reduce pain and improve function in patients with chronic pain. Nonopioid pharmacologic therapy should be used when benefits outweigh risks and should be combined with nonpharmacologic therapy to reduce pain and improve function. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate, to provide greater benefits to patients in improving pain and function.

2. **Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety (recommendation category: A, evidence type: 4).**

The clinical evidence review found insufficient evidence to determine long-term benefits of opioid therapy for chronic pain and found an increased risk for serious harms related to long-term opioid therapy that appears to be dose-dependent. In addition, studies on currently available risk assessment instruments were sparse and showed inconsistent results (KQ4). The clinical evidence review for the current guideline considered studies with outcomes examined at ≥1 year that compared opioid use versus nonuse or placebo. Studies of opioid therapy for chronic pain that did not have a nonopioid control group have found that although many patients discontinue opioid therapy for chronic noncancer pain due to adverse effects or insufficient pain relief, there is weak evidence that patients who are able to continue opioid therapy for at least 6 months can experience clinically significant pain relief and insufficient evidence that function or quality of life improves (*185*). These findings suggest that it is very difficult for clinicians to predict whether benefits of opioids for chronic pain will outweigh risks of ongoing treatment for individual patients. Opioid therapy should not be initiated without consideration of an "exit strategy" to be used if the therapy is unsuccessful.

Experts agreed that before opioid therapy is initiated for chronic pain outside of active cancer, palliative, and end-of-life care, clinicians should determine how effectiveness will be evaluated and should establish treatment goals with patients. Because the line between acute pain and initial chronic pain is not always clear, it might be difficult for clinicians to determine when they are initiating opioids for chronic pain rather than treating acute pain. Pain lasting longer than 3 months or past the time of normal tissue healing (which could be substantially shorter than 3 months, depending on the condition) is generally no longer considered acute. However, establishing treatment goals with a patient who has already received opioid therapy for 3 months would defer this discussion well past the point of

initiation of opioid therapy for chronic pain. Clinicians often write prescriptions for long-term use in 30-day increments, and opioid prescriptions written for ≥30 days are likely to represent initiation or continuation of long-term opioid therapy. Before writing an opioid prescription for ≥30 days, clinicians should establish treatment goals with patients. Clinicians seeing new patients already receiving opioids should establish treatment goals for continued opioid therapy. Although the clinical evidence review did not find studies evaluating the effectiveness of written agreements or treatment plans (KQ4), clinicians and patients who set a plan in advance will clarify expectations regarding how opioids will be prescribed and monitored, as well as situations in which opioids will be discontinued or doses tapered (e.g., if treatment goals are not met, opioids are no longer needed, or adverse events put the patient at risk) to improve patient safety.

Experts thought that goals should include improvement in both pain relief and function (and therefore in quality of life). However, there are some clinical circumstances under which reductions in pain without improvement in physical function might be a more realistic goal (e.g., diseases typically associated with progressive functional impairment or catastrophic injuries such as spinal cord trauma). Experts noted that function can include emotional and social as well as physical dimensions. In addition, experts emphasized that mood has important interactions with pain and function. Experts agreed that clinicians may use validated instruments such as the three-item "Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale (*186*) to track patient outcomes. Clinically meaningful improvement has been defined as a 30% improvement in scores for both pain and function (*187*). Monitoring progress toward patient-centered functional goals (e.g., walking the dog or walking around the block, returning to part-time work, attending family sports or recreational activities) can also contribute to the assessment of functional improvement. Clinicians should use these goals in assessing benefits of opioid therapy for individual patients and in weighing benefits against risks of continued opioid therapy (see Recommendation 7, including recommended intervals for follow-up). Because depression, anxiety, and other psychological co-morbidities often coexist with and can interfere with resolution of pain, clinicians should use validated instruments to assess for these conditions (see Recommendation 8) and ensure that treatment for these conditions is optimized. If patients receiving opioid therapy for chronic pain do not experience meaningful improvements in both pain and function compared with prior to initiation of opioid therapy, clinicians should consider working with patients to taper and discontinue opioids (see Recommendation 7) and should use nonpharmacologic and nonopioid pharmacologic approaches to pain management (see Recommendation 1).

**3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy (recommendation category: A, evidence type: 3).**

The clinical evidence review did not find studies evaluating effectiveness of patient education or opioid treatment plans as risk-mitigation strategies (KQ4). However, the contextual evidence review found that many patients lack information about opioids and identified concerns that some clinicians miss opportunities to effectively communicate about safety. Given the substantial evidence gaps on opioids, uncertain benefits of long-term use, and potential for serious harms, patient education and discussion before starting opioid therapy are critical so that patient preferences and values can be understood and used to inform clinical decisions. Experts agreed that essential elements to communicate to patients before starting and periodically during opioid therapy include realistic expected benefits, common and serious harms, and expectations for clinician and patient responsibilities to mitigate risks of opioid therapy.

Clinicians should involve patients in decisions about whether to start or continue opioid therapy. Given potentially serious risks of long-term opioid therapy, clinicians should ensure that patients are aware of potential benefits of, harms of, and alternatives to opioids before starting or continuing opioid therapy. Clinicians are encouraged to have open and honest discussions with patients to inform mutual decisions about whether to start or continue opioid therapy. Important considerations include the following:

- Be explicit and realistic about expected benefits of opioids, explaining that while opioids can reduce pain during short-term use, there is no good evidence that opioids improve pain or function with long-term use, and that complete relief of pain is unlikely (clinical evidence review, KQ1).
- Emphasize improvement in function as a primary goal and that function can improve even when pain is still present.
- Advise patients about serious adverse effects of opioids, including potentially fatal respiratory depression and development of a potentially serious lifelong opioid use disorder that can cause distress and inability to fulfill major role obligations.
- Advise patients about common effects of opioids, such as constipation, dry mouth, nausea, vomiting, drowsiness, confusion, tolerance, physical dependence, and withdrawal symptoms when stopping opioids. To prevent constipation associated with opioid use, advise patients to increase

hydration and fiber intake and to maintain or increase physical activity. Stool softeners or laxatives might be needed.
- Discuss effects that opioids might have on ability to safely operate a vehicle, particularly when opioids are initiated, when dosages are increased, or when other central nervous system depressants, such as benzodiazepines or alcohol, are used concurrently.
- Discuss increased risks for opioid use disorder, respiratory depression, and death at higher dosages, along with the importance of taking only the amount of opioids prescribed, i.e., not taking more opioids or taking them more often.
- Review increased risks for respiratory depression when opioids are taken with benzodiazepines, other sedatives, alcohol, illicit drugs such as heroin, or other opioids.
- Discuss risks to household members and other individuals if opioids are intentionally or unintentionally shared with others for whom they are not prescribed, including the possibility that others might experience overdose at the same or at lower dosage than prescribed for the patient, and that young children are susceptible to unintentional ingestion. Discuss storage of opioids in a secure, preferably locked location and options for safe disposal of unused opioids (*188*).
- Discuss the importance of periodic reassessment to ensure that opioids are helping to meet patient goals and to allow opportunities for opioid discontinuation and consideration of additional nonpharmacologic or nonopioid pharmacologic treatment options if opioids are not effective or are harmful.
- Discuss planned use of precautions to reduce risks, including use of prescription drug monitoring program information (see Recommendation 9) and urine drug testing (see Recommendation 10). Consider including discussion of naloxone use for overdose reversal (see Recommendation 8).
- Consider whether cognitive limitations might interfere with management of opioid therapy (for older adults in particular) and, if so, determine whether a caregiver can responsibly co-manage medication therapy. Discuss the importance of reassessing safer medication use with both the patient and caregiver.

Given the possibility that benefits of opioid therapy might diminish or that risks might become more prominent over time, it is important that clinicians review expected benefits and risks of continued opioid therapy with patients periodically, at least every 3 months (see Recommendation 7).

## Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

**4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids (recommendation category: A, evidence type: 4).**

ER/LA opioids include methadone, transdermal fentanyl, and extended-release versions of opioids such as oxycodone, oxymorphone, hydrocodone, and morphine. The clinical evidence review found a fair-quality study showing a higher risk for overdose among patients initiating treatment with ER/LA opioids than among those initiating treatment with immediate-release opioids (*77*). The clinical evidence review did not find evidence that continuous, time-scheduled use of ER/LA opioids is more effective or safer than intermittent use of immediate-release opioids or that time-scheduled use of ER/LA opioids reduces risks for opioid misuse or addiction (KQ3).

In 2014, the FDA modified the labeling for ER/LA opioid pain medications, noting serious risks and recommending that ER/LA opioids be reserved for "management of pain severe enough to require daily, around-the-clock, long-term opioid treatment" when "alternative treatment options (e.g., nonopioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain" and not used as "as needed" pain relievers (*121*). FDA has also noted that some ER/LA opioids are only appropriate for opioid-tolerant patients, defined as patients who have received certain dosages of opioids (e.g., 60 mg daily of oral morphine, 30 mg daily of oral oxycodone, or equianalgesic dosages of other opioids) for at least 1 week (*189*). Time-scheduled opioid use can be associated with greater total average daily opioid dosage compared with intermittent, as-needed opioid use (contextual evidence review). In addition, experts indicated that there was not enough evidence to determine the safety of using immediate-release opioids for breakthrough pain when ER/LA opioids are used for chronic pain outside of active cancer pain, palliative care, or end-of-life care, and that this practice might be associated with dose escalation.

Abuse-deterrent technologies have been employed to prevent manipulation intended to defeat extended-release properties of ER/LA opioids and to prevent opioid use by unintended routes of administration, such as injection of oral opioids. As indicated in FDA guidance for industry on evaluation and labeling of abuse-deterrent opioids (*190*), although abuse-deterrent technologies are expected to make manipulation of opioids more difficult or less rewarding, they do not prevent

opioid abuse through oral intake, the most common route of opioid abuse, and can still be abused by nonoral routes. The "abuse-deterrent" label does not indicate that there is no risk for abuse. No studies were found in the clinical evidence review assessing the effectiveness of abuse-deterrent technologies as a risk mitigation strategy for deterring or preventing abuse. In addition, abuse-deterrent technologies do not prevent unintentional overdose through oral intake. Experts agreed that recommendations could not be offered at this time related to use of abuse-deterrent formulations.

In comparing different ER/LA formulations, the clinical evidence review found inconsistent results for overdose risk with methadone versus other ER/LA opioids used for chronic pain (KQ3). The contextual evidence review found that methadone has been associated with disproportionate numbers of overdose deaths relative to the frequency with which it is prescribed for chronic pain. In addition, methadone is associated with cardiac arrhythmias along with QT prolongation on the electrocardiogram, and it has complicated pharmacokinetics and pharmacodynamics, including a long and variable half-life and peak respiratory depressant effect occurring later and lasting longer than peak analgesic effect. Experts noted that the pharmacodynamics of methadone are subject to more inter-individual variability than other opioids. In regard to other ER/LA opioid formulations, experts noted that the absorption and pharmacodynamics of transdermal fentanyl are complex, with gradually increasing serum concentration during the first part of the 72-hour dosing interval, as well as variable absorption based on factors such as external heat. In addition, the dosing of transdermal fentanyl in mcg/hour, which is not typical for a drug used by outpatients, can be confusing. Experts thought that these complexities might increase the risk for fatal overdose when methadone or transdermal fentanyl is prescribed to a patient who has not used it previously or by clinicians who are not familiar with its effects.

Experts agreed that for patients not already receiving opioids, clinicians should not initiate opioid treatment with ER/LA opioids and should not prescribe ER/LA opioids for intermittent use. ER/LA opioids should be reserved for severe, continuous pain and should be considered only for patients who have received immediate-release opioids daily for at least 1 week. When changing to an ER/LA opioid for a patient previously receiving a different immediate-release opioid, clinicians should consult product labeling and reduce total daily dosage to account for incomplete opioid cross-tolerance. Clinicians should use additional caution with ER/LA opioids and consider a longer dosing interval when prescribing to patients with renal or hepatic dysfunction because decreased clearance of drugs among these patients can lead to accumulation of drugs to toxic levels and persistence in the body for longer durations. Although there might be situations in which clinicians need to prescribe immediate-release and ER/LA opioids together (e.g., transitioning patients from ER/LA opioids to immediate-release opioids by temporarily using lower dosages of both), in general, avoiding the use of immediate-release opioids in combination with ER/LA opioids is preferable, given potentially increased risk and diminishing returns of such an approach for chronic pain.

When an ER/LA opioid is prescribed, using one with predictable pharmacokinetics and pharmacodynamics is preferred to minimize unintentional overdose risk. In particular, unusual characteristics of methadone and of transdermal fentanyl make safe prescribing of these medications for pain especially challenging.

- Methadone should not be the first choice for an ER/LA opioid. Only clinicians who are familiar with methadone's unique risk profile and who are prepared to educate and closely monitor their patients, including risk assessment for QT prolongation and consideration of electrocardiographic monitoring, should consider prescribing methadone for pain. A clinical practice guideline that contains further guidance regarding methadone prescribing for pain has been published previously (*191*).
- Because dosing effects of transdermal fentanyl are often misunderstood by both clinicians and patients, only clinicians who are familiar with the dosing and absorption properties of transdermal fentanyl and are prepared to educate their patients about its use should consider prescribing it.

**5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day (recommendation category: A, evidence type: 3).**

Benefits of high-dose opioids for chronic pain are not established. The clinical evidence review found only one study (*84*) addressing effectiveness of dose titration for outcomes related to pain control, function, and quality of life (KQ3). This randomized trial found no difference in pain or function between a more liberal opioid dose escalation strategy and maintenance of current dosage. (These groups were prescribed average dosages of 52 and 40 MME/day, respectively, at the end of the trial.) At the same time, risks for serious harms

related to opioid therapy increase at higher opioid dosage. The clinical evidence review found that higher opioid dosages are associated with increased risks for motor vehicle injury, opioid use disorder, and overdose (KQ2). The clinical and contextual evidence reviews found that opioid overdose risk increases in a dose-response manner, that dosages of 50–<100 MME/day have been found to increase risks for opioid overdose by factors of 1.9 to 4.6 compared with dosages of 1–<20 MME/day, and that dosages ≥100 MME/day are associated with increased risks of overdose 2.0–8.9 times the risk at 1–<20 MME/day. In a national sample of Veterans Health Administration patients with chronic pain who were prescribed opioids, mean prescribed opioid dosage among patients who died from opioid overdose was 98 MME (median 60 MME) compared with mean prescribed opioid dosage of 48 MME (median 25 MME) among patients not experiencing fatal overdose (*127*).

The contextual evidence review found that although there is not a single dosage threshold below which overdose risk is eliminated, holding dosages <50 MME/day would likely reduce risk among a large proportion of patients who would experience fatal overdose at higher prescribed dosages. Experts agreed that lower dosages of opioids reduce the risk for overdose, but that a single dosage threshold for safe opioid use could not be identified. Experts noted that daily opioid dosages close to or greater than 100 MME/day are associated with significant risks, that dosages <50 MME/day are safer than dosages of 50–100 MME/day, and that dosages <20 MME/day are safer than dosages of 20–50 MME/day. One expert thought that a specific dosage at which the benefit/risk ratio of opioid therapy decreases could not be identified. Most experts agreed that, in general, increasing dosages to 50 or more MME/day increases overdose risk without necessarily adding benefits for pain control or function and that clinicians should carefully reassess evidence of individual benefits and risks when considering increasing opioid dosages to ≥50 MME/day. Most experts also agreed that opioid dosages should not be increased to ≥90 MME/day without careful justification based on diagnosis and on individualized assessment of benefits and risks.

When opioids are used for chronic pain outside of active cancer, palliative, and end-of-life care, clinicians should start opioids at the lowest possible effective dosage (the lowest starting dosage on product labeling for patients not already taking opioids and according to product labeling guidance regarding tolerance for patients already taking opioids). Clinicians should use additional caution when initiating opioids for patients aged ≥65 years and for patients with renal or hepatic insufficiency because decreased clearance of drugs in these patients can result in accumulation of drugs to toxic levels. Clinicians should use caution when increasing opioid dosages and increase dosage by the smallest practical amount because overdose risk increases with increases in opioid dosage. Although there is limited evidence to recommend specific intervals for dosage titration, a previous guideline recommended waiting at least five half-lives before increasing dosage and waiting at least a week before increasing dosage of methadone to make sure that full effects of the previous dosage are evident (*31*). Clinicians should re-evaluate patients after increasing dosage for changes in pain, function, and risk for harm (see Recommendation 7). Before increasing total opioid dosage to ≥50 MME/day, clinicians should reassess whether opioid treatment is meeting the patient's treatment goals (see Recommendation 2). If a patient's opioid dosage for all sources of opioids combined reaches or exceeds 50 MME/day, clinicians should implement additional precautions, including increased frequency of follow-up (see Recommendation 7) and considering offering naloxone and overdose prevention education to both patients and the patients' household members (see Recommendation 8). Clinicians should avoid increasing opioid dosages to ≥90 MME/day or should carefully justify a decision to increase dosage to ≥90 MME/day based on individualized assessment of benefits and risks and weighing factors such as diagnosis, incremental benefits for pain and function relative to harms as dosages approach 90 MME/day, other treatments and effectiveness, and recommendations based on consultation with pain specialists. If patients do not experience improvement in pain and function at ≥90 MME/day, or if there are escalating dosage requirements, clinicians should discuss other approaches to pain management with the patient, consider working with patients to taper opioids to a lower dosage or to taper and discontinue opioids (see Recommendation 7), and consider consulting a pain specialist. Some states require clinicians to implement clinical protocols at specific dosage levels. For example, before increasing long-term opioid therapy dosage to >120 MME/day, clinicians in Washington state must obtain consultation from a pain specialist who agrees that this is indicated and appropriate (*30*). Clinicians should be aware of rules related to MME thresholds and associated clinical protocols established by their states.

Established patients already taking high dosages of opioids, as well as patients transferring from other clinicians, might consider the possibility of opioid dosage reduction to be anxiety-provoking, and tapering opioids can be especially challenging after years on high dosages because of physical and psychological dependence. However, these patients should be offered the opportunity to re-evaluate their continued use of opioids at high dosages in light of recent evidence regarding the association of opioid dosage and overdose risk. Clinicians should explain in a nonjudgmental manner to patients already taking high opioid dosages (≥90 MME/day) that there is

now an established body of scientific evidence showing that overdose risk is increased at higher opioid dosages. Clinicians should empathically review benefits and risks of continued high-dosage opioid therapy and should offer to work with the patient to taper opioids to safer dosages. For patients who agree to taper opioids to lower dosages, clinicians should collaborate with the patient on a tapering plan (see Recommendation 7). Experts noted that patients tapering opioids after taking them for years might require very slow opioid tapers as well as pauses in the taper to allow gradual accommodation to lower opioid dosages. Clinicians should remain alert to signs of anxiety, depression, and opioid use disorder (see Recommendations 8 and 12) that might be unmasked by an opioid taper and arrange for management of these co-morbidities. For patients agreeing to taper to lower opioid dosages as well as for those remaining on high opioid dosages, clinicians should establish goals with the patient for continued opioid therapy (see Recommendation 2), maximize pain treatment with nonpharmacologic and nonopioid pharmacologic treatments as appropriate (see Recommendation 1), and consider consulting a pain specialist as needed to assist with pain management.

**6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed (recommendation category: A, evidence type: 4).**

The clinical evidence review found that opioid use for acute pain (i.e., pain with abrupt onset and caused by an injury or other process that is not ongoing) is associated with long-term opioid use, and that a greater amount of early opioid exposure is associated with greater risk for long-term use (KQ5). Several guidelines on opioid prescribing for acute pain from emergency departments (*192*–*194*) and other settings (*195*,*196*) have recommended prescribing ≤3 days of opioids in most cases, whereas others have recommended ≤7 days (*197*) or <14 days (*30*). Because physical dependence on opioids is an expected physiologic response in patients exposed to opioids for more than a few days (contextual evidence review), limiting days of opioids prescribed also should minimize the need to taper opioids to prevent distressing or unpleasant withdrawal symptoms. Experts noted that more than a few days of exposure to opioids significantly increases hazards, that each day of unnecessary opioid use increases likelihood of physical dependence without adding benefit, and that prescriptions with fewer days' supply will minimize the number of pills available for unintentional or intentional diversion.

Experts agreed that when opioids are needed for acute pain, clinicians should prescribe opioids at the lowest effective dose and for no longer than the expected duration of pain severe enough to require opioids to minimize unintentional initiation of long-term opioid use. The lowest effective dose can be determined using product labeling as a starting point with calibration as needed based on the severity of pain and on other clinical factors such as renal or hepatic insufficiency (see Recommendation 8). Experts thought, based on clinical experience regarding anticipated duration of pain severe enough to require an opioid, that in most cases of acute pain not related to surgery or trauma, a ≤3 days' supply of opioids will be sufficient. For example, in one study of the course of acute low back pain (not associated with malignancies, infections, spondylarthropathies, fractures, or neurological signs) in a primary care setting, there was a large decrease in pain until the fourth day after treatment with paracetamol, with smaller decreases thereafter (*198*). Some experts thought that because some types of acute pain might require more than 3 days of opioid treatment, it would be appropriate to recommend a range of ≤3–5 days or ≤3–7 days when opioids are needed. Some experts thought that a range including 7 days was too long given the expected course of severe acute pain for most acute pain syndromes seen in primary care.

Acute pain can often be managed without opioids. It is important to evaluate the patient for reversible causes of pain, for underlying etiologies with potentially serious sequelae, and to determine appropriate treatment. When the diagnosis and severity of nontraumatic, nonsurgical acute pain are reasonably assumed to warrant the use of opioids, clinicians should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids, often 3 days or less, unless circumstances clearly warrant additional opioid therapy. More than 7 days will rarely be needed. Opioid treatment for post-surgical pain is outside the scope of this guideline but has been addressed elsewhere (*30*). Clinicians should not prescribe additional opioids to patients "just in case" pain continues longer than expected. Clinicians should re-evaluate the subset of patients who experience severe acute pain that continues longer than the expected duration to confirm or revise the initial diagnosis and to adjust management accordingly. Given longer half-lives and longer duration of effects (e.g., respiratory depression) with ER/LA opioids such as methadone, fentanyl patches, or extended release versions of opioids such as oxycodone, oxymorphone, or morphine, clinicians should not prescribe ER/LA opioids for the treatment of acute pain.

7. **Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids (recommendation category: A, evidence type: 4).**

Although the clinical evidence review did not find studies evaluating the effectiveness of more frequent monitoring intervals (KQ4), it did find that continuing opioid therapy for 3 months substantially increases risk for opioid use disorder (KQ2); therefore, follow-up earlier than 3 months might be necessary to provide the greatest opportunity to prevent the development of opioid use disorder. In addition, risk for overdose associated with ER/LA opioids might be particularly high during the first 2 weeks of treatment (KQ3). The contextual evidence review found that patients who do not have pain relief with opioids at 1 month are unlikely to experience pain relief with opioids at 6 months. Although evidence is insufficient to determine at what point within the first 3 months of opioid therapy the risks for opioid use disorder increase, reassessment of pain and function within 1 month of initiating opioids provides an opportunity to minimize risks of long-term opioid use by discontinuing opioids among patients not receiving a clear benefit from these medications. Experts noted that risks for opioid overdose are greatest during the first 3–7 days after opioid initiation or increase in dosage, particularly when methadone or transdermal fentanyl are prescribed; that follow-up within 3 days is appropriate when initiating or increasing the dosage of methadone; and that follow-up within 1 week might be appropriate when initiating or increasing the dosage of other ER/LA opioids.

Clinicians should evaluate patients to assess benefits and harms of opioids within 1 to 4 weeks of starting long-term opioid therapy or of dose escalation. Clinicians should consider follow-up intervals within the lower end of this range when ER/LA opioids are started or increased or when total daily opioid dosage is ≥50 MME/day. Shorter follow-up intervals (within 3 days) should be strongly considered when starting or increasing the dosage of methadone. At follow up, clinicians should assess benefits in function, pain control, and quality of life using tools such as the three-item "Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale (*186*) and/or asking patients about progress toward functional goals that have meaning for them (see Recommendation 2). Clinicians should also ask patients about common adverse effects such as constipation and drowsiness (see Recommendation 3), as well as asking about and assessing for effects that might be early warning signs for more serious problems such as overdose (e.g., sedation or slurred speech) or opioid use disorder (e.g., craving, wanting to take opioids in greater quantities or more frequently than prescribed, or difficulty controlling use). Clinicians should ask patients about their preferences for continuing opioids, given their effects on pain and function relative to any adverse effects experienced.

Because of potential changes in the balance of benefits and risks of opioid therapy over time, clinicians should regularly reassess all patients receiving long-term opioid therapy, including patients who are new to the clinician but on long-term opioid therapy, at least every 3 months. At reassessment, clinicians should determine whether opioids continue to meet treatment goals, including sustained improvement in pain and function, whether the patient has experienced common or serious adverse events or early warning signs of serious adverse events, signs of opioid use disorder (e.g., difficulty controlling use, work or family problems related to opioid use), whether benefits of opioids continue to outweigh risks, and whether opioid dosage can be reduced or opioids can be discontinued. Ideally, these reassessments would take place in person and be conducted by the prescribing clinician. In practice contexts where virtual visits are part of standard care (e.g., in remote areas where distance or other issues make follow-up visits challenging), follow-up assessments that allow the clinician to communicate with and observe the patient through video and audio could be conducted, with in-person visits occurring at least once per year. Clinicians should re-evaluate patients who are exposed to greater risk of opioid use disorder or overdose (e.g., patients with depression or other mental health conditions, a history of substance use disorder, a history of overdose, taking ≥50 MME/day, or taking other central nervous system depressants with opioids) more frequently than every 3 months. If clinically meaningful improvements in pain and function are not sustained, if patients are taking high-risk regimens (e.g., dosages ≥50 MME/day or opioids combined with benzodiazepines) without evidence of benefit, if patients believe benefits no longer outweigh risks or if they request dosage reduction or discontinuation, or if patients experience overdose or other serious adverse events (e.g., an event leading to hospitalization or disability) or warning signs of serious adverse events, clinicians should work with patients to reduce opioid dosage or to discontinue opioids when possible. Clinicians should maximize pain treatment with nonpharmacologic and nonopioid pharmacologic treatments as appropriate (see Recommendation 1) and consider consulting a pain specialist as needed to assist with pain management.

### Considerations for Tapering Opioids

Although the clinical evidence review did not find high-quality studies comparing the effectiveness of different tapering protocols for use when opioid dosage is reduced or opioids are discontinued (KQ3), tapers reducing weekly dosage by 10%–50% of the original dosage have been recommended by other clinical guidelines (*199*), and a rapid taper over 2–3 weeks has been recommended in the case of a severe adverse event such as overdose (*30*). Experts noted that tapers slower than 10% per week (e.g., 10% per month) also might be appropriate and better tolerated than more rapid tapers, particularly when patients have been taking opioids for longer durations (e.g., for years). Opioid withdrawal during pregnancy has been associated with spontaneous abortion and premature labor.

When opioids are reduced or discontinued, a taper slow enough to minimize symptoms and signs of opioid withdrawal (e.g., drug craving, anxiety, insomnia, abdominal pain, vomiting, diarrhea, diaphoresis, mydriasis, tremor, tachycardia, or piloerection) should be used. A decrease of 10% of the original dose per week is a reasonable starting point; experts agreed that tapering plans may be individualized based on patient goals and concerns. Experts noted that at times, tapers might have to be paused and restarted again when the patient is ready and might have to be slowed once patients reach low dosages. Tapers may be considered successful as long as the patient is making progress. Once the smallest available dose is reached, the interval between doses can be extended. Opioids may be stopped when taken less frequently than once a day. More rapid tapers might be needed for patient safety under certain circumstances (e.g., for patients who have experienced overdose on their current dosage). Ultrarapid detoxification under anesthesia is associated with substantial risks, including death, and should not be used (*200*). Clinicians should access appropriate expertise if considering tapering opioids during pregnancy because of possible risk to the pregnant patient and to the fetus if the patient goes into withdrawal. Patients who are not taking opioids (including patients who are diverting all opioids they obtain) do not require tapers. Clinicians should discuss with patients undergoing tapering the increased risk for overdose on abrupt return to a previously prescribed higher dose. Primary care clinicians should collaborate with mental health providers and with other specialists as needed to optimize nonopioid pain management (see Recommendation 1), as well as psychosocial support for anxiety related to the taper. More detailed guidance on tapering, including management of withdrawal symptoms has been published previously (*30*,*201*). If a patient exhibits signs of opioid use disorder, clinicians should offer or arrange for treatment of opioid use disorder (see Recommendation 12) and consider offering naloxone for overdose prevention (see Recommendation 8).

## Assessing Risk and Addressing Harms of Opioid Use

**8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present (recommendation category: A, evidence type: 4).**

The clinical evidence review found insufficient evidence to determine how harms of opioids differ depending on patient demographics or patient comorbidities (KQ2). However, based on the contextual evidence review and expert opinion, certain risk factors are likely to increase susceptibility to opioid-associated harms and warrant incorporation of additional strategies into the management plan to mitigate risk. Clinicians should assess these risk factors periodically, with frequency varying by risk factor and patient characteristics. For example, factors that vary more frequently over time, such as alcohol use, require more frequent follow up. In addition, clinicians should consider offering naloxone, re-evaluating patients more frequently (see Recommendation 7), and referring to pain and/or behavioral health specialists when factors that increase risk for harm, such as history of overdose, history of substance use disorder, higher dosages of opioids (≥50 MME/day), and concurrent use of benzodiazepines with opioids, are present.

### Patients with Sleep-Disordered Breathing, Including Sleep Apnea

Risk factors for sleep-disordered breathing include congestive heart failure, and obesity. Experts noted that careful monitoring and cautious dose titration should be used if opioids are prescribed for patients with mild sleep-disordered breathing. Clinicians should avoid prescribing opioids to patients with moderate or severe sleep-disordered breathing whenever possible to minimize risks for opioid overdose (contextual evidence review).

### Pregnant Women

Opioids used in pregnancy might be associated with additional risks to both mother and fetus. Some studies have shown an association of opioid use in pregnancy with stillbirth, poor fetal growth, pre-term delivery, and birth defects (contextual evidence review). Importantly, in some cases, opioid use during pregnancy leads to neonatal opioid withdrawal syndrome. Clinicians and patients together should carefully weigh risks and benefits when making decisions

about whether to initiate opioid therapy for chronic pain during pregnancy. In addition, before initiating opioid therapy for chronic pain for reproductive-age women, clinicians should discuss family planning and how long-term opioid use might affect any future pregnancy. For pregnant women already receiving opioids, clinicians should access appropriate expertise if considering tapering opioids because of possible risk to the pregnant patient and to the fetus if the patient goes into withdrawal (see Recommendation 7). For pregnant women with opioid use disorder, medication-assisted therapy with buprenorphine or methadone has been associated with improved maternal outcomes and should be offered (*202*) (see Recommendation 12). Clinicians caring for pregnant women receiving opioids for pain or receiving buprenorphine or methadone for opioid use disorder should arrange for delivery at a facility prepared to monitor, evaluate for, and treat neonatal opioid withdrawal syndrome. In instances when travel to such a facility would present an undue burden on the pregnant woman, it is appropriate to deliver locally, monitor and evaluate the newborn for neonatal opioid withdrawal syndrome, and transfer the newborn for additional treatment if needed. Neonatal toxicity and death have been reported in breast-feeding infants whose mothers are taking codeine (contextual evidence review); previous guidelines have recommended that codeine be avoided whenever possible among mothers who are breast feeding and, if used, should be limited to the lowest possible dose and to a 4-day supply (*203*).

### Patients with Renal or Hepatic Insufficiency

Clinicians should use additional caution and increased monitoring (see Recommendation 7) to minimize risks of opioids prescribed for patients with renal or hepatic insufficiency, given their decreased ability to process and excrete drugs, susceptibility to accumulation of opioids, and reduced therapeutic window between safe dosages and dosages associated with respiratory depression and overdose (contextual evidence review; see Recommendations 4, 5, and 7).

### Patients Aged ≥65 Years

Inadequate pain treatment among persons aged ≥65 years has been documented (*204*). Pain management for older patients can be challenging given increased risks of both nonopioid pharmacologic therapies (see Recommendation 1) and opioid therapy in this population. Given reduced renal function and medication clearance even in the absence of renal disease, patients aged ≥65 years might have increased susceptibility to accumulation of opioids and a smaller therapeutic window between safe dosages and dosages associated with respiratory depression and overdose (contextual evidence review). Some older adults suffer from cognitive impairment, which can increase risk for medication errors and make opioid-related confusion more dangerous. In addition, older adults are more likely than younger adults to experience co-morbid medical conditions and more likely to receive multiple medications, some of which might interact with opioids (such as benzodiazepines). Clinicians should use additional caution and increased monitoring (see Recommendations 4, 5, and 7) to minimize risks of opioids prescribed for patients aged ≥65 years. Experts suggested that clinicians educate older adults receiving opioids to avoid risky medication-related behaviors such as obtaining controlled medications from multiple prescribers and saving unused medications. Clinicians should also implement interventions to mitigate common risks of opioid therapy among older adults, such as exercise or bowel regimens to prevent constipation, risk assessment for falls, and patient monitoring for cognitive impairment.

### Patients with Mental Health Conditions

Because psychological distress frequently interferes with improvement of pain and function in patients with chronic pain, using validated instruments such as the Generalized Anxiety Disorder (GAD)-7 and the Patient Health Questionnaire (PHQ)-9 or the PHQ-4 to assess for anxiety, post-traumatic stress disorder, and/or depression (*205*), might help clinicians improve overall pain treatment outcomes. Experts noted that clinicians should use additional caution and increased monitoring (see Recommendation 7) to lessen the increased risk for opioid use disorder among patients with mental health conditions (including depression, anxiety disorders, and PTSD), as well as increased risk for drug overdose among patients with depression. Previous guidelines have noted that opioid therapy should not be initiated during acute psychiatric instability or uncontrolled suicide risk, and that clinicians should consider behavioral health specialist consultation for any patient with a history of suicide attempt or psychiatric disorder (*31*). In addition, patients with anxiety disorders and other mental health conditions are more likely to receive benzodiazepines, which can exacerbate opioid-induced respiratory depression and increase risk for overdose (see Recommendation 11). Clinicians should ensure that treatment for depression and other mental health conditions is optimized, consulting with behavioral health specialists when needed. Treatment for depression can improve pain symptoms as well as depression and might decrease overdose risk (contextual evidence review). For treatment of chronic pain in patients with depression, clinicians should strongly consider using tricyclic or SNRI antidepressants for analgesic as well as antidepressant effects if these medications are not otherwise contraindicated (see Recommendation 1).

### Patients with Substance Use Disorder

Illicit drugs and alcohol are listed as contributory factors on a substantial proportion of death certificates for opioid-related overdose deaths (contextual evidence review). Previous guidelines have recommended screening or risk assessment tools to identify patients at higher risk for misuse or abuse of opioids. However, the clinical evidence review found that currently available risk-stratification tools (e.g., Opioid Risk Tool, Screener and Opioid Assessment for Patients with Pain Version 1, SOAPP-R, and Brief Risk Interview) show insufficient accuracy for classification of patients as at low or high risk for abuse or misuse (KQ4). Clinicians should always exercise caution when considering or prescribing opioids for any patient with chronic pain outside of active cancer, palliative, and end-of-life care and should not overestimate the ability of these tools to rule out risks from long-term opioid therapy.

Clinicians should ask patients about their drug and alcohol use. Single screening questions can be used (*206*). For example, the question "How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?" (with an answer of one or more considered positive) was found in a primary care setting to be 100% sensitive and 73.5% specific for the detection of a drug use disorder compared with a standardized diagnostic interview (*207*). Validated screening tools such as the Drug Abuse Screening Test (DAST) (*208*) and the Alcohol Use Disorders Identification Test (AUDIT) (*209*) can also be used. Clinicians should use PDMP data (see Recommendation 9) and drug testing (see Recommendation 10) as appropriate to assess for concurrent substance use that might place patients at higher risk for opioid use disorder and overdose. Clinicians should also provide specific counseling on increased risks for overdose when opioids are combined with other drugs or alcohol (see Recommendation 3) and ensure that patients receive effective treatment for substance use disorders when needed (see Recommendation 12).

The clinical evidence review found insufficient evidence to determine how harms of opioids differ depending on past or current substance use disorder (KQ2), although a history of substance use disorder was associated with misuse. Similarly, based on contextual evidence, patients with drug or alcohol use disorders are likely to experience greater risks for opioid use disorder and overdose than persons without these conditions. If clinicians consider opioid therapy for chronic pain outside of active cancer, palliative, and end-of-life care for patients with drug or alcohol use disorders, they should discuss increased risks for opioid use disorder and overdose with patients, carefully consider whether benefits of opioids outweigh increased risks, and incorporate strategies to mitigate risk into the management plan, such as considering offering naloxone (see Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present) and increasing frequency of monitoring (see Recommendation 7) when opioids are prescribed. Because pain management in patients with substance use disorder can be complex, clinicians should consider consulting substance use disorder specialists and pain specialists regarding pain management for persons with active or recent past history of substance abuse. Experts also noted that clinicians should communicate with patients' substance use disorder treatment providers if opioids are prescribed.

### Patients with Prior Nonfatal Overdose

Although studies were not identified that directly addressed the risk for overdose among patients with prior nonfatal overdose who are prescribed opioids, based on clinical experience, experts thought that prior nonfatal overdose would substantially increase risk for future nonfatal or fatal opioid overdose. If patients experience nonfatal opioid overdose, clinicians should work with them to reduce opioid dosage and to discontinue opioids when possible (see Recommendation 7). If clinicians continue opioid therapy for chronic pain outside of active cancer, palliative, and end-of-life care in patients with prior opioid overdose, they should discuss increased risks for overdose with patients, carefully consider whether benefits of opioids outweigh substantial risks, and incorporate strategies to mitigate risk into the management plan, such as considering offering naloxone (see Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present) and increasing frequency of monitoring (see Recommendation 7) when opioids are prescribed.

### Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present

Naloxone is an opioid antagonist that can reverse severe respiratory depression; its administration by lay persons, such as friends and family of persons who experience opioid overdose, can save lives. Naloxone precipitates acute withdrawal among patients physically dependent on opioids. Serious adverse effects, such as pulmonary edema, cardiovascular instability, and seizures, have been reported but are rare at doses consistent with labeled use for opioid overdose (*210*). The contextual evidence review did not find any studies on effectiveness of prescribing naloxone for overdose prevention among patients prescribed opioids for chronic pain. However, there is evidence for effectiveness of naloxone provision in preventing opioid-related overdose death at the community level through community-based distribution (e.g., through overdose education and naloxone distribution programs in community service agencies) to persons at risk for overdose

(mostly due to illicit opiate use), and it is plausible that effectiveness would be observed when naloxone is provided in the clinical setting as well. Experts agreed that it is preferable not to initiate opioid treatment when factors that increase risk for opioid-related harms are present. Opinions diverged about the likelihood of naloxone being useful to patients and the circumstances under which it should be offered. However, most experts agreed that clinicians should consider offering naloxone when prescribing opioids to patients at increased risk for overdose, including patients with a history of overdose, patients with a history of substance use disorder, patients taking benzodiazepines with opioids (see Recommendation 11), patients at risk for returning to a high dose to which they are no longer tolerant (e.g., patients recently released from prison), and patients taking higher dosages of opioids (≥50 MME/day). Practices should provide education on overdose prevention and naloxone use to patients receiving naloxone prescriptions and to members of their households. Experts noted that naloxone co-prescribing can be facilitated by clinics or practices with resources to provide naloxone training and by collaborative practice models with pharmacists. Resources for prescribing naloxone in primary care settings can be found through Prescribe to Prevent at http://prescribetoprevent.org.

**9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months (recommendation category: A, evidence type: 4).**

PDMPs are state-based databases that collect information on controlled prescription drugs dispensed by pharmacies in most states and, in select states, by dispensing physicians as well. In addition, some clinicians employed by the federal government, including some clinicians in the Indian Health Care Delivery System, are not licensed in the states where they practice, and do not have access to PDMP data. Certain states require clinicians to review PDMP data prior to writing each opioid prescription (see state-level PDMP-related policies on the National Alliance for Model State Drug Laws website at http://www.namsdl.org/prescription-monitoring-programs.cfm). The clinical evidence review did not find studies evaluating the effectiveness of PDMPs on outcomes related to overdose, addiction, abuse, or misuse (KQ4). However, even though evidence is limited on the effectiveness of PDMP implementation at the state level on prescribing and mortality outcomes (*28*), the contextual evidence review found that most fatal overdoses were associated with patients receiving opioids from multiple prescribers and/or with patients receiving high total daily opioid dosages; information on both of these risk factors for overdose are available to prescribers in the PDMP. PDMP data also can be helpful when patient medication history is not otherwise available (e.g., for patients from other locales) and when patients transition care to a new clinician. The contextual evidence review also found that PDMP information could be used in a way that is harmful to patients. For example, it has been used to dismiss patients from clinician practices (*211*), which might adversely affect patient safety.

The contextual review found variation in state policies that affect timeliness of PDMP data (and therefore benefits of reviewing PDMP data) as well as time and workload for clinicians in accessing PDMP data. In states that permit delegating access to other members of the health care team, workload for prescribers can be reduced. These differences might result in a different balance of benefits to clinician workload in different states. Experts agreed that PDMPs are useful tools that should be consulted when starting a patient on opioid therapy and periodically during long-term opioid therapy. However, experts disagreed on how frequently clinicians should check the PDMP during long-term opioid therapy, given PDMP access issues and the lag time in reporting in some states. Most experts agreed that PDMP data should be reviewed every 3 months or more frequently during long-term opioid therapy. A minority of experts noted that, given the current burden of accessing PDMP data in some states and the lack of evidence surrounding the most effective interval for PDMP review to improve patient outcomes, annual review of PDMP data during long-term opioid therapy would be reasonable when factors that increase risk for opioid-related harms are not present.

Clinicians should review PDMP data for opioids and other controlled medications patients might have received from additional prescribers to determine whether a patient is receiving high total opioid dosages or dangerous combinations (e.g., opioids combined with benzodiazepines) that put him or her at high risk for overdose. Ideally, PDMP data should be reviewed before every opioid prescription. This is recommended in all states with well-functioning PDMPs and where PDMP access policies make this practicable (e.g., clinician and delegate access permitted), but it is not currently possible in states without functional PDMPs or in those that do not permit certain prescribers to access them. As vendors and practices facilitate integration of PDMP information into regular clinical workflow (e.g., data made available in electronic health records), clinicians' ease of access in reviewing PDMP data is expected to improve.

In addition, improved timeliness of PDMP data will improve their value in identifying patient risks.

If patients are found to have high opioid dosages, dangerous combinations of medications, or multiple controlled substance prescriptions written by different clinicians, several actions can be taken to augment clinicians' abilities to improve patient safety:

- Clinicians should discuss information from the PDMP with their patient and confirm that the patient is aware of the additional prescriptions. Occasionally, PDMP information can be incorrect (e.g., if the wrong name or birthdate has been entered, the patient uses a nickname or maiden name, or another person has used the patient's identity to obtain prescriptions).
- Clinicians should discuss safety concerns, including increased risk for respiratory depression and overdose, with patients found to be receiving opioids from more than one prescriber or receiving medications that increase risk when combined with opioids (e.g., benzodiazepines) and consider offering naloxone (see Recommendation 8).
- Clinicians should avoid prescribing opioids and benzodiazepines concurrently whenever possible. Clinicians should communicate with others managing the patient to discuss the patient's needs, prioritize patient goals, weigh risks of concurrent benzodiazepine and opioid exposure, and coordinate care (see Recommendation 11).
- Clinicians should calculate the total MME/day for concurrent opioid prescriptions to help assess the patient's overdose risk (see Recommendation 5). If patients are found to be receiving high total daily dosages of opioids, clinicians should discuss their safety concerns with the patient, consider tapering to a safer dosage (see Recommendations 5 and 7), and consider offering naloxone (see Recommendation 8).
- Clinicians should discuss safety concerns with other clinicians who are prescribing controlled substances for their patient. Ideally clinicians should first discuss concerns with their patient and inform him or her that they plan to coordinate care with the patient's other prescribers to improve the patient's safety.
- Clinicians should consider the possibility of a substance use disorder and discuss concerns with their patient (see Recommendation 12).
- If clinicians suspect their patient might be sharing or selling opioids and not taking them, clinicians should consider urine drug testing to assist in determining whether opioids can be discontinued without causing withdrawal (see Recommendations 7 and 10). A negative drug test for prescribed opioids might indicate the patient is not taking prescribed opioids, although clinicians should consider other possible reasons for this test result (see Recommendation 10).

Experts agreed that clinicians should not dismiss patients from their practice on the basis of PDMP information. Doing so can adversely affect patient safety, could represent patient abandonment, and could result in missed opportunities to provide potentially lifesaving information (e.g., about risks of opioids and overdose prevention) and interventions (e.g., safer prescriptions, nonopioid pain treatment [see Recommendation 1], naloxone [see Recommendation 8], and effective treatment for substance use disorder [see Recommendation 12]).

**10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs (recommendation category: B, evidence type: 4).**

Concurrent use of opioid pain medications with other opioid pain medications, benzodiazepines, or heroin can increase patients' risk for overdose. Urine drug tests can provide information about drug use that is not reported by the patient. In addition, urine drug tests can assist clinicians in identifying when patients are not taking opioids prescribed for them, which might in some cases indicate diversion or other clinically important issues such as difficulties with adverse effects. Urine drug tests do not provide accurate information about how much or what dose of opioids or other drugs a patient took. The clinical evidence review did not find studies evaluating the effectiveness of urine drug screening for risk mitigation during opioid prescribing for pain (KQ4). The contextual evidence review found that urine drug testing can provide useful information about patients assumed not to be using unreported drugs. Urine drug testing results can be subject to misinterpretation and might sometimes be associated with practices that might harm patients (e.g., stigmatization, inappropriate termination from care). Routine use of urine drug tests with standardized policies at the practice or clinic level might destigmatize their use. Although random drug testing also might destigmatize urine drug testing, experts thought that truly random testing was not feasible in clinical practice. Some clinics obtain a urine specimen at every visit, but only send it for testing on a random schedule. Experts noted that in addition to direct costs of urine drug testing, which often are not covered fully by insurance and can be a burden for patients, clinician time is needed to interpret, confirm, and communicate results.

Experts agreed that prior to starting opioids for chronic pain and periodically during opioid therapy, clinicians should

use urine drug testing to assess for prescribed opioids as well as other controlled substances and illicit drugs that increase risk for overdose when combined with opioids, including nonprescribed opioids, benzodiazepines, and heroin. There was some difference of opinion among experts as to whether this recommendation should apply to all patients, or whether this recommendation should entail individual decision making with different choices for different patients based on values, preferences, and clinical situations. While experts agreed that clinicians should use urine drug testing before initiating opioid therapy for chronic pain, they disagreed on how frequently urine drug testing should be conducted during long-term opioid therapy. Most experts agreed that urine drug testing at least annually for all patients was reasonable. Some experts noted that this interval might be too long in some cases and too short in others, and that the follow-up interval should be left to the discretion of the clinician. Previous guidelines have recommended more frequent urine drug testing in patients thought to be at higher risk for substance use disorder (*30*). However, experts thought that predicting risk prior to urine drug testing is challenging and that currently available tools do not allow clinicians to reliably identify patients who are at low risk for substance use disorder.

In most situations, initial urine drug testing can be performed with a relatively inexpensive immunoassay panel for commonly prescribed opioids and illicit drugs. Patients prescribed less commonly used opioids might require specific testing for those agents. The use of confirmatory testing adds substantial costs and should be based on the need to detect specific opioids that cannot be identified on standard immunoassays or on the presence of unexpected urine drug test results. Clinicians should be familiar with the drugs included in urine drug testing panels used in their practice and should understand how to interpret results for these drugs. For example, a positive "opiates" immunoassay detects morphine, which might reflect patient use of morphine, codeine, or heroin, but this immunoassay does not detect synthetic opioids (e.g., fentanyl or methadone) and might not detect semisynthetic opioids (e.g., oxycodone). However, many laboratories use an oxycodone immunoassay that detects oxycodone and oxymorphone. In some cases, positive results for specific opioids might reflect metabolites from opioids the patient is taking and might not mean the patient is taking the specific opioid for which the test was positive. For example, hydromorphone is a metabolite of hydrocodone, and oxymorphone is a metabolite of oxycodone. Detailed guidance on interpretation of urine drug test results, including which tests to order and expected results, drug detection time in urine, drug metabolism, and other considerations has been published previously (*30*). Clinicians should not test for substances for which results would not affect patient management or for which implications for patient management are unclear. For example, experts noted that there might be uncertainty about the clinical implications of a positive urine drug test for tetrahyrdocannabinol (THC). In addition, restricting confirmatory testing to situations and substances for which results can reasonably be expected to affect patient management can reduce costs of urine drug testing, given the substantial costs associated with confirmatory testing methods. Before ordering urine drug testing, clinicians should have a plan for responding to unexpected results. Clinicians should explain to patients that urine drug testing is intended to improve their safety and should also explain expected results (e.g., presence of prescribed medication and absence of drugs, including illicit drugs, not reported by the patient). Clinicians should ask patients about use of prescribed and other drugs and ask whether there might be unexpected results. This will provide an opportunity for patients to provide information about changes in their use of prescribed opioids or other drugs. Clinicians should discuss unexpected results with the local laboratory or toxicologist and with the patient. Discussion with patients prior to specific confirmatory testing can sometimes yield a candid explanation of why a particular substance is present or absent and obviate the need for expensive confirmatory testing on that visit. For example, a patient might explain that the test is negative for prescribed opioids because she felt opioids were no longer helping and discontinued them. If unexpected results are not explained, a confirmatory test using a method selective enough to differentiate specific opioids and metabolites (e.g., gas or liquid chromatography/mass spectrometry) might be warranted to clarify the situation.

Clinicians should use unexpected results to improve patient safety (e.g., change in pain management strategy [see Recommendation 1], tapering or discontinuation of opioids [see Recommendation 7], more frequent re-evaluation [see Recommendation 7], offering naloxone [see Recommendation 8], or referral for treatment for substance use disorder [see Recommendation 12], all as appropriate). If tests for prescribed opioids are repeatedly negative, confirming that the patient is not taking the prescribed opioid, clinicians can discontinue the prescription without a taper. Clinicians should not dismiss patients from care based on a urine drug test result because this could constitute patient abandonment and could have adverse consequences for patient safety, potentially including the patient obtaining opioids from alternative sources and the clinician missing opportunities to facilitate treatment for substance use disorder.

**11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently**

**whenever possible (recommendation category: A, evidence type: 3).**

Benzodiazepines and opioids both cause central nervous system depression and can decrease respiratory drive. Concurrent use is likely to put patients at greater risk for potentially fatal overdose. The clinical evidence review did not address risks of benzodiazepine co-prescription among patients prescribed opioids. However, the contextual evidence review found evidence in epidemiologic series of concurrent benzodiazepine use in large proportions of opioid-related overdose deaths, and a case-cohort study found concurrent benzodiazepine prescription with opioid prescription to be associated with a near quadrupling of risk for overdose death compared with opioid prescription alone (*212*). Experts agreed that although there are circumstances when it might be appropriate to prescribe opioids to a patient receiving benzodiazepines (e.g., severe acute pain in a patient taking long-term, stable low-dose benzodiazepine therapy), clinicians should avoid prescribing opioids and benzodiazepines concurrently whenever possible. In addition, given that other central nervous system depressants (e.g., muscle relaxants, hypnotics) can potentiate central nervous system depression associated with opioids, clinicians should consider whether benefits outweigh risks of concurrent use of these drugs. Clinicians should check the PDMP for concurrent controlled medications prescribed by other clinicians (see Recommendation 9) and should consider involving pharmacists and pain specialists as part of the management team when opioids are co-prescribed with other central nervous system depressants. Because of greater risks of benzodiazepine withdrawal relative to opioid withdrawal, and because tapering opioids can be associated with anxiety, when patients receiving both benzodiazepines and opioids require tapering to reduce risk for fatal respiratory depression, it might be safer and more practical to taper opioids first (see Recommendation 7). Clinicians should taper benzodiazepines gradually if discontinued because abrupt withdrawal can be associated with rebound anxiety, hallucinations, seizures, delirium tremens, and, in rare cases, death (contextual evidence review). A commonly used tapering schedule that has been used safely and with moderate success is a reduction of the benzodiazepine dose by 25% every 1–2 weeks (*213*,*214*). CBT increases tapering success rates and might be particularly helpful for patients struggling with a benzodiazepine taper (*213*). If benzodiazepines prescribed for anxiety are tapered or discontinued, or if patients receiving opioids require treatment for anxiety, evidence-based psychotherapies (e.g., CBT) and/or specific anti-depressants or other nonbenzodiazepine medications approved for anxiety should be offered. Experts emphasized that clinicians should communicate with mental health professionals managing the patient to discuss the patient's needs, prioritize patient goals, weigh risks of concurrent benzodiazepine and opioid exposure, and coordinate care.

**12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder (recommendation category: A, evidence type: 2).**

Opioid use disorder (previously classified as opioid abuse or opioid dependence) is defined in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) as a problematic pattern of opioid use leading to clinically significant impairment or distress, manifested by at least two defined criteria occurring within a year (http://pcssmat.org/wp-content/uploads/2014/02/5B-DSM-5-Opioid-Use-Disorder-Diagnostic-Criteria.pdf) (*20*).

The clinical evidence review found prevalence of opioid dependence (using DSM-IV diagnosis criteria) in primary care settings among patients with chronic pain on opioid therapy to be 3%–26% (KQ2). As found in the contextual evidence review and supported by moderate quality evidence, opioid agonist or partial agonist treatment with methadone maintenance therapy or buprenorphine has been shown to be more effective in preventing relapse among patients with opioid use disorder (*151–153*). Some studies suggest that using behavioral therapies in combination with these treatments can reduce opioid misuse and increase retention during maintenance therapy and improve compliance after detoxification (*154*,*155*); behavioral therapies are also recommended by clinical practice guidelines (*215*). The cited studies primarily evaluated patients with a history of illicit opioid use, rather than prescription opioid use for chronic pain. Recent studies among patients with prescription opioid dependence (based on DSM-IV criteria) have found maintenance therapy with buprenorphine and buprenorphine-naloxone effective in preventing relapse (*216*,*217*). Treatment need in a community is often not met by capacity to provide buprenorphine or methadone maintenance therapy (*218*), and patient cost can be a barrier to buprenorphine treatment because insurance coverage of buprenorphine for opioid use disorder is often limited (*219*). Oral or long-acting injectable formulations of naltrexone can also be used as medication-assisted treatment for opioid use disorder in nonpregnant adults, particularly for highly motivated persons (*220*,*221*). Experts agreed that clinicians prescribing opioids should identify treatment resources for opioid use disorder in the community and should work together to ensure sufficient treatment capacity for opioid use disorder at the practice level.

If clinicians suspect opioid use disorder based on patient concerns or behaviors or on findings in prescription drug monitoring program data (see Recommendation 9) or from urine drug testing (see Recommendation 10), they should discuss their concern with their patient and provide an opportunity for the patient to disclose related concerns or problems. Clinicians should assess for the presence of opioid use disorder using DSM-5 criteria (*20*). Alternatively, clinicians can arrange for a substance use disorder treatment specialist to assess for the presence of opioid use disorder. For patients meeting criteria for opioid use disorder, clinicians should offer or arrange for patients to receive evidence-based treatment, usually medication-assisted treatment with buprenorphine or methadone maintenance therapy in combination with behavioral therapies. Oral or long-acting injectable naltrexone, a long-acting opioid antagonist, can also be used in nonpregnant adults. Naltrexone blocks the effects of opioids if they are used but requires adherence to daily oral therapy or monthly injections. For pregnant women with opioid use disorder, medication-assisted therapy with buprenorphine (without naloxone) or methadone has been associated with improved maternal outcomes and should be offered (see Recommendation 8). Clinicians should also consider offering naloxone for overdose prevention to patients with opioid use disorder (see Recommendation 8). For patients with problematic opioid use that does not meet criteria for opioid use disorder, experts noted that clinicians can offer to taper and discontinue opioids (see Recommendation 7). For patients who choose to but are unable to taper, clinicians may reassess for opioid use disorder and offer opioid agonist therapy if criteria are met.

Physicians not already certified to provide buprenorphine in an office-based setting can undergo training to receive a waiver from the Substance Abuse and Mental Health Services Administration (SAMHSA) that allows them to prescribe buprenorphine to treat patients with opioid use disorder. Physicians prescribing opioids in communities without sufficient treatment capacity for opioid use disorder should strongly consider obtaining this waiver. Information about qualifications and the process to obtain a waiver are available from SAMHSA (*222*). Clinicians do not need a waiver to offer naltrexone for opioid use disorder as part of their practice.

Additional guidance has been published previously (*215*) on induction, use, and monitoring of buprenorphine treatment (see Part 5) and naltrexone treatment (see Part 6) for opioid use disorder and on goals, components of, and types of effective psychosocial treatment that are recommended in conjunction with pharmacological treatment of opioid use disorder (see Part 7). Clinicians unable to provide treatment themselves should arrange for patients with opioid use disorder to receive care from a substance use disorder treatment specialist, such as an office-based buprenorphine or naltrexone treatment provider, or from an opioid treatment program certified by SAMHSA to provide supervised medication-assisted treatment for patients with opioid use disorder. Clinicians should assist patients in finding qualified treatment providers and should arrange for patients to follow up with these providers, as well as arranging for ongoing coordination of care. Clinicians should not dismiss patients from their practice because of a substance use disorder because this can adversely affect patient safety and could represent patient abandonment. Identification of substance use disorder represents an opportunity for a clinician to initiate potentially life-saving interventions, and it is important for the clinician to collaborate with the patient regarding their safety to increase the likelihood of successful treatment. In addition, although identification of an opioid use disorder can alter the expected benefits and risks of opioid therapy for pain, patients with co-occurring pain and substance use disorder require ongoing pain management that maximizes benefits relative to risks. Clinicians should continue to use nonpharmacologic and nonopioid pharmacologic pain treatments as appropriate (see Recommendation 1) and consider consulting a pain specialist as needed to provide optimal pain management.

Resources to help with arranging for treatment include SAMHSA's buprenorphine physician locator (http://buprenorphine.samhsa.gov/bwns_locator); SAMHSA's Opioid Treatment Program Directory (http://dpt2.samhsa.gov/treatment/directory.aspx); SAMHSA's Provider Clinical Support System for Opioid Therapies (http://pcss-o.org), which offers extensive experience in the treatment of substance use disorders and specifically of opioid use disorder, as well as expertise on the interface of pain and opioid misuse; and SAMHSA's Provider's Clinical Support System for Medication-Assisted Treatment (http://pcssmat.org), which offers expert physician mentors to answer questions about assessment for and treatment of substance use disorders.

## Conclusions and Future Directions

Clinical guidelines represent one strategy for improving prescribing practices and health outcomes. Efforts are required to disseminate the guideline and achieve widespread adoption and implementation of the recommendations in clinical settings. CDC will translate this guideline into user-friendly materials for distribution and use by health systems, medical professional societies, insurers, public health departments, health information technology developers, and clinicians and engage in dissemination efforts. CDC has provided a

checklist for prescribing opioids for chronic pain (http://stacks.cdc.gov/view/cdc/38025), additional resources such as fact sheets (http://www.cdc.gov/drugoverdose/prescribing/resources.html), and will provide a mobile application to guide clinicians in implementing the recommendations. CDC will also work with partners to support clinician education on pain management options, opioid therapy, and risk mitigation strategies (e.g., urine drug testing). Activities such as development of clinical decision support in electronic health records to assist clinicians' treatment decisions at the point of care; identification of mechanisms that insurers and pharmacy benefit plan managers can use to promote safer prescribing within plans; and development of clinical quality improvement measures and initiatives to improve prescribing and patient care within health systems have promise for increasing guideline adoption and improving practice. In addition, policy initiatives that address barriers to implementation of the guidelines, such as increasing accessibility of PDMP data within and across states, e-prescribing, and availability of clinicians who can offer medication-assisted treatment for opioid use disorder, are strategies to consider to enhance implementation of the recommended practices. CDC will work with federal partners and payers to evaluate strategies such as payment reform and health care delivery models that could improve patient health and safety. For example, strategies might include strengthened coverage for nonpharmacologic treatments, appropriate urine drug testing, and medication-assisted treatment; reimbursable time for patient counseling; and payment models that improve access to interdisciplinary, coordinated care.

As highlighted in the forthcoming report on the National Pain Strategy, an overarching federal effort that outlines a comprehensive population-level health strategy for addressing pain as a public health problem, clinical guidelines complement other strategies aimed at preventing illnesses and injuries that lead to pain. A draft of the National Pain Strategy has been published previously (*180*). These strategies include strengthening the evidence base for pain prevention and treatment strategies, reducing disparities in pain treatment, improving service delivery and reimbursement, supporting professional education and training, and providing public education. It is important that overall improvements be made in developing the workforce to address pain management in general, in addition to opioid prescribing specifically. This guideline also complements other federal efforts focused on addressing the opioid overdose epidemic including prescriber training and education, improving access to treatment for opioid use disorder, safe storage and disposal programs, utilization management mechanisms, naloxone distribution programs, law enforcement and supply reduction efforts, prescription drug monitoring program improvements, and support for community coalitions and state prevention programs.

This guideline provides recommendations that are based on the best available evidence that was interpreted and informed by expert opinion. The clinical scientific evidence informing the recommendations is low in quality. To inform future guideline development, more research is necessary to fill in critical evidence gaps. The evidence reviews forming the basis of this guideline clearly illustrate that there is much yet to be learned about the effectiveness, safety, and economic efficiency of long-term opioid therapy. As highlighted by an expert panel in a recent workshop sponsored by the National Institutes of Health on the role of opioid pain medications in the treatment of chronic pain, "evidence is insufficient for every clinical decision that a provider needs to make about the use of opioids for chronic pain" (*223*). The National Institutes of Health panel recommended that research is needed to improve our understanding of which types of pain, specific diseases, and patients are most likely to be associated with benefit and harm from opioid pain medications; evaluate multidisciplinary pain interventions; estimate cost-benefit; develop and validate tools for identification of patient risk and outcomes; assess the effectiveness and harms of opioid pain medications with alternative study designs; and investigate risk identification and mitigation strategies and their effects on patient and public health outcomes. It is also important to obtain data to inform the cost feasibility and cost-effectiveness of recommended actions, such as use of nonpharmacologic therapy and urine drug testing. Research that contributes to safer and more effective pain treatment can be implemented across public health entities and federal agencies (*4*). Additional research can inform the development of future guidelines for special populations that could not be adequately addressed in this guideline, such as children and adolescents, where evidence and guidance is needed but currently lacking. CDC is committed to working with partners to identify the highest priority research areas to build the evidence base. Yet, given that chronic pain is recognized as a significant public health problem, the risks associated with long-term opioid therapy, the availability of effective nonpharmacological and nonopioid pharmacologic treatment options for pain, and the potential for improvement in the quality of health care with the implementation of recommended practices, a guideline for prescribing is warranted with the evidence that is currently available. The balance between the benefits and the risks of long-term opioid therapy for chronic pain based on both clinical and contextual evidence is strong enough to support the issuance of category A recommendations in most cases.

CDC will revisit this guideline as new evidence becomes available to determine when evidence gaps have been sufficiently closed to warrant an update of the guideline. Until this research is conducted, clinical practice guidelines will have to be based on the best available evidence and expert opinion. This guideline is intended to improve communication between clinicians and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death. CDC is committed to evaluating the guideline to identify the impact of the recommendations on clinician and patient outcomes, both intended and unintended, and revising the recommendations in future updates when warranted.

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**TABLE 1. Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain**

| Outcome | Studies | Limitations | Inconsistency | Imprecision | Type of evidence | Other factors | Estimates of effect/findings |
|---|---|---|---|---|---|---|---|
| **Effectiveness and comparative effectiveness (KQ1)** | | | | | | | |
| **Effectiveness of long-term opioid therapy versus placebo or no opioid therapy for long-term (≥1 year) outcomes** | | | | | | | |
| Pain, function, and quality of life | None | —[†] | — | — | Insufficient | — | No evidence |
| **Harms and adverse events (KQ2)** | | | | | | | |
| **Risks of opioids versus placebo or no opioids on opioid abuse, addiction, and related outcomes; overdose; and other harms** | | | | | | | |
| Abuse or addiction | 1 cohort study (n = 568,640) | Serious limitations | Unknown (1 study) | No imprecision | 3 | None identified | One retrospective cohort study found long-term use of prescribed opioids associated with an increased risk of abuse or dependence diagnosis versus no opioid use (adjusted OR ranged from 14.9 to 122.5, depending on dose). |
| Abuse or addiction | 10 uncontrolled studies (n = 3,780) | Very serious limitations | Very serious inconsistency | No imprecision | 4 | None identified | In primary care settings, prevalence of opioid abuse ranged from 0.6% to 8% and prevalence of dependence from 3% to 26%. In pain clinic settings, prevalence of misuse ranged from 8% to 16% and addiction from 2% to 14%. Prevalence of aberrant drug-related behaviors ranged from 6% to 37%. |
| Overdose | 1 cohort study (n = 9,940) | Serious limitations | Unknown (1 study) | Serious imprecision | 3 | None identified | Current opioid use associated with increased risk of any overdose events (adjusted HR 5.2, 95% CI = 2.1–12) and serious overdose events (adjusted HR 8.4, 95% CI = 2.5–28) versus current nonuse. |
| Fractures | 1 cohort study (n = 2,341) and 1 case–control study (n = 21,739 case patients) | Serious limitations | No inconsistency | No imprecision | 3 | None identified | Opioid use associated with increased risk of fracture in 1 cohort study (adjusted HR 1.28, 95% CI = 0.99–1.64) and 1 case-control study (adjusted OR 1.27, 95% CI = 1.21–1.33). |
| Myocardial infarction | 1 cohort study (n = 426,124) and 1 case–control study (n = 11,693 case patients) | No limitations | No inconsistency | No imprecision | 3 | None identified | Current opioid use associated with increased risk of myocardial infarction versus nonuse (adjusted OR 1.28, 95% CI = 1.19–1.37 and incidence rate ratio 2.66, 95% CI = 2.30–3.08). |
| Endocrinologic harms | 1 cross-sectional study (n = 11,327) | Serious limitations | Unknown (1 study) | No imprecision | 3 | None identified | Long-term opioid use associated with increased risk for use of medications for erectile dysfunction or testosterone replacement versus nonuse (adjusted OR 1.5, 95% CI = 1.1–1.9). |
| **How do harms vary depending on the opioid dose used?** | | | | | | | |
| Abuse or addiction | 1 cohort study (n = 568,640) | Serious limitations | Unknown (1 study) | No imprecision | 3 | None identified | One retrospective cohort study found higher doses of long-term opioid therapy associated with increased risk of opioid abuse or dependence than lower doses. Compared to no opioid prescription, the adjusted odds ratios were 15 (95% CI = 10–21) for 1 to 36 MME/day, 29 (95 % CI = 20–41) for 36 to120 MME/day, and 122 (95 % CI = 73–205) for ≥120 MME/day. |
| Overdose | 1 cohort study (n = 9,940) and 1 case–control study (n = 593 case patients in primary analysis) | Serious limitations | No inconsistency | No imprecision | 3 | Magnitude of effect, dose response relationship | Versus 1 to <20 MME/day, one cohort study found an adjusted HR for an overdose event of 1.44 (95% CI = 0.57–3.62) for 20 to <50 MME/day that increased to 8.87 (95% CI = 3.99–19.72) at ≥100 MME/day; one case-control study found an adjusted OR for an opioid-related death of 1.32 (95% CI = 0.94–1.84) for 20 to 49 MME/day that increased to 2.88 (95% CI = 1.79–4.63) at ≥200 MME/day. |
| Fractures | 1 cohort study (n = 2,341) | Serious limitations | Unknown (1 study) | Serious imprecision | 3 | None identified | Risk of fracture increased from an adjusted HR of 1.20 (95% CI = 0.92–1.56) at 1 to <20 MME/day to 2.00 (95% CI = 1.24–3.24) at ≥50 MME/day; the trend was of borderline statistical significance. |

See table footnotes on page 47.

**TABLE 1. (*Continued*) Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain**

| Outcome | Studies | Limitations | Inconsistency | Imprecision | Type of evidence | Other factors | Estimates of effect/findings |
|---|---|---|---|---|---|---|---|
| Myocardial infarction | 1 cohort study (n = 426,124) | Serious limitations | Unknown (1 study) | No imprecision | 3 | None identified | Relative to a cumulative dose of 0 to 1,350 MME during a 90-day period, the incidence rate ratio for myocardial infarction for 1350 to <2700 MME was 1.21 (95% CI = 1.02–1.45), for 2,700 to <8,100 MME was 1.42 (95% CI = 1.21–1.67), for 8,100 to <18,000 MME was 1.89 (95% CI = 1.54–2.33), and for ≥18,000 MME was 1.73 (95% CI = 1.32–2.26). |
| Motor vehicle crash injuries | 1 case–control study (n = 5,300 case patients) | No limitations | Unknown (1 study) | No imprecision | 3 | None identified | No association between opioid dose and risk of motor vehicle crash injuries even though opioid doses >20 MME/day were associated with increased odds of road trauma among drivers. |
| Endocrinologic harms | 1 cross-sectional study (n = 11,327) New for update: 1 additional cross-sectional study (n=1,585) | Serious limitations | Consistent | No imprecision | 3 | None identified | Relative to 0 to <20 MME/day, the adjusted OR for ≥120 MME/day for use of medications for erectile dysfunction or testosterone replacement was 1.6 (95% CI = 1.0–2.4).<br>One new cross-sectional study found higher-dose long-term opioid therapy associated with increased risk of androgen deficiency among men receiving immediate-release opioids (adjusted OR per 10 MME/day 1.16, 95% CI = 1.09–1.23), but the dose response was very weak among men receiving ER/LA opioids. |
| **Dosing strategies (KQ3)** | | | | | | | |
| **Comparative effectiveness of different methods for initiating opioid therapy and titrating doses** | | | | | | | |
| Pain | 3 randomized trials (n = 93) | Serious limitations | Serious inconsistency | Very serious imprecision | 4 | None identified | Trials on effects of titration with immediate-release versus ER/LA opioids reported inconsistent results and had additional differences between treatment arms in dosing protocols (titrated versus fixed dosing) and doses of opioids used. |
| Overdose | New for update: 1 cohort study (n = 840,606) | Serious limitations | Unknown (1 study) | No imprecision | 4 | None identified | One new cross-sectional study found initiation of therapy with an ER/LA opioid associated with increased risk of overdose versus initiation with an immediate-release opioid (adjusted HR 2.33, 95% CI = 1.26–4.32). |
| **Comparative effectiveness of different ER/LA opioids** | | | | | | | |
| Pain and function | 3 randomized trials (n = 1,850) | Serious limitations | No inconsistency | No imprecision | 3 | None identified | No differences |
| All-cause mortality | 1 cohort study (n = 108,492)<br>New for update: 1 cohort study (n = 38,756) | Serious limitations | Serious inconsistency | No imprecision | 4 | None identified | One cohort study found methadone to be associated with lower all-cause mortality risk than sustained-release morphine in a propensity-adjusted analysis (adjusted HR 0.56, 95% CI = 0.51–0.62) and one cohort study among Tennessee Medicaid patients found methadone to be associated with higher risk of all-cause mortality than sustained-release morphine (adjusted HR 1.46, 95% CI = 1.17–1.73). |
| Abuse and related outcomes | 1 cohort study (n = 5,684) | Serious limitations | Unknown (1 study) | Serious imprecision | 4 | None identified | One cohort study found some differences between ER/LA opioids in rates of adverse outcomes related to abuse, but outcomes were nonspecific for opioid-related adverse events, precluding reliable conclusions. |
| **ER/LA versus immediate-release opioids** | | | | | | | |
| Endocrinologic harms | New for update: 1 cross-sectional study (n = 1,585) | Serious limitations | Unknown (1 study) | No imprecision | 4 | None identified | One cross-sectional study found ER/LA opioids associated with increased risk of androgen deficiency versus immediate-release opioids (adjusted OR 3.39, 95% CI = 2.39–4.77). |

See table footnotes on page 47.

**TABLE 1. (*Continued*) Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain**

| Outcome | Studies | Limitations | Inconsistency | Imprecision | Type of evidence | Other factors | Estimates of effect/findings |
|---|---|---|---|---|---|---|---|
| **Dose escalation versus dose maintenance or use of dose thresholds** | | | | | | | |
| Pain, function, or withdrawal due to opioid misuse | 1 randomized trial (n = 140) | Serious limitations | Unknown (1 study) | Very serious imprecision | 3 | None identified | No difference between more liberal dose escalation versus maintenance of current doses in pain, function, or risk of withdrawal due to opioid misuse, but there was limited separation in opioid doses between groups (52 versus 40 MME/day at the end of the trial). |
| **Immediate-release versus ER/LA opioids; immediate-release plus ER/LA opioids versus ER/LA opioids alone; scheduled and continuous versus as-needed dosing of opioids; or opioid rotation versus maintenance of current therapy** | | | | | | | |
| Pain, function, quality of life, and outcomes related to abuse | None | — | — | — | Insufficient | — | No evidence |
| **Effects of decreasing or tapering opioid doses versus continuation of opioid therapy** | | | | | | | |
| Pain and function | 1 randomized trial (n = 10) | Very serious limitations | Unknown (1 study) | Very serious imprecision | 4 | None identified | Abrupt cessation of morphine was associated with increased pain and decreased function compared with continuation of morphine. |
| **Comparative effectiveness of different tapering protocols and strategies** | | | | | | | |
| Opioid abstinence | 2 nonrandomized trials (n = 150) | Very serious limitations | No inconsistency | Very serious imprecision | 4 | None identified | No clear differences between different methods for opioid discontinuation or tapering in likelihood of opioid abstinence after 3–6 months |
| **Risk assessment and risk mitigation strategies (KQ4)** | | | | | | | |
| **Diagnostic accuracy of instruments for predicting risk for opioid overdose, addiction, abuse, or misuse among patients with chronic pain being considered for long-term opioid therapy** | | | | | | | |
| Opioid risk tool | 3 studies of diagnostic accuracy (n = 496)<br>New for update:<br>2 studies of diagnostic accuracy (n = 320) | Serious limitations | Very serious inconsistency | Serious imprecision | 4 | None identified | Based on a cutoff score of >4 (or unspecified), five studies (two fair-quality, three poor-quality) reported sensitivity that ranged from 0.20 to 0.99 and specificity that ranged from 0.16 to 0.88. |
| Screener and Opioid Assessment for Patients with Pain, Version 1 | 2 studies of diagnostic accuracy (n = 203) | Very serious limitations | No inconsistency | Serious imprecision | 3 | None identified | Based on a cutoff score of ≥8, sensitivity was 0.68 and specificity was 0.38 in one study, for a positive likelihood ratio of 1.11 and a negative likelihood ratio of 0.83. Based on a cutoff score of >6, sensitivity was 0.73 in one study. |
| Screener and Opioid Assessment for Patients with Pain-Revised | New for update:<br>2 studies of diagnostic accuracy (n = 320) | Very serious limitations | No inconsistency | Serious imprecision | 3 | None identified | Based on a cutoff score of >3 or unspecified, sensitivity was 0.25 and 0.53 and specificity was 0.62 and 0.73 in two studies, for likelihood ratios close to 1. |
| Brief Risk Interview | New for update:<br>2 studies of diagnostic accuracy (n = 320) | Very serious limitations | No inconsistency | Serious imprecision | 3 | None identified | Based on a "high risk" assessment, sensitivity was 0.73 and 0.83 and specificity was 0.43 and 0.88 in two studies, for positive likelihood ratios of 1.28 and 7.18 and negative likelihood ratios of 0.63 and 0.19. |

See table footnotes on page 47.

**TABLE 1. (*Continued*) Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain**

| Outcome | Studies | Limitations | Inconsistency | Imprecision | Type of evidence | Other factors | Estimates of effect/findings |
|---|---|---|---|---|---|---|---|
| **Effectiveness of risk prediction instruments on outcomes related to overdose, addiction, abuse, or misuse in patients with chronic pain** | | | | | | | |
| Outcomes related to abuse | None | — | — | — | Insufficient | — | No evidence |
| **Effectiveness of risk mitigation strategies, including opioid management plans, patient education, urine drug screening, use of prescription drug monitoring program data, use of monitoring instruments, more frequent monitoring intervals, pill counts, and use of abuse-deterrent formulations, on outcomes related to overdose, addiction, abuse, or misuse** | | | | | | | |
| Outcomes related to abuse | None | — | — | — | Insufficient | — | No evidence |
| **Effectiveness of risk prediction instruments on outcomes related to overdose, addiction, abuse, or misuse in patients with chronic pain** | | | | | | | |
| Outcomes related to abuse | None | — | — | — | Insufficient | — | No evidence |
| **Effectiveness of risk mitigation strategies, including opioid management plans, patient education, urine drug screening, use of prescription drug monitoring program data, use of monitoring instruments, more frequent monitoring intervals, pill counts, and use of abuse-deterrent formulations, on outcomes related to overdose, addiction, abuse, or misuse** | | | | | | | |
| Outcomes related to abuse | None | — | — | — | Insufficient | — | No evidence |
| **Comparative effectiveness of treatment strategies for managing patients with addiction to prescription opioids** | | | | | | | |
| Outcomes related to abuse | None | — | — | — | Insufficient | — | No evidence |
| **Effects of opioid therapy for acute pain on long-term use (KQ5)** | | | | | | | |
| Long-term opioid use | New for update: 2 cohort studies (n = 399,852) | Serious limitations | No inconsistency | No imprecision | 3 | None identified | One study found use of opioids within 7 days of low-risk surgery associated with increased likelihood of opioid use at 1 year (adjusted OR 1.44, 95% CI = 1.39–1.50), and one study found use of opioids within 15 days of onset of low back pain among workers with a compensation claim associated with increased risk of late opioid use (adjusted OR 2.08, 95% CI = 1.55–2.78 for 1 to 140 MME/day and OR 6.14, 95% CI = 4.92–7.66 for ≥450 MME/day). |

**Abbreviations:** CI = confidence interval; ER/LA = extended release/long-acting; HR = hazard ratio; MME = morphine milligram equivalents; OR = odds ratio.
* Ratings were made per GRADE quality assessment criteria; "no limitations" indicates that limitations assessed through the GRADE method were not identified.
† Not applicable as no evidence was available for rating.

**TABLE 2. Morphine milligram equivalent (MME) doses for commonly prescribed opioids**

| Opioid | Conversion factor* |
|---|---|
| Codeine | 0.15 |
| Fentanyl transdermal (in mcg/hr) | 2.4 |
| Hydrocodone | 1 |
| Hydromorphone | 4 |
| Methadone | |
| 1–20 mg/day | 4 |
| 21–40 mg/day | 8 |
| 41–60 mg/day | 10 |
| ≥61–80 mg/day | 12 |
| Morphine | 1 |
| Oxycodone | 1.5 |
| Oxymorphone | 3 |
| Tapentadol† | 0.4 |

**Source:** Adapted from Von Korff M, Saunders K, Ray GT, et al. Clin J Pain 2008;24:521–7 and Washington State Interagency Guideline on Prescribing Opioids for Pain (http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf).

* Multiply the dose for each opioid by the conversion factor to determine the dose in MMEs. For example, tablets containing hydrocodone 5 mg and acetaminophen 300 mg taken four times a day would contain a total of 20 mg of hydrocodone daily, equivalent to 20 MME daily; extended-release tablets containing oxycodone 10mg and taken twice a day would contain a total of 20mg of oxycodone daily, equivalent to 30 MME daily. The following cautions should be noted: 1) All doses are in mg/day except for fentanyl, which is mcg/hr. 2) Equianalgesic dose conversions are only estimates and cannot account for individual variability in genetics and pharmacokinetics. 3) Do not use the calculated dose in MMEs to determine the doses to use when converting opioid to another; when converting opioids the new opioid is typically dosed at substantially lower than the calculated MME dose to avoid accidental overdose due to incomplete cross-tolerance and individual variability in opioid pharmacokinetics. 4) Use particular caution with methadone dose conversions because the conversion factor increases at higher doses. 5) Use particular caution with fentanyl since it is dosed in mcg/hr instead of mg/day, and its absorption is affected by heat and other factors.

† Tapentadol is a mu receptor agonist and norepinephrine reuptake inhibitor. MMEs are based on degree of mu-receptor agonist activity, but it is unknown if this drug is associated with overdose in the same dose-dependent manner as observed with medications that are solely mu receptor agonists.

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# Local Coverage Determination (LCD): Controlled Substance Monitoring and Drugs of Abuse Testing (L35006)

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| Novitas Solutions, Inc. | A and B MAC | 04211 - MAC A | J - H | New Mexico |
| Novitas Solutions, Inc. | A and B MAC | 04212 - MAC B | J - H | New Mexico |
| Novitas Solutions, Inc. | A and B MAC | 04311 - MAC A | J - H | Oklahoma |
| Novitas Solutions, Inc. | A and B MAC | 04312 - MAC B | J - H | Oklahoma |
| Novitas Solutions, Inc. | A and B MAC | 04411 - MAC A | J - H | Texas |
| Novitas Solutions, Inc. | A and B MAC | 04412 - MAC B | J - H | Texas |
| Novitas Solutions, Inc. | A and B MAC | 04911 - MAC A | J - H | Colorado<br>New Mexico<br>Oklahoma<br>Texas |
| Novitas Solutions, Inc. | A and B MAC | 07101 - MAC A | J - H | Arkansas |
| Novitas Solutions, Inc. | A and B MAC | 07102 - MAC B | J - H | Arkansas |
| Novitas Solutions, Inc. | A and B MAC | 07201 - MAC A | J - H | Louisiana |
| Novitas Solutions, Inc. | A and B MAC | 07202 - MAC B | J - H | Louisiana |
| Novitas Solutions, Inc. | A and B MAC | 07301 - MAC A | J - H | Mississippi |
| Novitas Solutions, Inc. | A and B MAC | 07302 - MAC B | J - H | Mississippi |
| Novitas Solutions, Inc. | A and B MAC | 12101 - MAC A | J - L | Delaware |
| Novitas Solutions, Inc. | A and B MAC | 12102 - MAC B | J - L | Delaware |
| Novitas Solutions, Inc. | A and B MAC | 12201 - MAC A | J - L | District of Columbia |
| Novitas Solutions, Inc. | A and B MAC | 12202 - MAC B | J - L | District of Columbia |
| Novitas Solutions, Inc. | A and B MAC | 12301 - MAC A | J - L | Maryland |
| Novitas Solutions, Inc. | A and B MAC | 12302 - MAC B | J - L | Maryland |
| Novitas Solutions, Inc. | A and B MAC | 12401 - MAC A | J - L | New Jersey |
| Novitas Solutions, Inc. | A and B MAC | 12402 - MAC B | J - L | New Jersey |
| Novitas Solutions, Inc. | A and B MAC | 12501 - MAC A | J - L | Pennsylvania |
| Novitas Solutions, Inc. | A and B MAC | 12502 - MAC B | J - L | Pennsylvania |
| Novitas Solutions, Inc. | A and B MAC | 12901 - MAC A | J - L | District of Columbia<br>Delaware<br>Maryland<br>New Jersey<br>Pennsylvania |

Back to Top

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# LCD Information

## Document Information

LCD ID
L35006

Original Effective Date
For services performed on or after 10/01/2015

Original ICD-9 LCD ID
L32050

Revision Effective Date
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LCD Title
Controlled Substance Monitoring and Drugs of Abuse Testing

Revision Ending Date
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Retirement Date
N/A

Notice Period Start Date
11/05/2015

Notice Period End Date
12/30/2015



CMS National Coverage Policy This LCD supplements but does not replace, modify or supersede existing Medicare applicable National Coverage Determinations (NCDs) or payment policy rules and regulations for drug testing. Federal statute and subsequent Medicare regulations regarding provision and payment for medical services are lengthy. They are not repeated in this LCD. Neither Medicare payment policy rules nor this LCD replace, modify or supersede applicable state statutes regarding medical practice or other health practice professions acts, definitions and/or scopes of practice. All providers who report services for Medicare payment must fully understand and follow all existing laws, regulations and rules for Medicare payment for drug testing and must properly submit only valid claims for them. Please review and understand them and apply the medical necessity provisions in the policy within the context of the manual rules. Relevant CMS manual instructions and policies regarding drug testing are found in the following Internet-Only Manuals (IOMs) published on the CMS Web site:

CMS Internet-Only Manual (IOM) Publication 100-03, Medicare National Coverage Determinations Manual, Chapter 1, Section 130.6, Treatment of drug abuse

CMS Transmittal 653, Change Request 6852, Clinical Laboratory Fee Schedule (CLFS)- Special Instructions for Specific Test Codes (CPT CODE 80100, CPT Code 80101, CPT Code 80101QW, G0430, G0430QW and G0431QW)

CMS Transmittal 1905, Change Request 6800, February New Waived Tests

Code of Federal Regulations (CFR) Title 42, Part 410.32 indicates that diagnostic tests may only be ordered by the treating physician (or other treating practitioner acting within the scope of his or her license and Medicare requirements) who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem. Tests not ordered by the physician (or other qualified non-physician provider) who is treating the beneficiary are not reasonable and necessary (see section 411.15 (k)(1) of this chapter).

Medicare regulations at 42 CFR 410.32(a) state in part, that "…diagnostic tests must be ordered by the physician who is treating the beneficiary, that is, the physician (or other treating practitioner acting within the scope of his or her license and Medicare requirements) who furnishes a consultation or treats a beneficiary for a specific

medical problem and who uses the results in the management of the beneficiary's specific medical problem." Thus, **except where other uses have been authorized by statute, Medicare does not cover diagnostic testing used for routine screening or surveillance.**

Social Security Act (Title XVIII) Standard References:

- Title XVIII of the Social Security Act, Section 1862(a)(1)(A) states that no Medicare payment shall be made for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury.
- Title XVIII of the Social Security Act, Section 1862(a)(7). This section excludes routine physical examinations.
- Title XVIII of the Social Security Act, Section 1833(e) states that no payment shall be made to any provider for any claim that lacks the necessary information to process the claim.

Coverage Guidance
**Coverage Indications, Limitations, and/or Medical Necessity**

**Notice:** It is not appropriate to bill Medicare for services that are not covered (as described by this entire LCD) as if they are covered. When billing for non-covered services, use the appropriate modifier.

Compliance with the provisions in this policy may be monitored and addressed through post payment data analysis and subsequent medical review audits.

**Introduction and Overview**

For purposes of clarification the term physician or clinician refers to a Physician (or other treating practitioner acting within the scope of his or her license and Medicare requirements).

Urine drug testing (UDT) provides objective information to assist clinicians in identifying the presence or absence of drugs or drug classes in the body and making treatment decisions. A presumptive drug screen is used to detect the presence of a drug in the body. A blood or urine sample may be used. However, urine is the best specimen for presumptive screening, as blood is relatively insensitive for many common drugs, including psychotropic agents, opioids, and stimulants.

Common methods of drug analysis include chromatography, immunoassay, chemical ("spot") tests, and spectrometry. Analysis is comparative, matching the properties or behavior of a substance with that of a valid reference compound (a laboratory must possess a valid reference agent for every substance that it identifies). Drugs or classes of drugs are commonly assayed by presumptive testing. A presumptive test may be followed by definitive testing, when there is a positive inconsistent finding from the presumptive test in the setting of a symptomatic patient, as described below. Typically, the "spot" chemical tests (referred to above) are urine dipsticks or multiple drug cup devices.

Examples of drugs or classes of drugs that are commonly assayed by presumptive tests, followed by definitive testing, are: alcohols, amphetamines, barbituates/sedatives, benzodiazepines, cocaine and metabolites, methadone, antihistamines, stimulants, opioid analgesics, salicylates, cardiovascular drugs, antipsychotics, cyclic antidepressants, and others. Focused drug screens, most commonly for illicit drug use, may be more useful clinically.

There should be a direct correlation between those positive findings generated from presumptive testing and those requested definitive tests to specifically confirm such findings.

This policy provides:

- The appropriate indications and expected frequency of testing for safe medication management of prescribed substances in risk stratified pain management patients or in identifying and treating substance use disorders.
- Documentation requirements, by the clinician in the patient's medical record, to support the medical necessity for drug testing on an individual patient basis.
- An overview of presumptive urine drug testing (UDT) and definitive UDT testing by various methodologies.

**Definitions:**

By way of definition and as used in this document, the following terminology relates to the basic forms of UDT:

1. Presumptive (Qualitative) Drug Testing (hereafter called "presumptive" UDT)

    - Used when medically necessary to determine the presence or absence of drugs or drug classes in a urine sample;
    - Results expressed as negative or positive or as a numerical result;
    - Includes competitive immunoassays (IA) and thin layer chromatography.

2. Definitive (Quantitative) Confirmation (hereafter called "definitive" UDT)

    - Used when medically necessary to identify specific medications, illicit substances and metabolites; Reports the results of drugs absent or present in concentrations of ng/ml;
    - Limited to GC-MS and LC-MS/MS testing methods only.

3. Specimen Validity Testing

    - Urine specimen testing to ensure that it is consistent with normal human urine and has not been adulterated or substituted;
    - May include pH, specific gravity, oxidants and creatinine.

4. Point of Care Testing (POCT)

    - Used when medically necessary by clinicians for immediate test results for the immediate management of the patient;
    - Available when the patient and physician are in the same location;
    - IA test method that primarily identifies drug classes and a few specific drugs;
    - Platform consists of cups, dipsticks, cassettes, or strips; Read by the human eye.

5. Immunoassay (IA)

    - Ordered by clinicians primarily to identify the presence or absence of drug classes and some specific drugs;
    - Biochemical tests that measure the presence above a cutoff level of a substance (drug) with the use of an antibody;
    - Read by photometric technology.

6. Standing Orders

    - Test request for a specific patient representing repetitive testing to monitor a condition or disease for a limited number of sequential visits;
    - Individualized orders for certain patients for pre-determined tests based on historical use, risk and community trend patient profiles;
    - Clinician can alter the standing order.

      **Note:** A "profile" differs from a "panel" in that a profile responds to the clinical risks of a particular patient, whereas a panel encourages unnecessary or excessive testing when no clinical cause exists.

7. Blanket Orders

    - Test request that is not for a specific patient; rather, it is an identical order for all patient's in a clinician's practice without individualized decision making at every visit.

8. Reflex Testing

- Laboratory testing that is performed reflexively after initial test results to identify further diagnostic information essential to patient care.
- Testing Indications, performed as a step necessary to complete a physician's order is not considered reflex testing.

**Drug Test Methods**

The Clinical Laboratory Improvement Amendments (CLIA) regulates laboratory testing and requires clinical labs to be certified by their State as well as the CMS before they can accept human samples for diagnostic testing. Multiple types of CLIA certificates may be obtained based on the complexity of testing a lab conducts. CLIA levels of complexity (CLIA-waived, moderate complexity and high complexity) are addressed only as they relate to the HCPCS code description.

**A. Presumptive Testing Methods:**

1. CLIA-waived Presumptive UDT:

   CLIA-waived presumptive UDT consist of various platforms including cards, dipsticks, cassettes and cups based on qualitative competitive immunoassay methodology with one or more analytes in the test.

   - Positive test results are presumptive or not definitive due to sensitivity and cross-reactivity limitations.
   - Negative test results do not necessarily indicate the absence of a drug or substance in the urine specimen.
   - Presumptive UDT may be ordered when it is necessary to rapidly obtain and integrate results into clinical assessment and treatment decisions.
   - This type of test should only be used when results are needed immediately.

2. Presumptive UDT by FDA Approved/Cleared IA Analysis

   - Chemistry analyzers with IA UDT technology are used in an office or clinical laboratory setting. When FDA approved/cleared platforms and reagents are used, testing is classified as moderately complex.
   - This test may be used when less immediate test results are required.
   - At no time is IA technology by chemistry analyzer analysis considered confirmatory (definitive) testing.
   - Presumptive positive tests are not definitive due to sensitivity, specificity, and cross-reactivity limitations.
   - Negative test results do not necessarily indicate the absence of a drug or substance in the urine specimen.

3. Presumptive UDT by Laboratory Developed Test (LDT) IA Analysis:

   - Similar to #2 above except only performed in a clinical laboratory setting.

**Limitations of Presumptive UDT:**

Presumptive UDT testing is limited for the following reasons:

- Primarily screens for drug classes rather than specific drugs, and therefore, the practitioner may not be able to determine if a different drug within the same class is causing the positive result;
- Produces erroneous results due to cross-reactivity with other compounds or does not detect all drugs within a drug class;
- Given that not all prescription medications or synthetic/analog drugs are detectable or have assays available, it is unclear as to whether other drugs are present when some tests are reported as positive;
- Cut-off may be too high to detect presence of a drug. This information could cause a practitioner to make a wrong assumption or clinical decision.

**B. Definitive UDT:**

Gas Chromatography coupled with Mass Spectrometry (GC-MS) and High Performance Liquid Chromatography coupled with Tandem Mass Spectrometry (LC-MS/MS) are complex technologies that use the separation capabilities of gaseous or liquid chromatography with the analytical capabilities of mass spectrometry.

Both methodologies require the competency of on-site highly trained experts in this technology and interpretation of results. While these tests require different sample preparation and analytical runs, they are quantitative tests that identify all specific drugs, metabolites, and most illicit substances and report the results as absent or present in concentrations of ng/mL.

Quantification should not be used to determine adherence with a specific dosage or time of dose of a pain medication or illicit drug for clinical purposes. Rather, the use of quantitative drug data may be important for many reasons such as in a differential patient assessment.

For example, when several opioids are present in the urine of a patient prescribed a single opioid, quantification may help the clinician decide whether the presence of the other opioids is consistent with metabolism of the prescribed opioid, opioid contamination during manufacturing, or if more than one drug within a class is being used.

Quantification may also provide information in the setting of illicit drug use. Serial creatinine-corrected quantitative values may assist in the differential assessment of ongoing drug use or cessation of drug use with continued drug excretion.

Definitive UDT is reasonable and necessary in order to:

- Identify a specific substance or metabolite that is inadequately detected by a presumptive UDT;
- Definitively identify specific drugs in a large family of drugs;
- Identify a specific substance or metabolite that is not detected by presumptive UDT such as fentanyl, meperidine, synthetic cannabinoids and other synthetic/analog drugs;
- Identify drugs when a definitive concentration of a drug is needed to guide management (e.g., discontinuation of THC use according to a treatment plan);
- Identify a negative, or confirm a positive, presumptive UDT result that is inconsistent with a patient's self-report, presentation, medical history, or current prescribed pain medication plan;
- Rule out an error as the cause of a presumptive UDT result;
- Identify non-prescribed medication or illicit use for ongoing safe prescribing of controlled substances; and
- Use in a differential assessment of medication efficacy, side effects, or drug-drug interactions.

Definitive UDT may be reasonable and necessary based on patient specific indications, including historical use, medication response, and clinical assessment, when accurate results are necessary to make clinical decisions. The clinician's rationale for the definitive UDT and the tests ordered must be documented in the patient's medical record.

**Covered Indications for UDT**

**Group A** – Symptomatic patients, multiple drug ingestion or patients with unreliable history.

A patient who presents in a variety of medical settings with signs or symptoms of substance use toxicity will be treated presumptively to stabilize the patient while awaiting rapid, then definitive testing to determine the cause(s) of the presentation.

The need for definitive UDT is based upon rapid test findings, responses to medical interventions, and treatment plan.

A presumptive UDT should be performed as part of the evaluation and management of a patient who presents in an urgent care setting with any one of the following:

- Coma
- Altered mental status in the absence of a clinically defined toxic syndrome or toxidrome
- Severe or unexplained cardiovascular instability (cardiotoxicity)
- Unexplained metabolic or respiratory acidosis in the absence of a clinically defined toxic syndrome or toxidrome
- Seizures with an undetermined history
- To provide antagonist to specific drug

The presumptive findings, definitive drug tests ordered and reasons for the testing must be documented in the patient's medical record.

**Group B** - Diagnosis and treatment for substance abuse or dependence.

A patient in active treatment for substance use disorder (SUD) or monitoring across different phases of recovery may undergo medical management for a variety of medical conditions.

A physician who is writing prescriptions for medications to treat either the SUD or other conditions may need to know if the patient is taking substances which can interact with prescribed medications or taking prescribed medications as expected.

The risk of drug-drug interactions is inherent to the patient, and may be compounded by prescribed medications.

UDT is a medically necessary and useful component of chemical dependency diagnosis and treatment. The UDT result influences treatment and level of care decisions.

Ordered tests and testing methods (presumptive or definitive) must match the stage of screening, treatment, or recovery; the documented history; and Diagnostic and Statistical Manual of Mental Disorders (DSM V) diagnosis.

For patients with no known indicators of risk for SUDs, the clinician may screen for a broad range of commonly abused drugs using presumptive UDT.

For patients with known indicators of risk for SUDs, the clinician may screen for a broad range of commonly abused drugs using definitive UDT.

For patients with a diagnosed SUD, the clinician should perform random UDT, at random intervals in order to properly monitor the patient. Testing profiles must be determined by the clinician based on the following medical necessity guidance criteria:

- Patient history, physical examination, and previous laboratory findings
- Stage of treatment or recovery;
- Suspected abused substance;
- Substances that may present high risk for additive or synergistic interactions with prescribed medication (e.g., benzodiazepines, alcohol).

The patient’s medical record must include an appropriate testing frequency based on the stage of screening, treatment, or recovery; the rationale for the drugs/drug classes ordered; and the results must be documented in the medical record and used to direct care.

**Group C** - Treatment for patients on chronic opioid therapy (COT).

A physician who is writing prescriptions for medications to treat chronic pain can manage a patient better if the physician knows whether the patient is consuming another medication or substance, which could suggest the possibility of SUD or lead to drug-drug interactions. Additionally, UDT may help the physician monitor for medication adherence, efficacy, side effects, and patient safety in general.

A broad cross section of the general population will develop either cancer pain syndrome or non-cancer pain which will require prolonged or chronic opioid therapy for management. The risk of addiction in this population is considered equivalent to the risk in the general population. In contrast to the population of individuals who have a history of SUD, in the cancer and non-cancer pain population the risk of SUD is inherent to the substance(s) to which the patient is exposed.

1. COT UDT Testing Objectives:

a. Identifies absence of prescribed medication and potential for abuse, misuse, and diversion;
b. Identifies undisclosed substances, such as alcohol, unsanctioned prescription medication, or illicit substances;
c. Identifies substances that contribute to adverse events or drug-drug interactions;
d. Provides objectivity to the treatment plan;
e. Reinforces therapeutic compliance with the patient;
f. Provides additional documentation demonstrating compliance with patient evaluation and monitoring;
g. Provides diagnostic information to help assess individual patient response to medications (e.g., metabolism, side effects, drug-drug interaction, etc.) over time for ongoing management of prescribed medications.

2. Medical Necessity Guidance:

Criteria to establish medical necessity for drug testing must be based on patient- specific elements identified during the clinical assessment, and documented by the clinician in the patient's medical record and minimally include the following elements:

- Patient history, physical examination and previous laboratory findings;
- Current treatment plan;
- Prescribed medication(s); and
- Risk assessment plan.

National pain organizations, physician societies, and the Federation of State Medical Boards recommend a practical approach to definitive UDT for COT.

Frequency of testing beyond the baseline presumptive UDT must be based on individual patient needs substantiated by documentation in the patient's medical record. Recommendations for the ordering of presumptive and definitive UDT for patients on COT are as follows:

a. COT Baseline Testing:

Initial presumptive or definitive COT patient testing may include amphetamine/methamphetamine, barbiturates, benzodiazepines, cocaine, methadone, oxycodone, tricyclic antidepressants, tetrahydrocannabinoid, opioids, opiates, heroin, and synthetic/analog or "designer" drugs.

b. COT Monitoring Testing:

Ongoing testing may be medically reasonable and necessary based on the patient history, clinical assessment, including medication side effects or inefficacy, suspicious behaviors, self -escalation of dose, doctor-shopping, indications/symptoms of illegal drug use, evidence of diversion, or other clinician documented change in affect or behavioral pattern.

The frequency of testing must be based on a complete clinical assessment of the individual's risk potential for abuse and diversion using a validated risk assessment interview or questionnaire and should include the patient's response to prescribed medications and the side effects of medications.

The clinician should perform random UDT at random intervals, in order to properly monitor a patient. UDT testing does not have to be associated with an office visit.

**Drug Testing Panels**

A. Presumptive UDT Panels

Presumptive UDT testing may be ordered as a panel because the Medicare billing codes are defined on a "per patient encounter" basis regardless of the number of analytes tested.

Presumptive UDT orders should be individualized based on clinical history and risk assessment, and must be documented in the medical record.

B. Definitive UDT Panels

At the current time, physician-directed definitive profile testing is reasonable and necessary when ordered for a particular patient based upon historical use and community trends. However, the same physician-defined profile is not reasonable and necessary for every patient in a physician's practice.

Definitive UDT orders should be individualized based on clinical history and risk assessment, and must be documented in the medical record.

**Specimen Type**

Urine or oral fluid is the preferred biologic specimen for testing because of the ease of collection, storage, and cost-effectiveness. UDT cannot detect the dosage of drug ingested/used, the time of use, or the means of delivery (intravenous vs. oral vs. inhaled). Detection time of a substance in urine is typically 1-3 days depending on the drug, rate of metabolism, and rate of excretion. Lipid-soluble drugs, such as marijuana, may remain in body fat and be detected upwards of a week or more.

**Other Covered Services**

1. Reflex Testing by Reference Laboratories – since reference laboratories do not have access to patient-specific data, reflex testing under the following circumstances is reasonable and necessary:

    - To verify a presumptive positive UDT using definitive UDT (GC-MS or LCMS/MS) before reporting the presumptive finding to the ordering clinician and without an additional order from the clinician;

      Or

    - To confirm the absence of prescribed medications when a negative result is obtained by presumptive UDT in the laboratory for a prescribed medication listed by the ordering clinician.

2. Direct to definitive UDT without a presumptive UDT is reasonable and necessary, when individualized for a particular patient, in the following circumstances:

    - To identify a specific substance or its metabolite that is in a large class of drugs, or that is inadequately detected or not detected by presumptive UDT, such as fentanyl, meperidine, synthetic cannabinoids, and other synthetic/analog drugs;
    - For use in a differential assessment of medication efficacy, side effects, or drug-drug interactions;
    - To identify non-prescribed medication or illicit substance use for ongoing safe prescribing of controlled substances, where clinician has documented concerns related to safety risks attendant to failure to identify specific substances suspected based upon clinical review and judgment; or
    - To identify drugs when a definitive concentration of a drug is needed to guide management (e.g., discontinuation of THC use according to a treatment plan).

3. Definitive testing to confirm a negative presumptive UDT result, upon the order of the clinician, is reasonable and necessary in the following circumstances:

a. The result is inconsistent with a patient's self-report, presentation, medical history, or current prescribed medication plan (should be present in the sample);
b. Following a review of clinical findings, the clinician suspects use of a substance that is inadequately detected or not detected by a presumptive UDT; or
c. To rule out an error as the cause of a negative presumptive UDT result.
d. Definitive testing to confirm a presumptive UDT positive result, upon the order of the clinician, is reasonable and necessary when the result is inconsistent with the expected result, a patient's self-report, presentation, medical history, or current prescribed medication plan.

**Limitations**

**Non-Covered Services**

1. Blanket Orders.

2. Reflex definitive UDT is not reasonable and necessary when presumptive testing is performed at point of care because the clinician may have sufficient information to manage the patient. If the clinician is not satisfied, he/she must determine the clinical appropriateness of and order specific subsequent definitive testing (e.g., the patient admits to using a particular drug, or the IA cut-off is set at such a point that is sufficiently low that the physician is satisfied with the presumptive test result).

3. Routine standing orders for all patients in a physician's practice are not reasonable and necessary.

4. It is not reasonable and necessary for a physician to perform presumptive POCT and order presumptive IA testing from a reference laboratory. In other words, Medicare will only pay for one presumptive test result per patient per date of service regardless of the number of billing providers.

5. It is not reasonable and necessary for a physician to perform presumptive IA testing and order presumptive IA testing from a reference laboratory with or without reflex testing. Medicare will only pay for one presumptive test result per patient per date of service regardless of the number of billing providers.

6. It is not reasonable and necessary for a reference laboratory to perform and bill IA presumptive UDT prior to definitive testing without a specific physician's order for the presumptive testing.

7. IA testing, regardless of whether it is qualitative or semi-quantitative (numerical), may not be used to "confirm" or definitively identify a presumptive test result obtained by cups, dipsticks, cards, cassettes or other IA testing methods. Definitive UDT provides specific identification or quantification by GC-MS or LCMS/MS.

8. Drug testing of two different specimen types from the same patient on the same date of service for the same drugs/metabolites/analytes.

9. UDT for medico-legal or employment purposes or to protect a physician from drug diversion charges.

10. Specimen validity testing including, but not limited to, pH, specific gravity, oxidants, creatinine.

As published in CMS IOM Pub. 100-08, Chapter 13, Section 13.5.1, in order to be covered under Medicare, a service shall be reasonable and necessary. When appropriate, contractors shall describe the circumstances under which the proposed LCD for the service is considered reasonable and necessary under Section 1862(a)(1)(A). Contractors shall consider a service to be reasonable and necessary if the contractor determines that the service is:

- Safe and effective.
- Not experimental or investigational (exception: routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 that meet the requirements of the Clinical Trials NCD are considered reasonable and necessary).
- Appropriate, including the duration and frequency that is considered appropriate for the service, in terms of whether it is:

    - Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member.
    - Furnished in a setting appropriate to the patient's medical needs and condition.
    - Ordered and furnished by qualified personnel.
    - One that meets, but does not exceed, the patient's medical needs.
    - At least as beneficial as an existing and available medically appropriate alternative.

Back to Top

# Coding Information

Bill Type Codes:

Contractors may specify Bill Types to help providers identify those Bill Types typically used to report this service. Absence of a Bill Type does not guarantee that the policy does not apply to that Bill Type. Complete absence of all Bill Types indicates that coverage is not influenced by Bill Type and the policy should be assumed to apply equally to all claims.

012x Hospital Inpatient (Medicare Part B only)
013x Hospital Outpatient
014x Hospital - Laboratory Services Provided to Non-patients
021x Skilled Nursing - Inpatient (Including Medicare Part A)
022x Skilled Nursing - Inpatient (Medicare Part B only)
023x Skilled Nursing - Outpatient
071x Clinic - Rural Health
072x Clinic - Hospital Based or Independent Renal Dialysis Center
073x Clinic - Freestanding
077x Clinic - Federally Qualified Health Center (FQHC)
085x Critical Access Hospital

Revenue Codes:

Contractors may specify Revenue Codes to help providers identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory. Unless specified in the policy, services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to apply equally to all Revenue Codes.

Note: The contractor has identified the Bill Type and Revenue Codes applicable for use with the CPT/HCPCS codes included in this LCD. Providers are reminded that not all CPT/HCPCS codes listed can be billed with all Bill Type and/or Revenue Codes listed. CPT/HCPCS codes are required to be billed with specific Bill Type and Revenue Codes. Providers are encouraged to refer to the CMS Internet-Only Manual (IOM) Pub. 100-04, Claims Processing Manual, for further guidance.

0300 Laboratory - General Classification
0301 Laboratory - Chemistry
0309 Laboratory - Other Laboratory

0971 Professional Fees - Laboratory

CPT/HCPCS Codes
**Group 1 Paragraph: Note:** Providers are reminded to refer to the long descriptors of the CPT codes in their CPT book.

**Presumptive UDT**

**Group 1 Codes:**
G0477 Drug test presump optical
G0478 Drug test presump opt inst
G0479 Drug test presump not opt

**Group 2 Paragraph:**
**Definitive UDT**

**Group 2 Codes:**
80159 Drug assay clozapine
80171 Drug screen quant gabapentin
80173 Assay of haloperidol
80183 Drug scrn quant oxcarbazepin
80184 Assay of phenobarbital
83789 Mass spectrometry qual/quan
83992 Assay for phencyclidine
84999 Clinical chemistry test
G0480 Drug test def 1-7 classes
G0481 Drug test def 8-14 classes
G0482 Drug test def 15-21 classes
G0483 Drug test def 22+ classes

ICD-10 Codes that Support Medical Necessity
**Group 1 Paragraph:** It is the provider's responsibility to select codes carried out to the highest level of specificity and selected from the ICD-10-CM code book appropriate to the year in which the service is rendered for the claim(s) submitted.

**Presumptive UDT**

**Group 1 Codes:**

| ICD-10 Codes | Description |
|---|---|
| E87.2 | Acidosis |
| F10.120* | Alcohol abuse with intoxication, uncomplicated |
| F11.20* | Opioid dependence, uncomplicated |
| F12.120* | Cannabis abuse with intoxication, uncomplicated |
| F12.220* | Cannabis dependence with intoxication, uncomplicated |
| F13.120* | Sedative, hypnotic or anxiolytic abuse with intoxication, uncomplicated |
| F14.120* | Cocaine abuse with intoxication, uncomplicated |
| F14.220* | Cocaine dependence with intoxication, uncomplicated |
| F16.120* | Hallucinogen abuse with intoxication, uncomplicated |
| F18.10* | Inhalant abuse, uncomplicated |
| F18.120* | Inhalant abuse with intoxication, uncomplicated |
| F18.90* | Inhalant use, unspecified, uncomplicated |
| F19.20* | Other psychoactive substance dependence, uncomplicated |
| F20.0 | Paranoid schizophrenia |
| F20.1 | Disorganized schizophrenia |

| ICD-10 Codes | Description |
|---|---|
| F20.2 | Catatonic schizophrenia |
| F20.89 | Other schizophrenia |
| F55.3* | Abuse of steroids or hormones |
| F55.4* | Abuse of vitamins |
| F55.8* | Abuse of other non-psychoactive substances |
| G40.301 | Generalized idiopathic epilepsy and epileptic syndromes, not intractable, with status epilepticus |
| G40.309 | Generalized idiopathic epilepsy and epileptic syndromes, not intractable, without status epilepticus |
| G40.311 | Generalized idiopathic epilepsy and epileptic syndromes, intractable, with status epilepticus |
| G40.319 | Generalized idiopathic epilepsy and epileptic syndromes, intractable, without status epilepticus |
| G40.901 | Epilepsy, unspecified, not intractable, with status epilepticus |
| G40.909 | Epilepsy, unspecified, not intractable, without status epilepticus |
| G40.911 | Epilepsy, unspecified, intractable, with status epilepticus |
| G40.919 | Epilepsy, unspecified, intractable, without status epilepticus |
| I44.0 | Atrioventricular block, first degree |
| I44.1 | Atrioventricular block, second degree |
| I44.30 | Unspecified atrioventricular block |
| I45.81 | Long QT syndrome |
| I47.1 | Supraventricular tachycardia |
| I47.2 | Ventricular tachycardia |
| M25.50 | Pain in unspecified joint |
| M47.811 | Spondylosis without myelopathy or radiculopathy, occipito-atlanto-axial region |
| M47.812 | Spondylosis without myelopathy or radiculopathy, cervical region |
| M47.813 | Spondylosis without myelopathy or radiculopathy, cervicothoracic region |
| M47.816 | Spondylosis without myelopathy or radiculopathy, lumbar region |
| M47.817 | Spondylosis without myelopathy or radiculopathy, lumbosacral region |
| M47.818 | Spondylosis without myelopathy or radiculopathy, sacral and sacrococcygeal region |
| M51.14 | Intervertebral disc disorders with radiculopathy, thoracic region |
| M51.15 | Intervertebral disc disorders with radiculopathy, thoracolumbar region |
| M51.16 | Intervertebral disc disorders with radiculopathy, lumbar region |
| M51.17 | Intervertebral disc disorders with radiculopathy, lumbosacral region |
| M51.36 | Other intervertebral disc degeneration, lumbar region |
| M51.37 | Other intervertebral disc degeneration, lumbosacral region |
| M54.10 | Radiculopathy, site unspecified |
| M54.14 | Radiculopathy, thoracic region |
| M54.15 | Radiculopathy, thoracolumbar region |
| M54.16 | Radiculopathy, lumbar region |
| M54.17 | Radiculopathy, lumbosacral region |
| M54.18 | Radiculopathy, sacral and sacrococcygeal region |
| M54.2 | Cervicalgia |
| M54.5 | Low back pain |
| M60.811 | Other myositis, right shoulder |
| M60.812 | Other myositis, left shoulder |
| M60.821 | Other myositis, right upper arm |
| M60.822 | Other myositis, left upper arm |
| M60.831 | Other myositis, right forearm |
| M60.832 | Other myositis, left forearm |
| M60.841 | Other myositis, right hand |
| M60.842 | Other myositis, left hand |
| M60.851 | Other myositis, right thigh |
| M60.852 | Other myositis, left thigh |
| M60.861 | Other myositis, right lower leg |
| M60.862 | Other myositis, left lower leg |
| M60.871 | Other myositis, right ankle and foot |
| M60.872 | Other myositis, left ankle and foot |
| M60.88 | Other myositis, other site |
| M60.89 | Other myositis, multiple sites |
| M79.1 | Myalgia |
| M79.2 | Neuralgia and neuritis, unspecified |

| ICD-10 Codes | Description |
|---|---|
| M79.7 | Fibromyalgia |
| R40.0 | Somnolence |
| R40.1 | Stupor |
| R40.2111 | Coma scale, eyes open, never, in the field [EMT or ambulance] |
| R40.2112 | Coma scale, eyes open, never, at arrival to emergency department |
| R40.2113 | Coma scale, eyes open, never, at hospital admission |
| R40.2114 | Coma scale, eyes open, never, 24 hours or more after hospital admission |
| R40.2121 | Coma scale, eyes open, to pain, in the field [EMT or ambulance] |
| R40.2122 | Coma scale, eyes open, to pain, at arrival to emergency department |
| R40.2123 | Coma scale, eyes open, to pain, at hospital admission |
| R40.2124 | Coma scale, eyes open, to pain, 24 hours or more after hospital admission |
| R40.2211 | Coma scale, best verbal response, none, in the field [EMT or ambulance] |
| R40.2212 | Coma scale, best verbal response, none, at arrival to emergency department |
| R40.2213 | Coma scale, best verbal response, none, at hospital admission |
| R40.2214 | Coma scale, best verbal response, none, 24 hours or more after hospital admission |
| R40.2221 | Coma scale, best verbal response, incomprehensible words, in the field [EMT or ambulance] |
| R40.2222 | Coma scale, best verbal response, incomprehensible words, at arrival to emergency department |
| R40.2223 | Coma scale, best verbal response, incomprehensible words, at hospital admission |
| R40.2224 | Coma scale, best verbal response, incomprehensible words, 24 hours or more after hospital admission |
| R40.2311 | Coma scale, best motor response, none, in the field [EMT or ambulance] |
| R40.2312 | Coma scale, best motor response, none, at arrival to emergency department |
| R40.2313 | Coma scale, best motor response, none, at hospital admission |
| R40.2314 | Coma scale, best motor response, none, 24 hours or more after hospital admission |
| R40.2321 | Coma scale, best motor response, extension, in the field [EMT or ambulance] |
| R40.2322 | Coma scale, best motor response, extension, at arrival to emergency department |
| R40.2323 | Coma scale, best motor response, extension, at hospital admission |
| R40.2324 | Coma scale, best motor response, extension, 24 hours or more after hospital admission |
| R40.2341 | Coma scale, best motor response, flexion withdrawal, in the field [EMT or ambulance] |
| R40.2342 | Coma scale, best motor response, flexion withdrawal, at arrival to emergency department |
| R40.2343 | Coma scale, best motor response, flexion withdrawal, at hospital admission |
| R40.2344 | Coma scale, best motor response, flexion withdrawal, 24 hours or more after hospital admission |
| R41.0 | Disorientation, unspecified |
| R41.82 | Altered mental status, unspecified |
| R44.0 | Auditory hallucinations |
| R44.3 | Hallucinations, unspecified |
| R56.9 | Unspecified convulsions |
| T39.011A | Poisoning by aspirin, accidental (unintentional), initial encounter |
| T39.012A | Poisoning by aspirin, intentional self-harm, initial encounter |
| T39.013A | Poisoning by aspirin, assault, initial encounter |
| T39.014A | Poisoning by aspirin, undetermined, initial encounter |
| T39.091A | Poisoning by salicylates, accidental (unintentional), initial encounter |
| T39.092A | Poisoning by salicylates, intentional self-harm, initial encounter |
| T39.093A | Poisoning by salicylates, assault, initial encounter |
| T39.094A | Poisoning by salicylates, undetermined, initial encounter |
| T39.1X1A | Poisoning by 4-Aminophenol derivatives, accidental (unintentional), initial encounter |
| T39.1X2A | Poisoning by 4-Aminophenol derivatives, intentional self-harm, initial encounter |
| T39.1X3A | Poisoning by 4-Aminophenol derivatives, assault, initial encounter |
| T39.1X4A | Poisoning by 4-Aminophenol derivatives, undetermined, initial encounter |
| T39.2X1A | Poisoning by pyrazolone derivatives, accidental (unintentional), initial encounter |
| T39.2X2A | Poisoning by pyrazolone derivatives, intentional self-harm, initial encounter |
| T39.2X3A | Poisoning by pyrazolone derivatives, assault, initial encounter |
| T39.2X4A | Poisoning by pyrazolone derivatives, undetermined, initial encounter |
| T39.311A | Poisoning by propionic acid derivatives, accidental (unintentional), initial encounter |
| T39.312A | Poisoning by propionic acid derivatives, intentional self-harm, initial encounter |
| T39.313A | Poisoning by propionic acid derivatives, assault, initial encounter |
| T39.314A | Poisoning by propionic acid derivatives, undetermined, initial encounter |
| T39.391A | |

| ICD-10 Codes | Description |
|---|---|
| | Poisoning by other nonsteroidal anti-inflammatory drugs [NSAID], accidental (unintentional), initial encounter |
| T39.392A | Poisoning by other nonsteroidal anti-inflammatory drugs [NSAID], intentional self-harm, initial encounter |
| T39.393A | Poisoning by other nonsteroidal anti-inflammatory drugs [NSAID], assault, initial encounter |
| T39.394A | Poisoning by other nonsteroidal anti-inflammatory drugs [NSAID], undetermined, initial encounter |
| T40.0X1A | Poisoning by opium, accidental (unintentional), initial encounter |
| T40.0X2A | Poisoning by opium, intentional self-harm, initial encounter |
| T40.0X3A | Poisoning by opium, assault, initial encounter |
| T40.0X4A | Poisoning by opium, undetermined, initial encounter |
| T40.1X1A | Poisoning by heroin, accidental (unintentional), initial encounter |
| T40.1X2A | Poisoning by heroin, intentional self-harm, initial encounter |
| T40.1X3A | Poisoning by heroin, assault, initial encounter |
| T40.1X4A | Poisoning by heroin, undetermined, initial encounter |
| T40.2X1A | Poisoning by other opioids, accidental (unintentional), initial encounter |
| T40.2X2A | Poisoning by other opioids, intentional self-harm, initial encounter |
| T40.2X3A | Poisoning by other opioids, assault, initial encounter |
| T40.2X4A | Poisoning by other opioids, undetermined, initial encounter |
| T40.3X1A | Poisoning by methadone, accidental (unintentional), initial encounter |
| T40.3X2A | Poisoning by methadone, intentional self-harm, initial encounter |
| T40.3X3A | Poisoning by methadone, assault, initial encounter |
| T40.3X4A | Poisoning by methadone, undetermined, initial encounter |
| T40.4X1A | Poisoning by other synthetic narcotics, accidental (unintentional), initial encounter |
| T40.4X2A | Poisoning by other synthetic narcotics, intentional self-harm, initial encounter |
| T40.4X3A | Poisoning by other synthetic narcotics, assault, initial encounter |
| T40.4X4A | Poisoning by other synthetic narcotics, undetermined, initial encounter |
| T40.5X1A | Poisoning by cocaine, accidental (unintentional), initial encounter |
| T40.5X2A | Poisoning by cocaine, intentional self-harm, initial encounter |
| T40.5X3A | Poisoning by cocaine, assault, initial encounter |
| T40.5X4A | Poisoning by cocaine, undetermined, initial encounter |
| T40.601A | Poisoning by unspecified narcotics, accidental (unintentional), initial encounter |
| T40.602A | Poisoning by unspecified narcotics, intentional self-harm, initial encounter |
| T40.603A | Poisoning by unspecified narcotics, assault, initial encounter |
| T40.604A | Poisoning by unspecified narcotics, undetermined, initial encounter |
| T40.691A | Poisoning by other narcotics, accidental (unintentional), initial encounter |
| T40.692A | Poisoning by other narcotics, intentional self-harm, initial encounter |
| T40.693A | Poisoning by other narcotics, assault, initial encounter |
| T40.694A | Poisoning by other narcotics, undetermined, initial encounter |
| T40.7X1A | Poisoning by cannabis (derivatives), accidental (unintentional), initial encounter |
| T40.7X2A | Poisoning by cannabis (derivatives), intentional self-harm, initial encounter |
| T40.7X3A | Poisoning by cannabis (derivatives), assault, initial encounter |
| T40.7X4A | Poisoning by cannabis (derivatives), undetermined, initial encounter |
| T40.8X2A | Poisoning by lysergide [LSD], intentional self-harm, initial encounter |
| T40.8X3A | Poisoning by lysergide [LSD], assault, initial encounter |
| T40.8X4A | Poisoning by lysergide [LSD], undetermined, initial encounter |
| T40.901A | Poisoning by unspecified psychodysleptics [hallucinogens], accidental (unintentional), initial encounter |
| T40.902A | Poisoning by unspecified psychodysleptics [hallucinogens], intentional self-harm, initial encounter |
| T40.903A | Poisoning by unspecified psychodysleptics [hallucinogens], assault, initial encounter |
| T40.904A | Poisoning by unspecified psychodysleptics [hallucinogens], undetermined, initial encounter |
| T40.991A | Poisoning by other psychodysleptics [hallucinogens], accidental (unintentional), initial encounter |
| T40.992A | Poisoning by other psychodysleptics [hallucinogens], intentional self-harm, initial encounter |
| T40.993A | Poisoning by other psychodysleptics [hallucinogens], assault, initial encounter |
| T40.994A | Poisoning by other psychodysleptics [hallucinogens], undetermined, initial encounter |
| T42.0X1A | Poisoning by hydantoin derivatives, accidental (unintentional), initial encounter |
| T42.0X2A | Poisoning by hydantoin derivatives, intentional self-harm, initial encounter |
| T42.0X3A | Poisoning by hydantoin derivatives, assault, initial encounter |
| T42.0X4A | Poisoning by hydantoin derivatives, undetermined, initial encounter |

| ICD-10 Codes | Description |
|---|---|
| T42.3X1A | Poisoning by barbiturates, accidental (unintentional), initial encounter |
| T42.3X2A | Poisoning by barbiturates, intentional self-harm, initial encounter |
| T42.3X3A | Poisoning by barbiturates, assault, initial encounter |
| T42.3X4A | Poisoning by barbiturates, undetermined, initial encounter |
| T42.4X1A | Poisoning by benzodiazepines, accidental (unintentional), initial encounter |
| T42.4X2A | Poisoning by benzodiazepines, intentional self-harm, initial encounter |
| T42.4X3A | Poisoning by benzodiazepines, assault, initial encounter |
| T42.4X4A | Poisoning by benzodiazepines, undetermined, initial encounter |
| T42.6X1A | Poisoning by other antiepileptic and sedative-hypnotic drugs, accidental (unintentional), initial encounter |
| T42.6X2A | Poisoning by other antiepileptic and sedative-hypnotic drugs, intentional self-harm, initial encounter |
| T42.6X3A | Poisoning by other antiepileptic and sedative-hypnotic drugs, assault, initial encounter |
| T42.6X4A | Poisoning by other antiepileptic and sedative-hypnotic drugs, undetermined, initial encounter |
| T43.011A | Poisoning by tricyclic antidepressants, accidental (unintentional), initial encounter |
| T43.012A | Poisoning by tricyclic antidepressants, intentional self-harm, initial encounter |
| T43.013A | Poisoning by tricyclic antidepressants, assault, initial encounter |
| T43.014A | Poisoning by tricyclic antidepressants, undetermined, initial encounter |
| T43.021A | Poisoning by tetracyclic antidepressants, accidental (unintentional), initial encounter |
| T43.022A | Poisoning by tetracyclic antidepressants, intentional self-harm, initial encounter |
| T43.023A | Poisoning by tetracyclic antidepressants, assault, initial encounter |
| T43.024A | Poisoning by tetracyclic antidepressants, undetermined, initial encounter |
| T43.1X1A | Poisoning by monoamine-oxidase-inhibitor antidepressants, accidental (unintentional), initial encounter |
| T43.1X2A | Poisoning by monoamine-oxidase-inhibitor antidepressants, intentional self-harm, initial encounter |
| T43.1X3A | Poisoning by monoamine-oxidase-inhibitor antidepressants, assault, initial encounter |
| T43.1X4A | Poisoning by monoamine-oxidase-inhibitor antidepressants, undetermined, initial encounter |
| T43.201A | Poisoning by unspecified antidepressants, accidental (unintentional), initial encounter |
| T43.202A | Poisoning by unspecified antidepressants, intentional self-harm, initial encounter |
| T43.203A | Poisoning by unspecified antidepressants, assault, initial encounter |
| T43.204A | Poisoning by unspecified antidepressants, undetermined, initial encounter |
| T43.211A | Poisoning by selective serotonin and norepinephrine reuptake inhibitors, accidental (unintentional), initial encounter |
| T43.212A | Poisoning by selective serotonin and norepinephrine reuptake inhibitors, intentional self-harm, initial encounter |
| T43.213A | Poisoning by selective serotonin and norepinephrine reuptake inhibitors, assault, initial encounter |
| T43.214A | Poisoning by selective serotonin and norepinephrine reuptake inhibitors, undetermined, initial encounter |
| T43.221A | Poisoning by selective serotonin reuptake inhibitors, accidental (unintentional), initial encounter |
| T43.222A | Poisoning by selective serotonin reuptake inhibitors, intentional self-harm, initial encounter |
| T43.223A | Poisoning by selective serotonin reuptake inhibitors, assault, initial encounter |
| T43.224A | Poisoning by selective serotonin reuptake inhibitors, undetermined, initial encounter |
| T43.291A | Poisoning by other antidepressants, accidental (unintentional), initial encounter |
| T43.292A | Poisoning by other antidepressants, intentional self-harm, initial encounter |
| T43.293A | Poisoning by other antidepressants, assault, initial encounter |
| T43.294A | Poisoning by other antidepressants, undetermined, initial encounter |
| T43.3X1A | Poisoning by phenothiazine antipsychotics and neuroleptics, accidental (unintentional), initial encounter |
| T43.3X2A | Poisoning by phenothiazine antipsychotics and neuroleptics, intentional self-harm, initial encounter |
| T43.3X3A | Poisoning by phenothiazine antipsychotics and neuroleptics, assault, initial encounter |
| T43.3X4A | Poisoning by phenothiazine antipsychotics and neuroleptics, undetermined, initial encounter |
| T43.4X1A | Poisoning by butyrophenone and thiothixene neuroleptics, accidental (unintentional), initial encounter |
| T43.4X2A | Poisoning by butyrophenone and thiothixene neuroleptics, intentional self-harm, initial encounter |
| T43.4X3A | Poisoning by butyrophenone and thiothixene neuroleptics, assault, initial encounter |
| T43.4X4A | Poisoning by butyrophenone and thiothixene neuroleptics, undetermined, initial encounter |
| T43.501A | Poisoning by unspecified antipsychotics and neuroleptics, accidental (unintentional), initial encounter |
| T43.502A | Poisoning by unspecified antipsychotics and neuroleptics, intentional self-harm, initial encounter |

| ICD-10 Codes | Description |
|---|---|
| T43.503A | Poisoning by unspecified antipsychotics and neuroleptics, assault, initial encounter |
| T43.504A | Poisoning by unspecified antipsychotics and neuroleptics, undetermined, initial encounter |
| T43.591A | Poisoning by other antipsychotics and neuroleptics, accidental (unintentional), initial encounter |
| T43.592A | Poisoning by other antipsychotics and neuroleptics, intentional self-harm, initial encounter |
| T43.593A | Poisoning by other antipsychotics and neuroleptics, assault, initial encounter |
| T43.594A | Poisoning by other antipsychotics and neuroleptics, undetermined, initial encounter |
| T43.601A | Poisoning by unspecified psychostimulants, accidental (unintentional), initial encounter |
| T43.602A | Poisoning by unspecified psychostimulants, intentional self-harm, initial encounter |
| T43.603A | Poisoning by unspecified psychostimulants, assault, initial encounter |
| T43.604A | Poisoning by unspecified psychostimulants, undetermined, initial encounter |
| T43.611A | Poisoning by caffeine, accidental (unintentional), initial encounter |
| T43.612A | Poisoning by caffeine, intentional self-harm, initial encounter |
| T43.613A | Poisoning by caffeine, assault, initial encounter |
| T43.614A | Poisoning by caffeine, undetermined, initial encounter |
| T43.621A | Poisoning by amphetamines, accidental (unintentional), initial encounter |
| T43.622A | Poisoning by amphetamines, intentional self-harm, initial encounter |
| T43.623A | Poisoning by amphetamines, assault, initial encounter |
| T43.624A | Poisoning by amphetamines, undetermined, initial encounter |
| T43.631A | Poisoning by methylphenidate, accidental (unintentional), initial encounter |
| T43.632A | Poisoning by methylphenidate, intentional self-harm, initial encounter |
| T43.633A | Poisoning by methylphenidate, assault, initial encounter |
| T43.634A | Poisoning by methylphenidate, undetermined, initial encounter |
| T43.691A | Poisoning by other psychostimulants, accidental (unintentional), initial encounter |
| T43.692A | Poisoning by other psychostimulants, intentional self-harm, initial encounter |
| T43.693A | Poisoning by other psychostimulants, assault, initial encounter |
| T43.694A | Poisoning by other psychostimulants, undetermined, initial encounter |
| T43.8X1A | Poisoning by other psychotropic drugs, accidental (unintentional), initial encounter |
| T43.8X2A | Poisoning by other psychotropic drugs, intentional self-harm, initial encounter |
| T43.8X3A | Poisoning by other psychotropic drugs, assault, initial encounter |
| T43.8X4A | Poisoning by other psychotropic drugs, undetermined, initial encounter |
| T43.91XA | Poisoning by unspecified psychotropic drug, accidental (unintentional), initial encounter |
| T43.92XA | Poisoning by unspecified psychotropic drug, intentional self-harm, initial encounter |
| T43.93XA | Poisoning by unspecified psychotropic drug, assault, initial encounter |
| T43.94XA | Poisoning by unspecified psychotropic drug, undetermined, initial encounter |
| T45.0X1A | Poisoning by antiallergic and antiemetic drugs, accidental (unintentional), initial encounter |
| T45.0X2A | Poisoning by antiallergic and antiemetic drugs, intentional self-harm, initial encounter |
| T45.0X3A | Poisoning by antiallergic and antiemetic drugs, assault, initial encounter |
| T45.0X4A | Poisoning by antiallergic and antiemetic drugs, undetermined, initial encounter |
| T46.0X1A | Poisoning by cardiac-stimulant glycosides and drugs of similar action, accidental (unintentional), initial encounter |
| T46.0X2A | Poisoning by cardiac-stimulant glycosides and drugs of similar action, intentional self-harm, initial encounter |
| T46.0X3A | Poisoning by cardiac-stimulant glycosides and drugs of similar action, assault, initial encounter |
| T46.0X4A | Poisoning by cardiac-stimulant glycosides and drugs of similar action, undetermined, initial encounter |
| T50.901A | Poisoning by unspecified drugs, medicaments and biological substances, accidental (unintentional), initial encounter |
| T50.902A | Poisoning by unspecified drugs, medicaments and biological substances, intentional self-harm, initial encounter |
| T50.903A | Poisoning by unspecified drugs, medicaments and biological substances, assault, initial encounter |
| T50.904A | Poisoning by unspecified drugs, medicaments and biological substances, undetermined, initial encounter |
| T50.991A | Poisoning by other drugs, medicaments and biological substances, accidental (unintentional), initial encounter |
| Z71.51* | Drug abuse counseling and surveillance of drug abuser |
| Z79.891 | Long term (current) use of opiate analgesic |
| Z79.899 | Other long term (current) drug therapy |
| Z91.120 | Patient's intentional underdosing of medication regimen due to financial hardship |

| ICD-10 Codes | Description |
|---|---|
| Z91.128 | Patient's intentional underdosing of medication regimen for other reason |
| Z91.130 | Patient's unintentional underdosing of medication regimen due to age-related debility |
| Z91.138 | Patient's unintentional underdosing of medication regimen for other reason |
| Z91.14 | Patient's other noncompliance with medication regimen |
| Z91.19 | Patient's noncompliance with other medical treatment and regimen |

**Group 1 Medical Necessity ICD-10 Codes Asterisk Explanation: ***F10.120, F11.20, F12.120, F12.220, F13.120, F14.120, F14.220, F16.120, F18.10, F18.120, F18.90, F19.20, F55.3, F55.4, F55.8: Signify diagnosis codes which are exempt from Group 1 codes one per calendar year frequency limit, given their status as substance use disorder (SUD) codes.

*Report monitoring of patient compliance in a drug treatment program using Z71.51 as the primary diagnosis and the specific drug dependence diagnosis as the secondary diagnosis.

Physicians are to select the most appropriate diagnosis code. Labs are not to prepopulate requisition forms with diagnosis codes.

**Group 2 Paragraph: Definitive UDT**

**Group 2 Codes:**

| ICD-10 Codes | Description |
|---|---|
| E03.5 | Myxedema coma |
| E87.2 | Acidosis |
| F10.120 | Alcohol abuse with intoxication, uncomplicated |
| F10.121 | Alcohol abuse with intoxication delirium |
| F10.129 | Alcohol abuse with intoxication, unspecified |
| F10.14 | Alcohol abuse with alcohol-induced mood disorder |
| F10.150 | Alcohol abuse with alcohol-induced psychotic disorder with delusions |
| F10.151 | Alcohol abuse with alcohol-induced psychotic disorder with hallucinations |
| F10.159 | Alcohol abuse with alcohol-induced psychotic disorder, unspecified |
| F10.180 | Alcohol abuse with alcohol-induced anxiety disorder |
| F10.181 | Alcohol abuse with alcohol-induced sexual dysfunction |
| F10.182 | Alcohol abuse with alcohol-induced sleep disorder |
| F10.188 | Alcohol abuse with other alcohol-induced disorder |
| F10.19 | Alcohol abuse with unspecified alcohol-induced disorder |
| F10.20 | Alcohol dependence, uncomplicated |
| F10.21 | Alcohol dependence, in remission |
| F10.220 | Alcohol dependence with intoxication, uncomplicated |
| F10.221 | Alcohol dependence with intoxication delirium |
| F10.229 | Alcohol dependence with intoxication, unspecified |
| F10.230 | Alcohol dependence with withdrawal, uncomplicated |
| F10.231 | Alcohol dependence with withdrawal delirium |
| F10.232 | Alcohol dependence with withdrawal with perceptual disturbance |
| F10.239 | Alcohol dependence with withdrawal, unspecified |
| F10.24 | Alcohol dependence with alcohol-induced mood disorder |
| F10.250 | Alcohol dependence with alcohol-induced psychotic disorder with delusions |
| F10.251 | Alcohol dependence with alcohol-induced psychotic disorder with hallucinations |
| F10.259 | Alcohol dependence with alcohol-induced psychotic disorder, unspecified |
| F10.26 | Alcohol dependence with alcohol-induced persisting amnestic disorder |
| F10.27 | Alcohol dependence with alcohol-induced persisting dementia |
| F10.280 | Alcohol dependence with alcohol-induced anxiety disorder |
| F10.281 | Alcohol dependence with alcohol-induced sexual dysfunction |
| F10.282 | Alcohol dependence with alcohol-induced sleep disorder |
| F10.288 | Alcohol dependence with other alcohol-induced disorder |
| F10.29 | Alcohol dependence with unspecified alcohol-induced disorder |
| F10.920 | Alcohol use, unspecified with intoxication, uncomplicated |
| F10.921 | Alcohol use, unspecified with intoxication delirium |

| ICD-10 Codes | Description |
|---|---|
| F10.929 | Alcohol use, unspecified with intoxication, unspecified |
| F10.94 | Alcohol use, unspecified with alcohol-induced mood disorder |
| F10.950 | Alcohol use, unspecified with alcohol-induced psychotic disorder with delusions |
| F10.951 | Alcohol use, unspecified with alcohol-induced psychotic disorder with hallucinations |
| F10.959 | Alcohol use, unspecified with alcohol-induced psychotic disorder, unspecified |
| F10.96 | Alcohol use, unspecified with alcohol-induced persisting amnestic disorder |
| F10.97 | Alcohol use, unspecified with alcohol-induced persisting dementia |
| F10.980 | Alcohol use, unspecified with alcohol-induced anxiety disorder |
| F10.981 | Alcohol use, unspecified with alcohol-induced sexual dysfunction |
| F10.982 | Alcohol use, unspecified with alcohol-induced sleep disorder |
| F10.988 | Alcohol use, unspecified with other alcohol-induced disorder |
| F10.99 | Alcohol use, unspecified with unspecified alcohol-induced disorder |
| F11.120 | Opioid abuse with intoxication, uncomplicated |
| F11.121 | Opioid abuse with intoxication delirium |
| F11.122 | Opioid abuse with intoxication with perceptual disturbance |
| F11.129 | Opioid abuse with intoxication, unspecified |
| F11.14 | Opioid abuse with opioid-induced mood disorder |
| F11.150 | Opioid abuse with opioid-induced psychotic disorder with delusions |
| F11.151 | Opioid abuse with opioid-induced psychotic disorder with hallucinations |
| F11.159 | Opioid abuse with opioid-induced psychotic disorder, unspecified |
| F11.181 | Opioid abuse with opioid-induced sexual dysfunction |
| F11.182 | Opioid abuse with opioid-induced sleep disorder |
| F11.188 | Opioid abuse with other opioid-induced disorder |
| F11.19 | Opioid abuse with unspecified opioid-induced disorder |
| F11.20 | Opioid dependence, uncomplicated |
| F11.21 | Opioid dependence, in remission |
| F11.220 | Opioid dependence with intoxication, uncomplicated |
| F11.221 | Opioid dependence with intoxication delirium |
| F11.222 | Opioid dependence with intoxication with perceptual disturbance |
| F11.229 | Opioid dependence with intoxication, unspecified |
| F11.23 | Opioid dependence with withdrawal |
| F11.24 | Opioid dependence with opioid-induced mood disorder |
| F11.250 | Opioid dependence with opioid-induced psychotic disorder with delusions |
| F11.251 | Opioid dependence with opioid-induced psychotic disorder with hallucinations |
| F11.281 | Opioid dependence with opioid-induced sexual dysfunction |
| F11.282 | Opioid dependence with opioid-induced sleep disorder |
| F11.288 | Opioid dependence with other opioid-induced disorder |
| F11.29 | Opioid dependence with unspecified opioid-induced disorder |
| F11.90 | Opioid use, unspecified, uncomplicated |
| F11.920 | Opioid use, unspecified with intoxication, uncomplicated |
| F11.921 | Opioid use, unspecified with intoxication delirium |
| F11.922 | Opioid use, unspecified with intoxication with perceptual disturbance |
| F11.929 | Opioid use, unspecified with intoxication, unspecified |
| F11.93 | Opioid use, unspecified with withdrawal |
| F11.94 | Opioid use, unspecified with opioid-induced mood disorder |
| F11.950 | Opioid use, unspecified with opioid-induced psychotic disorder with delusions |
| F11.951 | Opioid use, unspecified with opioid-induced psychotic disorder with hallucinations |
| F11.959 | Opioid use, unspecified with opioid-induced psychotic disorder, unspecified |
| F11.981 | Opioid use, unspecified with opioid-induced sexual dysfunction |
| F11.982 | Opioid use, unspecified with opioid-induced sleep disorder |
| F11.988 | Opioid use, unspecified with other opioid-induced disorder |
| F11.99 | Opioid use, unspecified with unspecified opioid-induced disorder |
| F12.120 | Cannabis abuse with intoxication, uncomplicated |
| F12.121 | Cannabis abuse with intoxication delirium |
| F12.122 | Cannabis abuse with intoxication with perceptual disturbance |
| F12.129 | Cannabis abuse with intoxication, unspecified |
| F12.150 | Cannabis abuse with psychotic disorder with delusions |
| F12.151 | Cannabis abuse with psychotic disorder with hallucinations |

| ICD-10 Codes | Description |
|---|---|
| F12.159 | Cannabis abuse with psychotic disorder, unspecified |
| F12.180 | Cannabis abuse with cannabis-induced anxiety disorder |
| F12.188 | Cannabis abuse with other cannabis-induced disorder |
| F12.19 | Cannabis abuse with unspecified cannabis-induced disorder |
| F12.20 | Cannabis dependence, uncomplicated |
| F12.21 | Cannabis dependence, in remission |
| F12.220 | Cannabis dependence with intoxication, uncomplicated |
| F12.221 | Cannabis dependence with intoxication delirium |
| F12.222 | Cannabis dependence with intoxication with perceptual disturbance |
| F12.229 | Cannabis dependence with intoxication, unspecified |
| F12.250 | Cannabis dependence with psychotic disorder with delusions |
| F12.251 | Cannabis dependence with psychotic disorder with hallucinations |
| F12.259 | Cannabis dependence with psychotic disorder, unspecified |
| F12.280 | Cannabis dependence with cannabis-induced anxiety disorder |
| F12.288 | Cannabis dependence with other cannabis-induced disorder |
| F12.29 | Cannabis dependence with unspecified cannabis-induced disorder |
| F12.90 | Cannabis use, unspecified, uncomplicated |
| F12.920 | Cannabis use, unspecified with intoxication, uncomplicated |
| F12.921 | Cannabis use, unspecified with intoxication delirium |
| F12.922 | Cannabis use, unspecified with intoxication with perceptual disturbance |
| F12.929 | Cannabis use, unspecified with intoxication, unspecified |
| F12.950 | Cannabis use, unspecified with psychotic disorder with delusions |
| F12.951 | Cannabis use, unspecified with psychotic disorder with hallucinations |
| F12.959 | Cannabis use, unspecified with psychotic disorder, unspecified |
| F12.980 | Cannabis use, unspecified with anxiety disorder |
| F12.988 | Cannabis use, unspecified with other cannabis-induced disorder |
| F12.99 | Cannabis use, unspecified with unspecified cannabis-induced disorder |
| F13.10 | Sedative, hypnotic or anxiolytic abuse, uncomplicated |
| F13.120 | Sedative, hypnotic or anxiolytic abuse with intoxication, uncomplicated |
| F13.121 | Sedative, hypnotic or anxiolytic abuse with intoxication delirium |
| F13.129 | Sedative, hypnotic or anxiolytic abuse with intoxication, unspecified |
| F13.14 | Sedative, hypnotic or anxiolytic abuse with sedative, hypnotic or anxiolytic-induced mood disorder |
| F13.150 | Sedative, hypnotic or anxiolytic abuse with sedative, hypnotic or anxiolytic-induced psychotic disorder with delusions |
| F13.151 | Sedative, hypnotic or anxiolytic abuse with sedative, hypnotic or anxiolytic-induced psychotic disorder with hallucinations |
| F13.159 | Sedative, hypnotic or anxiolytic abuse with sedative, hypnotic or anxiolytic-induced psychotic disorder, unspecified |
| F13.180 | Sedative, hypnotic or anxiolytic abuse with sedative, hypnotic or anxiolytic-induced anxiety disorder |
| F13.181 | Sedative, hypnotic or anxiolytic abuse with sedative, hypnotic or anxiolytic-induced sexual dysfunction |
| F13.182 | Sedative, hypnotic or anxiolytic abuse with sedative, hypnotic or anxiolytic-induced sleep disorder |
| F13.188 | Sedative, hypnotic or anxiolytic abuse with other sedative, hypnotic or anxiolytic-induced disorder |
| F13.19 | Sedative, hypnotic or anxiolytic abuse with unspecified sedative, hypnotic or anxiolytic-induced disorder |
| F13.20 | Sedative, hypnotic or anxiolytic dependence, uncomplicated |
| F13.21 | Sedative, hypnotic or anxiolytic dependence, in remission |
| F13.220 | Sedative, hypnotic or anxiolytic dependence with intoxication, uncomplicated |
| F13.221 | Sedative, hypnotic or anxiolytic dependence with intoxication delirium |
| F13.229 | Sedative, hypnotic or anxiolytic dependence with intoxication, unspecified |
| F13.230 | Sedative, hypnotic or anxiolytic dependence with withdrawal, uncomplicated |
| F13.231 | Sedative, hypnotic or anxiolytic dependence with withdrawal delirium |
| F13.232 | Sedative, hypnotic or anxiolytic dependence with withdrawal with perceptual disturbance |
| F13.239 | Sedative, hypnotic or anxiolytic dependence with withdrawal, unspecified |
| F13.24 | Sedative, hypnotic or anxiolytic dependence with sedative, hypnotic or anxiolytic-induced mood disorder |
| F13.250 | Sedative, hypnotic or anxiolytic dependence with sedative, hypnotic or anxiolytic-induced psychotic disorder with delusions |

| ICD-10 Codes | Description |
|---|---|
| F13.251 | Sedative, hypnotic or anxiolytic dependence with sedative, hypnotic or anxiolytic-induced psychotic disorder with hallucinations |
| F13.259 | Sedative, hypnotic or anxiolytic dependence with sedative, hypnotic or anxiolytic-induced psychotic disorder, unspecified |
| F13.26 | Sedative, hypnotic or anxiolytic dependence with sedative, hypnotic or anxiolytic-induced persisting amnestic disorder |
| F13.27 | Sedative, hypnotic or anxiolytic dependence with sedative, hypnotic or anxiolytic-induced persisting dementia |
| F13.280 | Sedative, hypnotic or anxiolytic dependence with sedative, hypnotic or anxiolytic-induced anxiety disorder |
| F13.281 | Sedative, hypnotic or anxiolytic dependence with sedative, hypnotic or anxiolytic-induced sexual dysfunction |
| F13.282 | Sedative, hypnotic or anxiolytic dependence with sedative, hypnotic or anxiolytic-induced sleep disorder |
| F13.288 | Sedative, hypnotic or anxiolytic dependence with other sedative, hypnotic or anxiolytic-induced disorder |
| F13.29 | Sedative, hypnotic or anxiolytic dependence with unspecified sedative, hypnotic or anxiolytic-induced disorder |
| F13.90 | Sedative, hypnotic, or anxiolytic use, unspecified, uncomplicated |
| F13.920 | Sedative, hypnotic or anxiolytic use, unspecified with intoxication, uncomplicated |
| F13.921 | Sedative, hypnotic or anxiolytic use, unspecified with intoxication delirium |
| F13.929 | Sedative, hypnotic or anxiolytic use, unspecified with intoxication, unspecified |
| F13.930 | Sedative, hypnotic or anxiolytic use, unspecified with withdrawal, uncomplicated |
| F13.931 | Sedative, hypnotic or anxiolytic use, unspecified with withdrawal delirium |
| F13.932 | Sedative, hypnotic or anxiolytic use, unspecified with withdrawal with perceptual disturbances |
| F13.939 | Sedative, hypnotic or anxiolytic use, unspecified with withdrawal, unspecified |
| F13.94 | Sedative, hypnotic or anxiolytic use, unspecified with sedative, hypnotic or anxiolytic-induced mood disorder |
| F13.950 | Sedative, hypnotic or anxiolytic use, unspecified with sedative, hypnotic or anxiolytic-induced psychotic disorder with delusions |
| F13.951 | Sedative, hypnotic or anxiolytic use, unspecified with sedative, hypnotic or anxiolytic-induced psychotic disorder with hallucinations |
| F13.959 | Sedative, hypnotic or anxiolytic use, unspecified with sedative, hypnotic or anxiolytic-induced psychotic disorder, unspecified |
| F13.96 | Sedative, hypnotic or anxiolytic use, unspecified with sedative, hypnotic or anxiolytic-induced persisting amnestic disorder |
| F13.97 | Sedative, hypnotic or anxiolytic use, unspecified with sedative, hypnotic or anxiolytic-induced persisting dementia |
| F13.980 | Sedative, hypnotic or anxiolytic use, unspecified with sedative, hypnotic or anxiolytic-induced anxiety disorder |
| F13.981 | Sedative, hypnotic or anxiolytic use, unspecified with sedative, hypnotic or anxiolytic-induced sexual dysfunction |
| F13.982 | Sedative, hypnotic or anxiolytic use, unspecified with sedative, hypnotic or anxiolytic-induced sleep disorder |
| F13.988 | Sedative, hypnotic or anxiolytic use, unspecified with other sedative, hypnotic or anxiolytic-induced disorder |
| F13.99 | Sedative, hypnotic or anxiolytic use, unspecified with unspecified sedative, hypnotic or anxiolytic-induced disorder |
| F14.10 | Cocaine abuse, uncomplicated |
| F14.120 | Cocaine abuse with intoxication, uncomplicated |
| F14.121 | Cocaine abuse with intoxication with delirium |
| F14.122 | Cocaine abuse with intoxication with perceptual disturbance |
| F14.14 | Cocaine abuse with cocaine-induced mood disorder |
| F14.150 | Cocaine abuse with cocaine-induced psychotic disorder with delusions |
| F14.151 | Cocaine abuse with cocaine-induced psychotic disorder with hallucinations |
| F14.159 | Cocaine abuse with cocaine-induced psychotic disorder, unspecified |
| F14.180 | Cocaine abuse with cocaine-induced anxiety disorder |
| F14.181 | Cocaine abuse with cocaine-induced sexual dysfunction |
| F14.182 | Cocaine abuse with cocaine-induced sleep disorder |
| F14.188 | Cocaine abuse with other cocaine-induced disorder |

| ICD-10 Codes | Description |
|---|---|
| F14.19 | Cocaine abuse with unspecified cocaine-induced disorder |
| F14.20 | Cocaine dependence, uncomplicated |
| F14.220 | Cocaine dependence with intoxication, uncomplicated |
| F14.221 | Cocaine dependence with intoxication delirium |
| F14.222 | Cocaine dependence with intoxication with perceptual disturbance |
| F14.229 | Cocaine dependence with intoxication, unspecified |
| F14.250 | Cocaine dependence with cocaine-induced psychotic disorder with delusions |
| F14.251 | Cocaine dependence with cocaine-induced psychotic disorder with hallucinations |
| F14.259 | Cocaine dependence with cocaine-induced psychotic disorder, unspecified |
| F14.280 | Cocaine dependence with cocaine-induced anxiety disorder |
| F14.281 | Cocaine dependence with cocaine-induced sexual dysfunction |
| F14.282 | Cocaine dependence with cocaine-induced sleep disorder |
| F14.288 | Cocaine dependence with other cocaine-induced disorder |
| F14.29 | Cocaine dependence with unspecified cocaine-induced disorder |
| F14.90 | Cocaine use, unspecified, uncomplicated |
| F14.920 | Cocaine use, unspecified with intoxication, uncomplicated |
| F14.921 | Cocaine use, unspecified with intoxication delirium |
| F14.922 | Cocaine use, unspecified with intoxication with perceptual disturbance |
| F14.929 | Cocaine use, unspecified with intoxication, unspecified |
| F14.94 | Cocaine use, unspecified with cocaine-induced mood disorder |
| F14.950 | Cocaine use, unspecified with cocaine-induced psychotic disorder with delusions |
| F14.951 | Cocaine use, unspecified with cocaine-induced psychotic disorder with hallucinations |
| F14.959 | Cocaine use, unspecified with cocaine-induced psychotic disorder, unspecified |
| F14.980 | Cocaine use, unspecified with cocaine-induced anxiety disorder |
| F14.981 | Cocaine use, unspecified with cocaine-induced sexual dysfunction |
| F14.982 | Cocaine use, unspecified with cocaine-induced sleep disorder |
| F14.988 | Cocaine use, unspecified with other cocaine-induced disorder |
| F14.99 | Cocaine use, unspecified with unspecified cocaine-induced disorder |
| F15.10 | Other stimulant abuse, uncomplicated |
| F15.120 | Other stimulant abuse with intoxication, uncomplicated |
| F15.121 | Other stimulant abuse with intoxication delirium |
| F15.122 | Other stimulant abuse with intoxication with perceptual disturbance |
| F15.129 | Other stimulant abuse with intoxication, unspecified |
| F15.14 | Other stimulant abuse with stimulant-induced mood disorder |
| F15.150 | Other stimulant abuse with stimulant-induced psychotic disorder with delusions |
| F15.151 | Other stimulant abuse with stimulant-induced psychotic disorder with hallucinations |
| F15.159 | Other stimulant abuse with stimulant-induced psychotic disorder, unspecified |
| F15.180 | Other stimulant abuse with stimulant-induced anxiety disorder |
| F15.181 | Other stimulant abuse with stimulant-induced sexual dysfunction |
| F15.182 | Other stimulant abuse with stimulant-induced sleep disorder |
| F15.188 | Other stimulant abuse with other stimulant-induced disorder |
| F15.19 | Other stimulant abuse with unspecified stimulant-induced disorder |
| F15.20 | Other stimulant dependence, uncomplicated |
| F15.21 | Other stimulant dependence, in remission |
| F15.220 | Other stimulant dependence with intoxication, uncomplicated |
| F15.221 | Other stimulant dependence with intoxication delirium |
| F15.222 | Other stimulant dependence with intoxication with perceptual disturbance |
| F15.229 | Other stimulant dependence with intoxication, unspecified |
| F15.23 | Other stimulant dependence with withdrawal |
| F15.24 | Other stimulant dependence with stimulant-induced mood disorder |
| F15.250 | Other stimulant dependence with stimulant-induced psychotic disorder with delusions |
| F15.251 | Other stimulant dependence with stimulant-induced psychotic disorder with hallucinations |
| F15.259 | Other stimulant dependence with stimulant-induced psychotic disorder, unspecified |
| F15.280 | Other stimulant dependence with stimulant-induced anxiety disorder |
| F15.281 | Other stimulant dependence with stimulant-induced sexual dysfunction |
| F15.282 | Other stimulant dependence with stimulant-induced sleep disorder |
| F15.288 | Other stimulant dependence with other stimulant-induced disorder |
| F15.29 | Other stimulant dependence with unspecified stimulant-induced disorder |

| ICD-10 Codes | Description |
|---|---|
| F15.90 | Other stimulant use, unspecified, uncomplicated |
| F15.920 | Other stimulant use, unspecified with intoxication, uncomplicated |
| F15.921 | Other stimulant use, unspecified with intoxication delirium |
| F15.922 | Other stimulant use, unspecified with intoxication with perceptual disturbance |
| F15.929 | Other stimulant use, unspecified with intoxication, unspecified |
| F15.93 | Other stimulant use, unspecified with withdrawal |
| F15.94 | Other stimulant use, unspecified with stimulant-induced mood disorder |
| F15.950 | Other stimulant use, unspecified with stimulant-induced psychotic disorder with delusions |
| F15.951 | Other stimulant use, unspecified with stimulant-induced psychotic disorder with hallucinations |
| F15.959 | Other stimulant use, unspecified with stimulant-induced psychotic disorder, unspecified |
| F15.980 | Other stimulant use, unspecified with stimulant-induced anxiety disorder |
| F15.981 | Other stimulant use, unspecified with stimulant-induced sexual dysfunction |
| F15.982 | Other stimulant use, unspecified with stimulant-induced sleep disorder |
| F15.988 | Other stimulant use, unspecified with other stimulant-induced disorder |
| F15.99 | Other stimulant use, unspecified with unspecified stimulant-induced disorder |
| F16.10 | Hallucinogen abuse, uncomplicated |
| F16.120 | Hallucinogen abuse with intoxication, uncomplicated |
| F16.121 | Hallucinogen abuse with intoxication with delirium |
| F16.122 | Hallucinogen abuse with intoxication with perceptual disturbance |
| F16.129 | Hallucinogen abuse with intoxication, unspecified |
| F16.150 | Hallucinogen abuse with hallucinogen-induced psychotic disorder with delusions |
| F16.151 | Hallucinogen abuse with hallucinogen-induced psychotic disorder with hallucinations |
| F16.159 | Hallucinogen abuse with hallucinogen-induced psychotic disorder, unspecified |
| F16.180 | Hallucinogen abuse with hallucinogen-induced anxiety disorder |
| F16.183 | Hallucinogen abuse with hallucinogen persisting perception disorder (flashbacks) |
| F16.188 | Hallucinogen abuse with other hallucinogen-induced disorder |
| F16.19 | Hallucinogen abuse with unspecified hallucinogen-induced disorder |
| F16.20 | Hallucinogen dependence, uncomplicated |
| F16.21 | Hallucinogen dependence, in remission |
| F16.220 | Hallucinogen dependence with intoxication, uncomplicated |
| F16.221 | Hallucinogen dependence with intoxication with delirium |
| F16.229 | Hallucinogen dependence with intoxication, unspecified |
| F16.24 | Hallucinogen dependence with hallucinogen-induced mood disorder |
| F16.250 | Hallucinogen dependence with hallucinogen-induced psychotic disorder with delusions |
| F16.251 | Hallucinogen dependence with hallucinogen-induced psychotic disorder with hallucinations |
| F16.259 | Hallucinogen dependence with hallucinogen-induced psychotic disorder, unspecified |
| F16.280 | Hallucinogen dependence with hallucinogen-induced anxiety disorder |
| F16.283 | Hallucinogen dependence with hallucinogen persisting perception disorder (flashbacks) |
| F16.288 | Hallucinogen dependence with other hallucinogen-induced disorder |
| F16.29 | Hallucinogen dependence with unspecified hallucinogen-induced disorder |
| F16.90 | Hallucinogen use, unspecified, uncomplicated |
| F16.920 | Hallucinogen use, unspecified with intoxication, uncomplicated |
| F16.921 | Hallucinogen use, unspecified with intoxication with delirium |
| F16.929 | Hallucinogen use, unspecified with intoxication, unspecified |
| F16.94 | Hallucinogen use, unspecified with hallucinogen-induced mood disorder |
| F16.950 | Hallucinogen use, unspecified with hallucinogen-induced psychotic disorder with delusions |
| F16.951 | Hallucinogen use, unspecified with hallucinogen-induced psychotic disorder with hallucinations |
| F16.959 | Hallucinogen use, unspecified with hallucinogen-induced psychotic disorder, unspecified |
| F16.980 | Hallucinogen use, unspecified with hallucinogen-induced anxiety disorder |
| F16.983 | Hallucinogen use, unspecified with hallucinogen persisting perception disorder (flashbacks) |
| F16.988 | Hallucinogen use, unspecified with other hallucinogen-induced disorder |
| F16.99 | Hallucinogen use, unspecified with unspecified hallucinogen-induced disorder |
| F18.10 | Inhalant abuse, uncomplicated |
| F18.120 | Inhalant abuse with intoxication, uncomplicated |
| F18.121 | Inhalant abuse with intoxication delirium |
| F18.129 | Inhalant abuse with intoxication, unspecified |
| F18.14 | Inhalant abuse with inhalant-induced mood disorder |

| ICD-10 Codes | Description |
|---|---|
| F18.150 | Inhalant abuse with inhalant-induced psychotic disorder with delusions |
| F18.151 | Inhalant abuse with inhalant-induced psychotic disorder with hallucinations |
| F18.159 | Inhalant abuse with inhalant-induced psychotic disorder, unspecified |
| F18.17 | Inhalant abuse with inhalant-induced dementia |
| F18.180 | Inhalant abuse with inhalant-induced anxiety disorder |
| F18.188 | Inhalant abuse with other inhalant-induced disorder |
| F18.19 | Inhalant abuse with unspecified inhalant-induced disorder |
| F18.20 | Inhalant dependence, uncomplicated |
| F18.21 | Inhalant dependence, in remission |
| F18.220 | Inhalant dependence with intoxication, uncomplicated |
| F18.221 | Inhalant dependence with intoxication delirium |
| F18.229 | Inhalant dependence with intoxication, unspecified |
| F18.24 | Inhalant dependence with inhalant-induced mood disorder |
| F18.250 | Inhalant dependence with inhalant-induced psychotic disorder with delusions |
| F18.251 | Inhalant dependence with inhalant-induced psychotic disorder with hallucinations |
| F18.259 | Inhalant dependence with inhalant-induced psychotic disorder, unspecified |
| F18.27 | Inhalant dependence with inhalant-induced dementia |
| F18.280 | Inhalant dependence with inhalant-induced anxiety disorder |
| F18.288 | Inhalant dependence with other inhalant-induced disorder |
| F18.29 | Inhalant dependence with unspecified inhalant-induced disorder |
| F18.90 | Inhalant use, unspecified, uncomplicated |
| F18.920 | Inhalant use, unspecified with intoxication, uncomplicated |
| F18.921 | Inhalant use, unspecified with intoxication with delirium |
| F18.929 | Inhalant use, unspecified with intoxication, unspecified |
| F18.94 | Inhalant use, unspecified with inhalant-induced mood disorder |
| F18.950 | Inhalant use, unspecified with inhalant-induced psychotic disorder with delusions |
| F18.951 | Inhalant use, unspecified with inhalant-induced psychotic disorder with hallucinations |
| F18.959 | Inhalant use, unspecified with inhalant-induced psychotic disorder, unspecified |
| F18.980 | Inhalant use, unspecified with inhalant-induced anxiety disorder |
| F18.988 | Inhalant use, unspecified with other inhalant-induced disorder |
| F18.99 | Inhalant use, unspecified with unspecified inhalant-induced disorder |
| F19.10 | Other psychoactive substance abuse, uncomplicated |
| F19.120 | Other psychoactive substance abuse with intoxication, uncomplicated |
| F19.121 | Other psychoactive substance abuse with intoxication delirium |
| F19.122 | Other psychoactive substance abuse with intoxication with perceptual disturbances |
| F19.129 | Other psychoactive substance abuse with intoxication, unspecified |
| F19.14 | Other psychoactive substance abuse with psychoactive substance-induced mood disorder |
| F19.150 | Other psychoactive substance abuse with psychoactive substance-induced psychotic disorder with delusions |
| F19.151 | Other psychoactive substance abuse with psychoactive substance-induced psychotic disorder with hallucinations |
| F19.159 | Other psychoactive substance abuse with psychoactive substance-induced psychotic disorder, unspecified |
| F19.16 | Other psychoactive substance abuse with psychoactive substance-induced persisting amnestic disorder |
| F19.17 | Other psychoactive substance abuse with psychoactive substance-induced persisting dementia |
| F19.180 | Other psychoactive substance abuse with psychoactive substance-induced anxiety disorder |
| F19.181 | Other psychoactive substance abuse with psychoactive substance-induced sexual dysfunction |
| F19.182 | Other psychoactive substance abuse with psychoactive substance-induced sleep disorder |
| F19.188 | Other psychoactive substance abuse with other psychoactive substance-induced disorder |
| F19.19 | Other psychoactive substance abuse with unspecified psychoactive substance-induced disorder |
| F19.20 | Other psychoactive substance dependence, uncomplicated |
| F19.21 | Other psychoactive substance dependence, in remission |
| F19.220 | Other psychoactive substance dependence with intoxication, uncomplicated |
| F19.221 | Other psychoactive substance dependence with intoxication delirium |
| F19.222 | Other psychoactive substance dependence with intoxication with perceptual disturbance |
| F19.229 | Other psychoactive substance dependence with intoxication, unspecified |
| F19.230 | Other psychoactive substance dependence with withdrawal, uncomplicated |

| ICD-10 Codes | Description |
|---|---|
| F19.231 | Other psychoactive substance dependence with withdrawal delirium |
| F19.232 | Other psychoactive substance dependence with withdrawal with perceptual disturbance |
| F19.239 | Other psychoactive substance dependence with withdrawal, unspecified |
| F19.24 | Other psychoactive substance dependence with psychoactive substance-induced mood disorder |
| F19.250 | Other psychoactive substance dependence with psychoactive substance-induced psychotic disorder with delusions |
| F19.251 | Other psychoactive substance dependence with psychoactive substance-induced psychotic disorder with hallucinations |
| F19.259 | Other psychoactive substance dependence with psychoactive substance-induced psychotic disorder, unspecified |
| F19.26 | Other psychoactive substance dependence with psychoactive substance-induced persisting amnestic disorder |
| F19.27 | Other psychoactive substance dependence with psychoactive substance-induced persisting dementia |
| F19.280 | Other psychoactive substance dependence with psychoactive substance-induced anxiety disorder |
| F19.281 | Other psychoactive substance dependence with psychoactive substance-induced sexual dysfunction |
| F19.282 | Other psychoactive substance dependence with psychoactive substance-induced sleep disorder |
| F19.288 | Other psychoactive substance dependence with other psychoactive substance-induced disorder |
| F19.29 | Other psychoactive substance dependence with unspecified psychoactive substance-induced disorder |
| F19.90 | Other psychoactive substance use, unspecified, uncomplicated |
| F19.920 | Other psychoactive substance use, unspecified with intoxication, uncomplicated |
| F19.921 | Other psychoactive substance use, unspecified with intoxication with delirium |
| F19.922 | Other psychoactive substance use, unspecified with intoxication with perceptual disturbance |
| F19.929 | Other psychoactive substance use, unspecified with intoxication, unspecified |
| F19.930 | Other psychoactive substance use, unspecified with withdrawal, uncomplicated |
| F19.931 | Other psychoactive substance use, unspecified with withdrawal delirium |
| F19.932 | Other psychoactive substance use, unspecified with withdrawal with perceptual disturbance |
| F19.939 | Other psychoactive substance use, unspecified with withdrawal, unspecified |
| F19.94 | Other psychoactive substance use, unspecified with psychoactive substance-induced mood disorder |
| F19.950 | Other psychoactive substance use, unspecified with psychoactive substance-induced psychotic disorder with delusions |
| F19.951 | Other psychoactive substance use, unspecified with psychoactive substance-induced psychotic disorder with hallucinations |
| F19.959 | Other psychoactive substance use, unspecified with psychoactive substance-induced psychotic disorder, unspecified |
| F19.96 | Other psychoactive substance use, unspecified with psychoactive substance-induced persisting amnestic disorder |
| F19.97 | Other psychoactive substance use, unspecified with psychoactive substance-induced persisting dementia |
| F19.980 | Other psychoactive substance use, unspecified with psychoactive substance-induced anxiety disorder |
| F19.981 | Other psychoactive substance use, unspecified with psychoactive substance-induced sexual dysfunction |
| F19.982 | Other psychoactive substance use, unspecified with psychoactive substance-induced sleep disorder |
| F19.988 | Other psychoactive substance use, unspecified with other psychoactive substance-induced disorder |
| F19.99 | Other psychoactive substance use, unspecified with unspecified psychoactive substance-induced disorder |
| F20.0 | Paranoid schizophrenia |
| F20.1 | Disorganized schizophrenia |
| F20.2 | Catatonic schizophrenia |
| F20.3 | Undifferentiated schizophrenia |
| F20.5 | Residual schizophrenia |
| F20.81 | Schizophreniform disorder |
| F20.89 | Other schizophrenia |
| F20.9 | Schizophrenia, unspecified |
| F23 | Brief psychotic disorder |
| F25.0 | Schizoaffective disorder, bipolar type |
| F25.1 | Schizoaffective disorder, depressive type |
| F25.8 | Other schizoaffective disorders |

| ICD-10 Codes | Description |
|---|---|
| F25.9 | Schizoaffective disorder, unspecified |
| F28 | Other psychotic disorder not due to a substance or known physiological condition |
| F29 | Unspecified psychosis not due to a substance or known physiological condition |
| F30.10 | Manic episode without psychotic symptoms, unspecified |
| F30.11 | Manic episode without psychotic symptoms, mild |
| F30.12 | Manic episode without psychotic symptoms, moderate |
| F30.13 | Manic episode, severe, without psychotic symptoms |
| F30.2 | Manic episode, severe with psychotic symptoms |
| F30.3 | Manic episode in partial remission |
| F30.4 | Manic episode in full remission |
| F30.8 | Other manic episodes |
| F30.9 | Manic episode, unspecified |
| F31.10 | Bipolar disorder, current episode manic without psychotic features, unspecified |
| F31.11 | Bipolar disorder, current episode manic without psychotic features, mild |
| F31.12 | Bipolar disorder, current episode manic without psychotic features, moderate |
| F31.13 | Bipolar disorder, current episode manic without psychotic features, severe |
| F31.2 | Bipolar disorder, current episode manic severe with psychotic features |
| F31.30 | Bipolar disorder, current episode depressed, mild or moderate severity, unspecified |
| F31.31 | Bipolar disorder, current episode depressed, mild |
| F31.32 | Bipolar disorder, current episode depressed, moderate |
| F31.4 | Bipolar disorder, current episode depressed, severe, without psychotic features |
| F31.5 | Bipolar disorder, current episode depressed, severe, with psychotic features |
| F31.60 | Bipolar disorder, current episode mixed, unspecified |
| F31.61 | Bipolar disorder, current episode mixed, mild |
| F31.62 | Bipolar disorder, current episode mixed, moderate |
| F31.63 | Bipolar disorder, current episode mixed, severe, without psychotic features |
| F31.64 | Bipolar disorder, current episode mixed, severe, with psychotic features |
| F31.70 | Bipolar disorder, currently in remission, most recent episode unspecified |
| F31.71 | Bipolar disorder, in partial remission, most recent episode hypomanic |
| F31.72 | Bipolar disorder, in full remission, most recent episode hypomanic |
| F31.73 | Bipolar disorder, in partial remission, most recent episode manic |
| F31.74 | Bipolar disorder, in full remission, most recent episode manic |
| F31.75 | Bipolar disorder, in partial remission, most recent episode depressed |
| F31.76 | Bipolar disorder, in full remission, most recent episode depressed |
| F31.77 | Bipolar disorder, in partial remission, most recent episode mixed |
| F31.78 | Bipolar disorder, in full remission, most recent episode mixed |
| F31.81 | Bipolar II disorder |
| F31.89 | Other bipolar disorder |
| F31.9 | Bipolar disorder, unspecified |
| F32.0 | Major depressive disorder, single episode, mild |
| F32.1 | Major depressive disorder, single episode, moderate |
| F32.2 | Major depressive disorder, single episode, severe without psychotic features |
| F32.3 | Major depressive disorder, single episode, severe with psychotic features |
| F32.4 | Major depressive disorder, single episode, in partial remission |
| F32.5 | Major depressive disorder, single episode, in full remission |
| F32.8 | Other depressive episodes |
| F32.9 | Major depressive disorder, single episode, unspecified |
| F33.0 | Major depressive disorder, recurrent, mild |
| F33.1 | Major depressive disorder, recurrent, moderate |
| F33.2 | Major depressive disorder, recurrent severe without psychotic features |
| F33.3 | Major depressive disorder, recurrent, severe with psychotic symptoms |
| F33.40 | Major depressive disorder, recurrent, in remission, unspecified |
| F33.41 | Major depressive disorder, recurrent, in partial remission |
| F33.42 | Major depressive disorder, recurrent, in full remission |
| F33.8 | Other recurrent depressive disorders |
| F33.9 | Major depressive disorder, recurrent, unspecified |
| F34.0 | Cyclothymic disorder |
| F34.1 | Dysthymic disorder |

| ICD-10 Codes | Description |
|---|---|
| F34.8 | Other persistent mood [affective] disorders |
| F34.9 | Persistent mood [affective] disorder, unspecified |
| F39 | Unspecified mood [affective] disorder |
| F43.0 | Acute stress reaction |
| F43.10 | Post-traumatic stress disorder, unspecified |
| F43.11 | Post-traumatic stress disorder, acute |
| F43.12 | Post-traumatic stress disorder, chronic |
| F43.20 | Adjustment disorder, unspecified |
| F43.21 | Adjustment disorder with depressed mood |
| F43.22 | Adjustment disorder with anxiety |
| F43.23 | Adjustment disorder with mixed anxiety and depressed mood |
| F43.24 | Adjustment disorder with disturbance of conduct |
| F43.25 | Adjustment disorder with mixed disturbance of emotions and conduct |
| F43.29 | Adjustment disorder with other symptoms |
| F43.8 | Other reactions to severe stress |
| F43.9 | Reaction to severe stress, unspecified |
| F44.0 | Dissociative amnesia |
| F44.1 | Dissociative fugue |
| F44.2 | Dissociative stupor |
| F44.4 | Conversion disorder with motor symptom or deficit |
| F44.5 | Conversion disorder with seizures or convulsions |
| F44.6 | Conversion disorder with sensory symptom or deficit |
| F44.7 | Conversion disorder with mixed symptom presentation |
| F44.81 | Dissociative identity disorder |
| F44.89 | Other dissociative and conversion disorders |
| F44.9 | Dissociative and conversion disorder, unspecified |
| F45.0 | Somatization disorder |
| F45.1 | Undifferentiated somatoform disorder |
| F45.20 | Hypochondriacal disorder, unspecified |
| F45.21 | Hypochondriasis |
| F45.22 | Body dysmorphic disorder |
| F45.29 | Other hypochondriacal disorders |
| F45.41 | Pain disorder exclusively related to psychological factors |
| F45.42 | Pain disorder with related psychological factors |
| F45.8 | Other somatoform disorders |
| F45.9 | Somatoform disorder, unspecified |
| F55.0 | Abuse of antacids |
| F55.1 | Abuse of herbal or folk remedies |
| F55.2 | Abuse of laxatives |
| F55.3 | Abuse of steroids or hormones |
| F55.4 | Abuse of vitamins |
| F55.8 | Abuse of other non-psychoactive substances |
| F60.0 | Paranoid personality disorder |
| F60.1 | Schizoid personality disorder |
| F60.2 | Antisocial personality disorder |
| F60.3 | Borderline personality disorder |
| F60.4 | Histrionic personality disorder |
| F60.5 | Obsessive-compulsive personality disorder |
| F60.6 | Avoidant personality disorder |
| F60.7 | Dependent personality disorder |
| F60.81 | Narcissistic personality disorder |
| F60.89 | Other specific personality disorders |
| F60.9 | Personality disorder, unspecified |
| G40.001 | Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, not intractable, with status epilepticus |
| G40.009 | Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, not intractable, without status epilepticus |
| G40.011 | |

| ICD-10 Codes | Description |
|---|---|
| | Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable, with status epilepticus |
| G40.019 | Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable, without status epilepticus |
| G40.101 | Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, not intractable, with status epilepticus |
| G40.109 | Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, not intractable, without status epilepticus |
| G40.111 | Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, intractable, with status epilepticus |
| G40.119 | Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, intractable, without status epilepticus |
| G40.201 | Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, not intractable, with status epilepticus |
| G40.209 | Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, not intractable, without status epilepticus |
| G40.211 | Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, intractable, with status epilepticus |
| G40.219 | Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, intractable, without status epilepticus |
| G40.301 | Generalized idiopathic epilepsy and epileptic syndromes, not intractable, with status epilepticus |
| G40.309 | Generalized idiopathic epilepsy and epileptic syndromes, not intractable, without status epilepticus |
| G40.311 | Generalized idiopathic epilepsy and epileptic syndromes, intractable, with status epilepticus |
| G40.319 | Generalized idiopathic epilepsy and epileptic syndromes, intractable, without status epilepticus |
| G40.A01 | Absence epileptic syndrome, not intractable, with status epilepticus |
| G40.A09 | Absence epileptic syndrome, not intractable, without status epilepticus |
| G40.A11 | Absence epileptic syndrome, intractable, with status epilepticus |
| G40.A19 | Absence epileptic syndrome, intractable, without status epilepticus |
| G40.B01 | Juvenile myoclonic epilepsy, not intractable, with status epilepticus |
| G40.B09 | Juvenile myoclonic epilepsy, not intractable, without status epilepticus |
| G40.B11 | Juvenile myoclonic epilepsy, intractable, with status epilepticus |
| G40.B19 | Juvenile myoclonic epilepsy, intractable, without status epilepticus |
| G40.401 | Other generalized epilepsy and epileptic syndromes, not intractable, with status epilepticus |
| G40.409 | Other generalized epilepsy and epileptic syndromes, not intractable, without status epilepticus |
| G40.411 | Other generalized epilepsy and epileptic syndromes, intractable, with status epilepticus |
| G40.419 | Other generalized epilepsy and epileptic syndromes, intractable, without status epilepticus |
| G40.501 | Epileptic seizures related to external causes, not intractable, with status epilepticus |
| G40.509 | Epileptic seizures related to external causes, not intractable, without status epilepticus |
| G40.801 | Other epilepsy, not intractable, with status epilepticus |
| G40.802 | Other epilepsy, not intractable, without status epilepticus |
| G40.803 | Other epilepsy, intractable, with status epilepticus |
| G40.804 | Other epilepsy, intractable, without status epilepticus |
| G40.811 | Lennox-Gastaut syndrome, not intractable, with status epilepticus |
| G40.812 | Lennox-Gastaut syndrome, not intractable, without status epilepticus |
| G40.813 | Lennox-Gastaut syndrome, intractable, with status epilepticus |
| G40.814 | Lennox-Gastaut syndrome, intractable, without status epilepticus |
| G40.821 | Epileptic spasms, not intractable, with status epilepticus |
| G40.822 | Epileptic spasms, not intractable, without status epilepticus |
| G40.823 | Epileptic spasms, intractable, with status epilepticus |
| G40.824 | Epileptic spasms, intractable, without status epilepticus |
| G40.89 | Other seizures |
| G40.901 | Epilepsy, unspecified, not intractable, with status epilepticus |
| G40.909 | Epilepsy, unspecified, not intractable, without status epilepticus |
| G40.911 | Epilepsy, unspecified, intractable, with status epilepticus |
| G40.919 | Epilepsy, unspecified, intractable, without status epilepticus |
| I44.0 | Atrioventricular block, first degree |
| I44.1 | Atrioventricular block, second degree |
| I44.2 | Atrioventricular block, complete |
| I44.30 | Unspecified atrioventricular block |

| ICD-10 Codes | Description |
|---|---|
| I45.81 | Long QT syndrome |
| I47.0 | Re-entry ventricular arrhythmia |
| I47.1 | Supraventricular tachycardia |
| I47.2 | Ventricular tachycardia |
| I49.2 | Junctional premature depolarization |
| M25.50 | Pain in unspecified joint |
| M47.811 | Spondylosis without myelopathy or radiculopathy, occipito-atlanto-axial region |
| M47.812 | Spondylosis without myelopathy or radiculopathy, cervical region |
| M47.813 | Spondylosis without myelopathy or radiculopathy, cervicothoracic region |
| M47.816 | Spondylosis without myelopathy or radiculopathy, lumbar region |
| M47.817 | Spondylosis without myelopathy or radiculopathy, lumbosacral region |
| M47.818 | Spondylosis without myelopathy or radiculopathy, sacral and sacrococcygeal region |
| M51.14 | Intervertebral disc disorders with radiculopathy, thoracic region |
| M51.15 | Intervertebral disc disorders with radiculopathy, thoracolumbar region |
| M51.16 | Intervertebral disc disorders with radiculopathy, lumbar region |
| M51.17 | Intervertebral disc disorders with radiculopathy, lumbosacral region |
| M51.36 | Other intervertebral disc degeneration, lumbar region |
| M51.37 | Other intervertebral disc degeneration, lumbosacral region |
| M54.10 | Radiculopathy, site unspecified |
| M54.14 | Radiculopathy, thoracic region |
| M54.15 | Radiculopathy, thoracolumbar region |
| M54.16 | Radiculopathy, lumbar region |
| M54.17 | Radiculopathy, lumbosacral region |
| M54.18 | Radiculopathy, sacral and sacrococcygeal region |
| M54.2 | Cervicalgia |
| M54.5 | Low back pain |
| M60.811 | Other myositis, right shoulder |
| M60.812 | Other myositis, left shoulder |
| M60.821 | Other myositis, right upper arm |
| M60.822 | Other myositis, left upper arm |
| M60.831 | Other myositis, right forearm |
| M60.832 | Other myositis, left forearm |
| M60.841 | Other myositis, right hand |
| M60.842 | Other myositis, left hand |
| M60.851 | Other myositis, right thigh |
| M60.852 | Other myositis, left thigh |
| M60.861 | Other myositis, right lower leg |
| M60.862 | Other myositis, left lower leg |
| M60.871 | Other myositis, right ankle and foot |
| M60.872 | Other myositis, left ankle and foot |
| M60.88 | Other myositis, other site |
| M60.89 | Other myositis, multiple sites |
| M79.1 | Myalgia |
| M79.2 | Neuralgia and neuritis, unspecified |
| M79.7 | Fibromyalgia |
| R40.0 | Somnolence |
| R40.1 | Stupor |
| R40.2111 | Coma scale, eyes open, never, in the field [EMT or ambulance] |
| R40.2112 | Coma scale, eyes open, never, at arrival to emergency department |
| R40.2113 | Coma scale, eyes open, never, at hospital admission |
| R40.2114 | Coma scale, eyes open, never, 24 hours or more after hospital admission |
| R40.2121 | Coma scale, eyes open, to pain, in the field [EMT or ambulance] |
| R40.2122 | Coma scale, eyes open, to pain, at arrival to emergency department |
| R40.2123 | Coma scale, eyes open, to pain, at hospital admission |
| R40.2124 | Coma scale, eyes open, to pain, 24 hours or more after hospital admission |
| R40.2131 | Coma scale, eyes open, to sound, in the field [EMT or ambulance] |
| R40.2132 | Coma scale, eyes open, to sound, at arrival to emergency department |
| R40.2133 | Coma scale, eyes open, to sound, at hospital admission |

| ICD-10 Codes | Description |
|---|---|
| R40.2134 | Coma scale, eyes open, to sound, 24 hours or more after hospital admission |
| R40.2141 | Coma scale, eyes open, spontaneous, in the field [EMT or ambulance] |
| R40.2142 | Coma scale, eyes open, spontaneous, at arrival to emergency department |
| R40.2143 | Coma scale, eyes open, spontaneous, at hospital admission |
| R40.2144 | Coma scale, eyes open, spontaneous, 24 hours or more after hospital admission |
| R40.2211 | Coma scale, best verbal response, none, in the field [EMT or ambulance] |
| R40.2212 | Coma scale, best verbal response, none, at arrival to emergency department |
| R40.2213 | Coma scale, best verbal response, none, at hospital admission |
| R40.2214 | Coma scale, best verbal response, none, 24 hours or more after hospital admission |
| R40.2221 | Coma scale, best verbal response, incomprehensible words, in the field [EMT or ambulance] |
| R40.2222 | Coma scale, best verbal response, incomprehensible words, at arrival to emergency department |
| R40.2223 | Coma scale, best verbal response, incomprehensible words, at hospital admission |
| R40.2224 | Coma scale, best verbal response, incomprehensible words, 24 hours or more after hospital admission |
| R40.2231 | Coma scale, best verbal response, inappropriate words, in the field [EMT or ambulance] |
| R40.2232 | Coma scale, best verbal response, inappropriate words, at arrival to emergency department |
| R40.2233 | Coma scale, best verbal response, inappropriate words, at hospital admission |
| R40.2234 | Coma scale, best verbal response, inappropriate words, 24 hours or more after hospital admission |
| R40.2241 | Coma scale, best verbal response, confused conversation, in the field [EMT or ambulance] |
| R40.2242 | Coma scale, best verbal response, confused conversation, at arrival to emergency department |
| R40.2243 | Coma scale, best verbal response, confused conversation, at hospital admission |
| R40.2244 | Coma scale, best verbal response, confused conversation, 24 hours or more after hospital admission |
| R40.2251 | Coma scale, best verbal response, oriented, in the field [EMT or ambulance] |
| R40.2252 | Coma scale, best verbal response, oriented, at arrival to emergency department |
| R40.2253 | Coma scale, best verbal response, oriented, at hospital admission |
| R40.2254 | Coma scale, best verbal response, oriented, 24 hours or more after hospital admission |
| R40.2311 | Coma scale, best motor response, none, in the field [EMT or ambulance] |
| R40.2312 | Coma scale, best motor response, none, at arrival to emergency department |
| R40.2313 | Coma scale, best motor response, none, at hospital admission |
| R40.2314 | Coma scale, best motor response, none, 24 hours or more after hospital admission |
| R40.2321 | Coma scale, best motor response, extension, in the field [EMT or ambulance] |
| R40.2322 | Coma scale, best motor response, extension, at arrival to emergency department |
| R40.2323 | Coma scale, best motor response, extension, at hospital admission |
| R40.2324 | Coma scale, best motor response, extension, 24 hours or more after hospital admission |
| R40.2331 | Coma scale, best motor response, abnormal, in the field [EMT or ambulance] |
| R40.2332 | Coma scale, best motor response, abnormal, at arrival to emergency department |
| R40.2333 | Coma scale, best motor response, abnormal, at hospital admission |
| R40.2334 | Coma scale, best motor response, abnormal, 24 hours or more after hospital admission |
| R40.2341 | Coma scale, best motor response, flexion withdrawal, in the field [EMT or ambulance] |
| R40.2342 | Coma scale, best motor response, flexion withdrawal, at arrival to emergency department |
| R40.2343 | Coma scale, best motor response, flexion withdrawal, at hospital admission |
| R40.2344 | Coma scale, best motor response, flexion withdrawal, 24 hours or more after hospital admission |
| R40.2351 | Coma scale, best motor response, localizes pain, in the field [EMT or ambulance] |
| R40.2352 | Coma scale, best motor response, localizes pain, at arrival to emergency department |
| R40.2353 | Coma scale, best motor response, localizes pain, at hospital admission |
| R40.2354 | Coma scale, best motor response, localizes pain, 24 hours or more after hospital admission |
| R40.2361 | Coma scale, best motor response, obeys commands, in the field [EMT or ambulance] |
| R40.2362 | Coma scale, best motor response, obeys commands, at arrival to emergency department |
| R40.2363 | Coma scale, best motor response, obeys commands, at hospital admission |
| R40.2364 | Coma scale, best motor response, obeys commands, 24 hours or more after hospital admission |
| R41.0 | Disorientation, unspecified |
| R41.82 | Altered mental status, unspecified |
| R44.0 | Auditory hallucinations |
| R44.3 | Hallucinations, unspecified |
| R56.00 | Simple febrile convulsions |
| R56.01 | Complex febrile convulsions |
| R56.1 | Post traumatic seizures |
| R56.9 | Unspecified convulsions |

| ICD-10 Codes | Description |
|---|---|
| T39.011A | Poisoning by aspirin, accidental (unintentional), initial encounter |
| T39.011D | Poisoning by aspirin, accidental (unintentional), subsequent encounter |
| T39.012A | Poisoning by aspirin, intentional self-harm, initial encounter |
| T39.012D | Poisoning by aspirin, intentional self-harm, subsequent encounter |
| T39.013A | Poisoning by aspirin, assault, initial encounter |
| T39.013D | Poisoning by aspirin, assault, subsequent encounter |
| T39.014A | Poisoning by aspirin, undetermined, initial encounter |
| T39.014D | Poisoning by aspirin, undetermined, subsequent encounter |
| T39.015A | Adverse effect of aspirin, initial encounter |
| T39.015D | Adverse effect of aspirin, subsequent encounter |
| T39.016A | Underdosing of aspirin, initial encounter |
| T39.016D | Underdosing of aspirin, subsequent encounter |
| T39.091A | Poisoning by salicylates, accidental (unintentional), initial encounter |
| T39.091D | Poisoning by salicylates, accidental (unintentional), subsequent encounter |
| T39.092A | Poisoning by salicylates, intentional self-harm, initial encounter |
| T39.092D | Poisoning by salicylates, intentional self-harm, subsequent encounter |
| T39.093A | Poisoning by salicylates, assault, initial encounter |
| T39.093D | Poisoning by salicylates, assault, subsequent encounter |
| T39.094A | Poisoning by salicylates, undetermined, initial encounter |
| T39.094D | Poisoning by salicylates, undetermined, subsequent encounter |
| T39.095A | Adverse effect of salicylates, initial encounter |
| T39.095D | Adverse effect of salicylates, subsequent encounter |
| T39.096A | Underdosing of salicylates, initial encounter |
| T39.096D | Underdosing of salicylates, subsequent encounter |
| T39.1X1A | Poisoning by 4-Aminophenol derivatives, accidental (unintentional), initial encounter |
| T39.1X1D | Poisoning by 4-Aminophenol derivatives, accidental (unintentional), subsequent encounter |
| T39.1X2A | Poisoning by 4-Aminophenol derivatives, intentional self-harm, initial encounter |
| T39.1X2D | Poisoning by 4-Aminophenol derivatives, intentional self-harm, subsequent encounter |
| T39.1X3A | Poisoning by 4-Aminophenol derivatives, assault, initial encounter |
| T39.1X3D | Poisoning by 4-Aminophenol derivatives, assault, subsequent encounter |
| T39.1X4A | Poisoning by 4-Aminophenol derivatives, undetermined, initial encounter |
| T39.1X4D | Poisoning by 4-Aminophenol derivatives, undetermined, subsequent encounter |
| T39.1X5A | Adverse effect of 4-Aminophenol derivatives, initial encounter |
| T39.1X5D | Adverse effect of 4-Aminophenol derivatives, subsequent encounter |
| T39.1X6A | Underdosing of 4-Aminophenol derivatives, initial encounter |
| T39.1X6D | Underdosing of 4-Aminophenol derivatives, subsequent encounter |
| T39.2X1A | Poisoning by pyrazolone derivatives, accidental (unintentional), initial encounter |
| T39.2X1D | Poisoning by pyrazolone derivatives, accidental (unintentional), subsequent encounter |
| T39.2X2A | Poisoning by pyrazolone derivatives, intentional self-harm, initial encounter |
| T39.2X2D | Poisoning by pyrazolone derivatives, intentional self-harm, subsequent encounter |
| T39.2X3A | Poisoning by pyrazolone derivatives, assault, initial encounter |
| T39.2X3D | Poisoning by pyrazolone derivatives, assault, subsequent encounter |
| T39.2X4A | Poisoning by pyrazolone derivatives, undetermined, initial encounter |
| T39.2X4D | Poisoning by pyrazolone derivatives, undetermined, subsequent encounter |
| T39.2X5A | Adverse effect of pyrazolone derivatives, initial encounter |
| T39.2X5D | Adverse effect of pyrazolone derivatives, subsequent encounter |
| T39.311A | Poisoning by propionic acid derivatives, accidental (unintentional), initial encounter |
| T39.311D | Poisoning by propionic acid derivatives, accidental (unintentional), subsequent encounter |
| T39.312A | Poisoning by propionic acid derivatives, intentional self-harm, initial encounter |
| T39.312D | Poisoning by propionic acid derivatives, intentional self-harm, subsequent encounter |
| T39.313A | Poisoning by propionic acid derivatives, assault, initial encounter |
| T39.313D | Poisoning by propionic acid derivatives, assault, subsequent encounter |
| T39.314A | Poisoning by propionic acid derivatives, undetermined, initial encounter |
| T39.314D | Poisoning by propionic acid derivatives, undetermined, subsequent encounter |
| T39.315A | Adverse effect of propionic acid derivatives, initial encounter |
| T39.315D | Adverse effect of propionic acid derivatives, subsequent encounter |
| T39.316A | Underdosing of propionic acid derivatives, initial encounter |

| ICD-10 Codes | Description |
|---|---|
| T39.316D | Underdosing of propionic acid derivatives, subsequent encounter |
| T39.391A | Poisoning by other nonsteroidal anti-inflammatory drugs [NSAID], accidental (unintentional), initial encounter |
| T39.391D | Poisoning by other nonsteroidal anti-inflammatory drugs [NSAID], accidental (unintentional), subsequent encounter |
| T39.392A | Poisoning by other nonsteroidal anti-inflammatory drugs [NSAID], intentional self-harm, initial encounter |
| T39.392D | Poisoning by other nonsteroidal anti-inflammatory drugs [NSAID], intentional self-harm, subsequent encounter |
| T39.393A | Poisoning by other nonsteroidal anti-inflammatory drugs [NSAID], assault, initial encounter |
| T39.393D | Poisoning by other nonsteroidal anti-inflammatory drugs [NSAID], assault, subsequent encounter |
| T39.394A | Poisoning by other nonsteroidal anti-inflammatory drugs [NSAID], undetermined, initial encounter |
| T39.394D | Poisoning by other nonsteroidal anti-inflammatory drugs [NSAID], undetermined, subsequent encounter |
| T39.395A | Adverse effect of other nonsteroidal anti-inflammatory drugs [NSAID], initial encounter |
| T39.395D | Adverse effect of other nonsteroidal anti-inflammatory drugs [NSAID], subsequent encounter |
| T39.396A | Underdosing of other nonsteroidal anti-inflammatory drugs [NSAID], initial encounter |
| T39.396D | Underdosing of other nonsteroidal anti-inflammatory drugs [NSAID], subsequent encounter |
| T40.0X1A | Poisoning by opium, accidental (unintentional), initial encounter |
| T40.0X1D | Poisoning by opium, accidental (unintentional), subsequent encounter |
| T40.0X2A | Poisoning by opium, intentional self-harm, initial encounter |
| T40.0X2D | Poisoning by opium, intentional self-harm, subsequent encounter |
| T40.0X3A | Poisoning by opium, assault, initial encounter |
| T40.0X3D | Poisoning by opium, assault, subsequent encounter |
| T40.0X4A | Poisoning by opium, undetermined, initial encounter |
| T40.0X4D | Poisoning by opium, undetermined, subsequent encounter |
| T40.0X5A | Adverse effect of opium, initial encounter |
| T40.0X5D | Adverse effect of opium, subsequent encounter |
| T40.0X6A | Underdosing of opium, initial encounter |
| T40.0X6D | Underdosing of opium, subsequent encounter |
| T40.1X1A | Poisoning by heroin, accidental (unintentional), initial encounter |
| T40.1X1D | Poisoning by heroin, accidental (unintentional), subsequent encounter |
| T40.1X2A | Poisoning by heroin, intentional self-harm, initial encounter |
| T40.1X2D | Poisoning by heroin, intentional self-harm, subsequent encounter |
| T40.1X3A | Poisoning by heroin, assault, initial encounter |
| T40.1X3D | Poisoning by heroin, assault, subsequent encounter |
| T40.1X4A | Poisoning by heroin, undetermined, initial encounter |
| T40.1X4D | Poisoning by heroin, undetermined, subsequent encounter |
| T40.2X1A | Poisoning by other opioids, accidental (unintentional), initial encounter |
| T40.2X1D | Poisoning by other opioids, accidental (unintentional), subsequent encounter |
| T40.2X2A | Poisoning by other opioids, intentional self-harm, initial encounter |
| T40.2X2D | Poisoning by other opioids, intentional self-harm, subsequent encounter |
| T40.2X3A | Poisoning by other opioids, assault, initial encounter |
| T40.2X3D | Poisoning by other opioids, assault, subsequent encounter |
| T40.2X4A | Poisoning by other opioids, undetermined, initial encounter |
| T40.2X4D | Poisoning by other opioids, undetermined, subsequent encounter |
| T40.2X5A | Adverse effect of other opioids, initial encounter |
| T40.2X5D | Adverse effect of other opioids, subsequent encounter |
| T40.2X6A | Underdosing of other opioids, initial encounter |
| T40.2X6D | Underdosing of other opioids, subsequent encounter |
| T40.3X1A | Poisoning by methadone, accidental (unintentional), initial encounter |
| T40.3X1D | Poisoning by methadone, accidental (unintentional), subsequent encounter |
| T40.3X2A | Poisoning by methadone, intentional self-harm, initial encounter |
| T40.3X2D | Poisoning by methadone, intentional self-harm, subsequent encounter |
| T40.3X3A | Poisoning by methadone, assault, initial encounter |
| T40.3X3D | Poisoning by methadone, assault, subsequent encounter |
| T40.3X4A | Poisoning by methadone, undetermined, initial encounter |
| T40.3X4D | Poisoning by methadone, undetermined, subsequent encounter |

| ICD-10 Codes | Description |
|---|---|
| T40.3X5A | Adverse effect of methadone, initial encounter |
| T40.3X5D | Adverse effect of methadone, subsequent encounter |
| T40.3X6A | Underdosing of methadone, initial encounter |
| T40.3X6D | Underdosing of methadone, subsequent encounter |
| T40.4X1A | Poisoning by other synthetic narcotics, accidental (unintentional), initial encounter |
| T40.4X1D | Poisoning by other synthetic narcotics, accidental (unintentional), subsequent encounter |
| T40.4X2A | Poisoning by other synthetic narcotics, intentional self-harm, initial encounter |
| T40.4X2D | Poisoning by other synthetic narcotics, intentional self-harm, subsequent encounter |
| T40.4X3A | Poisoning by other synthetic narcotics, assault, initial encounter |
| T40.4X3D | Poisoning by other synthetic narcotics, assault, subsequent encounter |
| T40.4X4A | Poisoning by other synthetic narcotics, undetermined, initial encounter |
| T40.4X4D | Poisoning by other synthetic narcotics, undetermined, subsequent encounter |
| T40.4X5A | Adverse effect of other synthetic narcotics, initial encounter |
| T40.4X5D | Adverse effect of other synthetic narcotics, subsequent encounter |
| T40.4X6A | Underdosing of other synthetic narcotics, initial encounter |
| T40.4X6D | Underdosing of other synthetic narcotics, subsequent encounter |
| T40.5X1A | Poisoning by cocaine, accidental (unintentional), initial encounter |
| T40.5X1D | Poisoning by cocaine, accidental (unintentional), subsequent encounter |
| T40.5X2A | Poisoning by cocaine, intentional self-harm, initial encounter |
| T40.5X2D | Poisoning by cocaine, intentional self-harm, subsequent encounter |
| T40.5X3A | Poisoning by cocaine, assault, initial encounter |
| T40.5X3D | Poisoning by cocaine, assault, subsequent encounter |
| T40.5X4A | Poisoning by cocaine, undetermined, initial encounter |
| T40.5X4D | Poisoning by cocaine, undetermined, subsequent encounter |
| T40.5X5A | Adverse effect of cocaine, initial encounter |
| T40.5X5D | Adverse effect of cocaine, subsequent encounter |
| T40.5X6A | Underdosing of cocaine, initial encounter |
| T40.5X6D | Underdosing of cocaine, subsequent encounter |
| T40.601A | Poisoning by unspecified narcotics, accidental (unintentional), initial encounter |
| T40.601D | Poisoning by unspecified narcotics, accidental (unintentional), subsequent encounter |
| T40.602A | Poisoning by unspecified narcotics, intentional self-harm, initial encounter |
| T40.602D | Poisoning by unspecified narcotics, intentional self-harm, subsequent encounter |
| T40.603A | Poisoning by unspecified narcotics, assault, initial encounter |
| T40.603D | Poisoning by unspecified narcotics, assault, subsequent encounter |
| T40.604A | Poisoning by unspecified narcotics, undetermined, initial encounter |
| T40.604D | Poisoning by unspecified narcotics, undetermined, subsequent encounter |
| T40.605A | Adverse effect of unspecified narcotics, initial encounter |
| T40.605D | Adverse effect of unspecified narcotics, subsequent encounter |
| T40.606A | Underdosing of unspecified narcotics, initial encounter |
| T40.606D | Underdosing of unspecified narcotics, subsequent encounter |
| T40.691A | Poisoning by other narcotics, accidental (unintentional), initial encounter |
| T40.691D | Poisoning by other narcotics, accidental (unintentional), subsequent encounter |
| T40.692A | Poisoning by other narcotics, intentional self-harm, initial encounter |
| T40.692D | Poisoning by other narcotics, intentional self-harm, subsequent encounter |
| T40.693A | Poisoning by other narcotics, assault, initial encounter |
| T40.693D | Poisoning by other narcotics, assault, subsequent encounter |
| T40.694A | Poisoning by other narcotics, undetermined, initial encounter |
| T40.694D | Poisoning by other narcotics, undetermined, subsequent encounter |
| T40.695A | Adverse effect of other narcotics, initial encounter |
| T40.695D | Adverse effect of other narcotics, subsequent encounter |
| T40.696A | Underdosing of other narcotics, initial encounter |
| T40.696D | Underdosing of other narcotics, subsequent encounter |
| T40.7X1A | Poisoning by cannabis (derivatives), accidental (unintentional), initial encounter |
| T40.7X1D | Poisoning by cannabis (derivatives), accidental (unintentional), subsequent encounter |
| T40.7X2A | Poisoning by cannabis (derivatives), intentional self-harm, initial encounter |
| T40.7X2D | Poisoning by cannabis (derivatives), intentional self-harm, subsequent encounter |
| T40.7X3A | Poisoning by cannabis (derivatives), assault, initial encounter |
| T40.7X3D | Poisoning by cannabis (derivatives), assault, subsequent encounter |

| ICD-10 Codes | Description |
|---|---|
| T40.7X4A | Poisoning by cannabis (derivatives), undetermined, initial encounter |
| T40.7X4D | Poisoning by cannabis (derivatives), undetermined, subsequent encounter |
| T40.7X5A | Adverse effect of cannabis (derivatives), initial encounter |
| T40.7X5D | Adverse effect of cannabis (derivatives), subsequent encounter |
| T40.7X6A | Underdosing of cannabis (derivatives), initial encounter |
| T40.7X6D | Underdosing of cannabis (derivatives), subsequent encounter |
| T40.8X1A | Poisoning by lysergide [LSD], accidental (unintentional), initial encounter |
| T40.8X1D | Poisoning by lysergide [LSD], accidental (unintentional), subsequent encounter |
| T40.8X2A | Poisoning by lysergide [LSD], intentional self-harm, initial encounter |
| T40.8X2D | Poisoning by lysergide [LSD], intentional self-harm, subsequent encounter |
| T40.8X4A | Poisoning by lysergide [LSD], undetermined, initial encounter |
| T40.8X4D | Poisoning by lysergide [LSD], undetermined, subsequent encounter |
| T40.901A | Poisoning by unspecified psychodysleptics [hallucinogens], accidental (unintentional), initial encounter |
| T40.901D | Poisoning by unspecified psychodysleptics [hallucinogens], accidental (unintentional), subsequent encounter |
| T40.902A | Poisoning by unspecified psychodysleptics [hallucinogens], intentional self-harm, initial encounter |
| T40.902D | Poisoning by unspecified psychodysleptics [hallucinogens], intentional self-harm, subsequent encounter |
| T40.903A | Poisoning by unspecified psychodysleptics [hallucinogens], assault, initial encounter |
| T40.903D | Poisoning by unspecified psychodysleptics [hallucinogens], assault, subsequent encounter |
| T40.904A | Poisoning by unspecified psychodysleptics [hallucinogens], undetermined, initial encounter |
| T40.904D | Poisoning by unspecified psychodysleptics [hallucinogens], undetermined, subsequent encounter |
| T40.905A | Adverse effect of unspecified psychodysleptics [hallucinogens], initial encounter |
| T40.905D | Adverse effect of unspecified psychodysleptics [hallucinogens], subsequent encounter |
| T40.906A | Underdosing of unspecified psychodysleptics, initial encounter |
| T40.906D | Underdosing of unspecified psychodysleptics, subsequent encounter |
| T40.991A | Poisoning by other psychodysleptics [hallucinogens], accidental (unintentional), initial encounter |
| T40.991D | Poisoning by other psychodysleptics [hallucinogens], accidental (unintentional), subsequent encounter |
| T40.992A | Poisoning by other psychodysleptics [hallucinogens], intentional self-harm, initial encounter |
| T40.992D | Poisoning by other psychodysleptics [hallucinogens], intentional self-harm, subsequent encounter |
| T40.993A | Poisoning by other psychodysleptics [hallucinogens], assault, initial encounter |
| T40.993D | Poisoning by other psychodysleptics [hallucinogens], assault, subsequent encounter |
| T40.994A | Poisoning by other psychodysleptics [hallucinogens], undetermined, initial encounter |
| T40.994D | Poisoning by other psychodysleptics [hallucinogens], undetermined, subsequent encounter |
| T40.995A | Adverse effect of other psychodysleptics [hallucinogens], initial encounter |
| T40.995D | Adverse effect of other psychodysleptics [hallucinogens], subsequent encounter |
| T40.996A | Underdosing of other psychodysleptics, initial encounter |
| T40.996D | Underdosing of other psychodysleptics, subsequent encounter |
| T42.0X1A | Poisoning by hydantoin derivatives, accidental (unintentional), initial encounter |
| T42.0X1D | Poisoning by hydantoin derivatives, accidental (unintentional), subsequent encounter |
| T42.0X2A | Poisoning by hydantoin derivatives, intentional self-harm, initial encounter |
| T42.0X2D | Poisoning by hydantoin derivatives, intentional self-harm, subsequent encounter |
| T42.0X3A | Poisoning by hydantoin derivatives, assault, initial encounter |
| T42.0X3D | Poisoning by hydantoin derivatives, assault, subsequent encounter |
| T42.0X4A | Poisoning by hydantoin derivatives, undetermined, initial encounter |
| T42.0X4D | Poisoning by hydantoin derivatives, undetermined, subsequent encounter |
| T42.0X5A | Adverse effect of hydantoin derivatives, initial encounter |
| T42.0X5D | Adverse effect of hydantoin derivatives, subsequent encounter |
| T42.0X6A | Underdosing of hydantoin derivatives, initial encounter |
| T42.0X6D | Underdosing of hydantoin derivatives, subsequent encounter |
| T42.3X1A | Poisoning by barbiturates, accidental (unintentional), initial encounter |
| T42.3X1D | Poisoning by barbiturates, accidental (unintentional), subsequent encounter |
| T42.3X2A | Poisoning by barbiturates, intentional self-harm, initial encounter |
| T42.3X2D | Poisoning by barbiturates, intentional self-harm, subsequent encounter |
| T42.3X3A | Poisoning by barbiturates, assault, initial encounter |
| T42.3X3D | Poisoning by barbiturates, assault, subsequent encounter |

| ICD-10 Codes | Description |
|---|---|
| T42.3X4A | Poisoning by barbiturates, undetermined, initial encounter |
| T42.3X4D | Poisoning by barbiturates, undetermined, subsequent encounter |
| T42.3X5A | Adverse effect of barbiturates, initial encounter |
| T42.3X5D | Adverse effect of barbiturates, subsequent encounter |
| T42.3X6A | Underdosing of barbiturates, initial encounter |
| T42.3X6D | Underdosing of barbiturates, subsequent encounter |
| T42.4X1A | Poisoning by benzodiazepines, accidental (unintentional), initial encounter |
| T42.4X1D | Poisoning by benzodiazepines, accidental (unintentional), subsequent encounter |
| T42.4X2A | Poisoning by benzodiazepines, intentional self-harm, initial encounter |
| T42.4X2D | Poisoning by benzodiazepines, intentional self-harm, subsequent encounter |
| T42.4X3A | Poisoning by benzodiazepines, assault, initial encounter |
| T42.4X3D | Poisoning by benzodiazepines, assault, subsequent encounter |
| T42.4X4A | Poisoning by benzodiazepines, undetermined, initial encounter |
| T42.4X4D | Poisoning by benzodiazepines, undetermined, subsequent encounter |
| T42.4X5A | Adverse effect of benzodiazepines, initial encounter |
| T42.4X5D | Adverse effect of benzodiazepines, subsequent encounter |
| T42.4X6A | Underdosing of benzodiazepines, initial encounter |
| T42.4X6D | Underdosing of benzodiazepines, subsequent encounter |
| T42.6X1A | Poisoning by other antiepileptic and sedative-hypnotic drugs, accidental (unintentional), initial encounter |
| T42.6X1D | Poisoning by other antiepileptic and sedative-hypnotic drugs, accidental (unintentional), subsequent encounter |
| T42.6X2A | Poisoning by other antiepileptic and sedative-hypnotic drugs, intentional self-harm, initial encounter |
| T42.6X2D | Poisoning by other antiepileptic and sedative-hypnotic drugs, intentional self-harm, subsequent encounter |
| T42.6X3A | Poisoning by other antiepileptic and sedative-hypnotic drugs, assault, initial encounter |
| T42.6X3D | Poisoning by other antiepileptic and sedative-hypnotic drugs, assault, subsequent encounter |
| T42.6X4A | Poisoning by other antiepileptic and sedative-hypnotic drugs, undetermined, initial encounter |
| T42.6X4D | Poisoning by other antiepileptic and sedative-hypnotic drugs, undetermined, subsequent encounter |
| T42.6X5A | Adverse effect of other antiepileptic and sedative-hypnotic drugs, initial encounter |
| T42.6X5D | Adverse effect of other antiepileptic and sedative-hypnotic drugs, subsequent encounter |
| T42.6X6A | Underdosing of other antiepileptic and sedative-hypnotic drugs, initial encounter |
| T42.6X6D | Underdosing of other antiepileptic and sedative-hypnotic drugs, subsequent encounter |
| T42.71XA | Poisoning by unspecified antiepileptic and sedative-hypnotic drugs, accidental (unintentional), initial encounter |
| T42.71XD | Poisoning by unspecified antiepileptic and sedative-hypnotic drugs, accidental (unintentional), subsequent encounter |
| T42.72XA | Poisoning by unspecified antiepileptic and sedative-hypnotic drugs, intentional self-harm, initial encounter |
| T42.72XD | Poisoning by unspecified antiepileptic and sedative-hypnotic drugs, intentional self-harm, subsequent encounter |
| T42.73XA | Poisoning by unspecified antiepileptic and sedative-hypnotic drugs, assault, initial encounter |
| T42.73XD | Poisoning by unspecified antiepileptic and sedative-hypnotic drugs, assault, subsequent encounter |
| T42.74XA | Poisoning by unspecified antiepileptic and sedative-hypnotic drugs, undetermined, initial encounter |
| T42.74XD | Poisoning by unspecified antiepileptic and sedative-hypnotic drugs, undetermined, subsequent encounter |
| T42.75XA | Adverse effect of unspecified antiepileptic and sedative-hypnotic drugs, initial encounter |
| T42.75XD | Adverse effect of unspecified antiepileptic and sedative-hypnotic drugs, subsequent encounter |
| T42.76XA | Underdosing of unspecified antiepileptic and sedative-hypnotic drugs, initial encounter |
| T42.76XD | Underdosing of unspecified antiepileptic and sedative-hypnotic drugs, subsequent encounter |
| T43.011A | Poisoning by tricyclic antidepressants, accidental (unintentional), initial encounter |
| T43.011D | Poisoning by tricyclic antidepressants, accidental (unintentional), subsequent encounter |
| T43.012A | Poisoning by tricyclic antidepressants, intentional self-harm, initial encounter |
| T43.012D | Poisoning by tricyclic antidepressants, intentional self-harm, subsequent encounter |
| T43.013A | Poisoning by tricyclic antidepressants, assault, initial encounter |
| T43.013D | Poisoning by tricyclic antidepressants, assault, subsequent encounter |
| T43.014A | Poisoning by tricyclic antidepressants, undetermined, initial encounter |
| T43.014D | Poisoning by tricyclic antidepressants, undetermined, subsequent encounter |

| ICD-10 Codes | Description |
|---|---|
| T43.015A | Adverse effect of tricyclic antidepressants, initial encounter |
| T43.015D | Adverse effect of tricyclic antidepressants, subsequent encounter |
| T43.016A | Underdosing of tricyclic antidepressants, initial encounter |
| T43.016D | Underdosing of tricyclic antidepressants, subsequent encounter |
| T43.021A | Poisoning by tetracyclic antidepressants, accidental (unintentional), initial encounter |
| T43.021D | Poisoning by tetracyclic antidepressants, accidental (unintentional), subsequent encounter |
| T43.022A | Poisoning by tetracyclic antidepressants, intentional self-harm, initial encounter |
| T43.022D | Poisoning by tetracyclic antidepressants, intentional self-harm, subsequent encounter |
| T43.023A | Poisoning by tetracyclic antidepressants, assault, initial encounter |
| T43.023D | Poisoning by tetracyclic antidepressants, assault, subsequent encounter |
| T43.024A | Poisoning by tetracyclic antidepressants, undetermined, initial encounter |
| T43.024D | Poisoning by tetracyclic antidepressants, undetermined, subsequent encounter |
| T43.025A | Adverse effect of tetracyclic antidepressants, initial encounter |
| T43.025D | Adverse effect of tetracyclic antidepressants, subsequent encounter |
| T43.026A | Underdosing of tetracyclic antidepressants, initial encounter |
| T43.026D | Underdosing of tetracyclic antidepressants, subsequent encounter |
| T43.1X1A | Poisoning by monoamine-oxidase-inhibitor antidepressants, accidental (unintentional), initial encounter |
| T43.1X1D | Poisoning by monoamine-oxidase-inhibitor antidepressants, accidental (unintentional), subsequent encounter |
| T43.1X2A | Poisoning by monoamine-oxidase-inhibitor antidepressants, intentional self-harm, initial encounter |
| T43.1X2D | Poisoning by monoamine-oxidase-inhibitor antidepressants, intentional self-harm, subsequent encounter |
| T43.1X3A | Poisoning by monoamine-oxidase-inhibitor antidepressants, assault, initial encounter |
| T43.1X3D | Poisoning by monoamine-oxidase-inhibitor antidepressants, assault, subsequent encounter |
| T43.1X4A | Poisoning by monoamine-oxidase-inhibitor antidepressants, undetermined, initial encounter |
| T43.1X4D | Poisoning by monoamine-oxidase-inhibitor antidepressants, undetermined, subsequent encounter |
| T43.1X5A | Adverse effect of monoamine-oxidase-inhibitor antidepressants, initial encounter |
| T43.1X5D | Adverse effect of monoamine-oxidase-inhibitor antidepressants, subsequent encounter |
| T43.1X6A | Underdosing of monoamine-oxidase-inhibitor antidepressants, initial encounter |
| T43.1X6D | Underdosing of monoamine-oxidase-inhibitor antidepressants, subsequent encounter |
| T43.201A | Poisoning by unspecified antidepressants, accidental (unintentional), initial encounter |
| T43.201D | Poisoning by unspecified antidepressants, accidental (unintentional), subsequent encounter |
| T43.202A | Poisoning by unspecified antidepressants, intentional self-harm, initial encounter |
| T43.202D | Poisoning by unspecified antidepressants, intentional self-harm, subsequent encounter |
| T43.203A | Poisoning by unspecified antidepressants, assault, initial encounter |
| T43.203D | Poisoning by unspecified antidepressants, assault, subsequent encounter |
| T43.204A | Poisoning by unspecified antidepressants, undetermined, initial encounter |
| T43.204D | Poisoning by unspecified antidepressants, undetermined, subsequent encounter |
| T43.205A | Adverse effect of unspecified antidepressants, initial encounter |
| T43.205D | Adverse effect of unspecified antidepressants, subsequent encounter |
| T43.206A | Underdosing of unspecified antidepressants, initial encounter |
| T43.206D | Underdosing of unspecified antidepressants, subsequent encounter |
| T43.211A | Poisoning by selective serotonin and norepinephrine reuptake inhibitors, accidental (unintentional), initial encounter |
| T43.211D | Poisoning by selective serotonin and norepinephrine reuptake inhibitors, accidental (unintentional), subsequent encounter |
| T43.212A | Poisoning by selective serotonin and norepinephrine reuptake inhibitors, intentional self-harm, initial encounter |
| T43.212D | Poisoning by selective serotonin and norepinephrine reuptake inhibitors, intentional self-harm, subsequent encounter |
| T43.213A | Poisoning by selective serotonin and norepinephrine reuptake inhibitors, assault, initial encounter |
| T43.213D | Poisoning by selective serotonin and norepinephrine reuptake inhibitors, assault, subsequent encounter |
| T43.214A | Poisoning by selective serotonin and norepinephrine reuptake inhibitors, undetermined, initial encounter |
| T43.214D | Poisoning by selective serotonin and norepinephrine reuptake inhibitors, undetermined, subsequent encounter |
| T43.215A | Adverse effect of selective serotonin and norepinephrine reuptake inhibitors, initial encounter |

| ICD-10 Codes | Description |
|---|---|
| T43.215D | Adverse effect of selective serotonin and norepinephrine reuptake inhibitors, subsequent encounter |
| T43.216A | Underdosing of selective serotonin and norepinephrine reuptake inhibitors, initial encounter |
| T43.216D | Underdosing of selective serotonin and norepinephrine reuptake inhibitors, subsequent encounter |
| T43.221A | Poisoning by selective serotonin reuptake inhibitors, accidental (unintentional), initial encounter |
| T43.221D | Poisoning by selective serotonin reuptake inhibitors, accidental (unintentional), subsequent encounter |
| T43.222A | Poisoning by selective serotonin reuptake inhibitors, intentional self-harm, initial encounter |
| T43.222D | Poisoning by selective serotonin reuptake inhibitors, intentional self-harm, subsequent encounter |
| T43.223A | Poisoning by selective serotonin reuptake inhibitors, assault, initial encounter |
| T43.223D | Poisoning by selective serotonin reuptake inhibitors, assault, subsequent encounter |
| T43.224A | Poisoning by selective serotonin reuptake inhibitors, undetermined, initial encounter |
| T43.224D | Poisoning by selective serotonin reuptake inhibitors, undetermined, subsequent encounter |
| T43.225A | Adverse effect of selective serotonin reuptake inhibitors, initial encounter |
| T43.225D | Adverse effect of selective serotonin reuptake inhibitors, subsequent encounter |
| T43.226A | Underdosing of selective serotonin reuptake inhibitors, initial encounter |
| T43.226D | Underdosing of selective serotonin reuptake inhibitors, subsequent encounter |
| T43.291A | Poisoning by other antidepressants, accidental (unintentional), initial encounter |
| T43.291D | Poisoning by other antidepressants, accidental (unintentional), subsequent encounter |
| T43.292A | Poisoning by other antidepressants, intentional self-harm, initial encounter |
| T43.292D | Poisoning by other antidepressants, intentional self-harm, subsequent encounter |
| T43.293A | Poisoning by other antidepressants, assault, initial encounter |
| T43.293D | Poisoning by other antidepressants, assault, subsequent encounter |
| T43.294A | Poisoning by other antidepressants, undetermined, initial encounter |
| T43.294D | Poisoning by other antidepressants, undetermined, subsequent encounter |
| T43.295A | Adverse effect of other antidepressants, initial encounter |
| T43.295D | Adverse effect of other antidepressants, subsequent encounter |
| T43.296A | Underdosing of other antidepressants, initial encounter |
| T43.296D | Underdosing of other antidepressants, subsequent encounter |
| T43.3X1A | Poisoning by phenothiazine antipsychotics and neuroleptics, accidental (unintentional), initial encounter |
| T43.3X1D | Poisoning by phenothiazine antipsychotics and neuroleptics, accidental (unintentional), subsequent encounter |
| T43.3X2A | Poisoning by phenothiazine antipsychotics and neuroleptics, intentional self-harm, initial encounter |
| T43.3X2D | Poisoning by phenothiazine antipsychotics and neuroleptics, intentional self-harm, subsequent encounter |
| T43.3X3A | Poisoning by phenothiazine antipsychotics and neuroleptics, assault, initial encounter |
| T43.3X3D | Poisoning by phenothiazine antipsychotics and neuroleptics, assault, subsequent encounter |
| T43.3X4A | Poisoning by phenothiazine antipsychotics and neuroleptics, undetermined, initial encounter |
| T43.3X4D | Poisoning by phenothiazine antipsychotics and neuroleptics, undetermined, subsequent encounter |
| T43.3X5A | Adverse effect of phenothiazine antipsychotics and neuroleptics, initial encounter |
| T43.3X5D | Adverse effect of phenothiazine antipsychotics and neuroleptics, subsequent encounter |
| T43.3X6A | Underdosing of phenothiazine antipsychotics and neuroleptics, initial encounter |
| T43.3X6D | Underdosing of phenothiazine antipsychotics and neuroleptics, subsequent encounter |
| T43.4X1A | Poisoning by butyrophenone and thiothixene neuroleptics, accidental (unintentional), initial encounter |
| T43.4X1D | Poisoning by butyrophenone and thiothixene neuroleptics, accidental (unintentional), subsequent encounter |
| T43.4X2A | Poisoning by butyrophenone and thiothixene neuroleptics, intentional self-harm, initial encounter |
| T43.4X2D | Poisoning by butyrophenone and thiothixene neuroleptics, intentional self-harm, subsequent encounter |
| T43.4X3A | Poisoning by butyrophenone and thiothixene neuroleptics, assault, initial encounter |
| T43.4X3D | Poisoning by butyrophenone and thiothixene neuroleptics, assault, subsequent encounter |
| T43.4X4A | Poisoning by butyrophenone and thiothixene neuroleptics, undetermined, initial encounter |
| T43.4X4D | Poisoning by butyrophenone and thiothixene neuroleptics, undetermined, subsequent encounter |
| T43.4X5A | Adverse effect of butyrophenone and thiothixene neuroleptics, initial encounter |
| T43.4X5D | Adverse effect of butyrophenone and thiothixene neuroleptics, subsequent encounter |
| T43.4X6A | Underdosing of butyrophenone and thiothixene neuroleptics, initial encounter |
| T43.4X6D | Underdosing of butyrophenone and thiothixene neuroleptics, subsequent encounter |

| ICD-10 Codes | Description |
|---|---|
| T43.501A | Poisoning by unspecified antipsychotics and neuroleptics, accidental (unintentional), initial encounter |
| T43.501D | Poisoning by unspecified antipsychotics and neuroleptics, accidental (unintentional), subsequent encounter |
| T43.502A | Poisoning by unspecified antipsychotics and neuroleptics, intentional self-harm, initial encounter |
| T43.502D | Poisoning by unspecified antipsychotics and neuroleptics, intentional self-harm, subsequent encounter |
| T43.503A | Poisoning by unspecified antipsychotics and neuroleptics, assault, initial encounter |
| T43.503D | Poisoning by unspecified antipsychotics and neuroleptics, assault, subsequent encounter |
| T43.504A | Poisoning by unspecified antipsychotics and neuroleptics, undetermined, initial encounter |
| T43.504D | Poisoning by unspecified antipsychotics and neuroleptics, undetermined, subsequent encounter |
| T43.505A | Adverse effect of unspecified antipsychotics and neuroleptics, initial encounter |
| T43.505D | Adverse effect of unspecified antipsychotics and neuroleptics, subsequent encounter |
| T43.506A | Underdosing of unspecified antipsychotics and neuroleptics, initial encounter |
| T43.506D | Underdosing of unspecified antipsychotics and neuroleptics, subsequent encounter |
| T43.591A | Poisoning by other antipsychotics and neuroleptics, accidental (unintentional), initial encounter |
| T43.591D | Poisoning by other antipsychotics and neuroleptics, accidental (unintentional), subsequent encounter |
| T43.592A | Poisoning by other antipsychotics and neuroleptics, intentional self-harm, initial encounter |
| T43.592D | Poisoning by other antipsychotics and neuroleptics, intentional self-harm, subsequent encounter |
| T43.593A | Poisoning by other antipsychotics and neuroleptics, assault, initial encounter |
| T43.593D | Poisoning by other antipsychotics and neuroleptics, assault, subsequent encounter |
| T43.594A | Poisoning by other antipsychotics and neuroleptics, undetermined, initial encounter |
| T43.594D | Poisoning by other antipsychotics and neuroleptics, undetermined, subsequent encounter |
| T43.595A | Adverse effect of other antipsychotics and neuroleptics, initial encounter |
| T43.595D | Adverse effect of other antipsychotics and neuroleptics, subsequent encounter |
| T43.596A | Underdosing of other antipsychotics and neuroleptics, initial encounter |
| T43.596D | Underdosing of other antipsychotics and neuroleptics, subsequent encounter |
| T43.601A | Poisoning by unspecified psychostimulants, accidental (unintentional), initial encounter |
| T43.601D | Poisoning by unspecified psychostimulants, accidental (unintentional), subsequent encounter |
| T43.602A | Poisoning by unspecified psychostimulants, intentional self-harm, initial encounter |
| T43.602D | Poisoning by unspecified psychostimulants, intentional self-harm, subsequent encounter |
| T43.603A | Poisoning by unspecified psychostimulants, assault, initial encounter |
| T43.603D | Poisoning by unspecified psychostimulants, assault, subsequent encounter |
| T43.604A | Poisoning by unspecified psychostimulants, undetermined, initial encounter |
| T43.604D | Poisoning by unspecified psychostimulants, undetermined, subsequent encounter |
| T43.605A | Adverse effect of unspecified psychostimulants, initial encounter |
| T43.605D | Adverse effect of unspecified psychostimulants, subsequent encounter |
| T43.606A | Underdosing of unspecified psychostimulants, initial encounter |
| T43.606D | Underdosing of unspecified psychostimulants, subsequent encounter |
| T43.611A | Poisoning by caffeine, accidental (unintentional), initial encounter |
| T43.611D | Poisoning by caffeine, accidental (unintentional), subsequent encounter |
| T43.612A | Poisoning by caffeine, intentional self-harm, initial encounter |
| T43.612D | Poisoning by caffeine, intentional self-harm, subsequent encounter |
| T43.613A | Poisoning by caffeine, assault, initial encounter |
| T43.613D | Poisoning by caffeine, assault, subsequent encounter |
| T43.614A | Poisoning by caffeine, undetermined, initial encounter |
| T43.614D | Poisoning by caffeine, undetermined, subsequent encounter |
| T43.615A | Adverse effect of caffeine, initial encounter |
| T43.615D | Adverse effect of caffeine, subsequent encounter |
| T43.616A | Underdosing of caffeine, initial encounter |
| T43.616D | Underdosing of caffeine, subsequent encounter |
| T43.621A | Poisoning by amphetamines, accidental (unintentional), initial encounter |
| T43.621D | Poisoning by amphetamines, accidental (unintentional), subsequent encounter |
| T43.622A | Poisoning by amphetamines, intentional self-harm, initial encounter |
| T43.622D | Poisoning by amphetamines, intentional self-harm, subsequent encounter |
| T43.623A | Poisoning by amphetamines, assault, initial encounter |
| T43.623D | Poisoning by amphetamines, assault, subsequent encounter |

| ICD-10 Codes | Description |
|---|---|
| T43.624A | Poisoning by amphetamines, undetermined, initial encounter |
| T43.624D | Poisoning by amphetamines, undetermined, subsequent encounter |
| T43.625A | Adverse effect of amphetamines, initial encounter |
| T43.625D | Adverse effect of amphetamines, subsequent encounter |
| T43.626A | Underdosing of amphetamines, initial encounter |
| T43.626D | Underdosing of amphetamines, subsequent encounter |
| T43.631A | Poisoning by methylphenidate, accidental (unintentional), initial encounter |
| T43.631D | Poisoning by methylphenidate, accidental (unintentional), subsequent encounter |
| T43.632A | Poisoning by methylphenidate, intentional self-harm, initial encounter |
| T43.632D | Poisoning by methylphenidate, intentional self-harm, subsequent encounter |
| T43.633A | Poisoning by methylphenidate, assault, initial encounter |
| T43.633D | Poisoning by methylphenidate, assault, subsequent encounter |
| T43.634A | Poisoning by methylphenidate, undetermined, initial encounter |
| T43.634D | Poisoning by methylphenidate, undetermined, subsequent encounter |
| T43.635A | Adverse effect of methylphenidate, initial encounter |
| T43.635D | Adverse effect of methylphenidate, subsequent encounter |
| T43.636A | Underdosing of methylphenidate, initial encounter |
| T43.636D | Underdosing of methylphenidate, subsequent encounter |
| T43.691A | Poisoning by other psychostimulants, accidental (unintentional), initial encounter |
| T43.691D | Poisoning by other psychostimulants, accidental (unintentional), subsequent encounter |
| T43.692A | Poisoning by other psychostimulants, intentional self-harm, initial encounter |
| T43.692D | Poisoning by other psychostimulants, intentional self-harm, subsequent encounter |
| T43.693A | Poisoning by other psychostimulants, assault, initial encounter |
| T43.693D | Poisoning by other psychostimulants, assault, subsequent encounter |
| T43.694A | Poisoning by other psychostimulants, undetermined, initial encounter |
| T43.694D | Poisoning by other psychostimulants, undetermined, subsequent encounter |
| T43.695A | Adverse effect of other psychostimulants, initial encounter |
| T43.695D | Adverse effect of other psychostimulants, subsequent encounter |
| T43.696A | Underdosing of other psychostimulants, initial encounter |
| T43.696D | Underdosing of other psychostimulants, subsequent encounter |
| T43.8X1A | Poisoning by other psychotropic drugs, accidental (unintentional), initial encounter |
| T43.8X1D | Poisoning by other psychotropic drugs, accidental (unintentional), subsequent encounter |
| T43.8X2A | Poisoning by other psychotropic drugs, intentional self-harm, initial encounter |
| T43.8X2D | Poisoning by other psychotropic drugs, intentional self-harm, subsequent encounter |
| T43.8X3A | Poisoning by other psychotropic drugs, assault, initial encounter |
| T43.8X3D | Poisoning by other psychotropic drugs, assault, subsequent encounter |
| T43.8X4A | Poisoning by other psychotropic drugs, undetermined, initial encounter |
| T43.8X4D | Poisoning by other psychotropic drugs, undetermined, subsequent encounter |
| T43.8X5A | Adverse effect of other psychotropic drugs, initial encounter |
| T43.8X5D | Adverse effect of other psychotropic drugs, subsequent encounter |
| T43.8X6A | Underdosing of other psychotropic drugs, initial encounter |
| T43.8X6D | Underdosing of other psychotropic drugs, subsequent encounter |
| T43.91XA | Poisoning by unspecified psychotropic drug, accidental (unintentional), initial encounter |
| T43.91XD | Poisoning by unspecified psychotropic drug, accidental (unintentional), subsequent encounter |
| T43.92XA | Poisoning by unspecified psychotropic drug, intentional self-harm, initial encounter |
| T43.92XD | Poisoning by unspecified psychotropic drug, intentional self-harm, subsequent encounter |
| T43.93XA | Poisoning by unspecified psychotropic drug, assault, initial encounter |
| T43.93XD | Poisoning by unspecified psychotropic drug, assault, subsequent encounter |
| T43.94XA | Poisoning by unspecified psychotropic drug, undetermined, initial encounter |
| T43.94XD | Poisoning by unspecified psychotropic drug, undetermined, subsequent encounter |
| T43.95XA | Adverse effect of unspecified psychotropic drug, initial encounter |
| T43.95XD | Adverse effect of unspecified psychotropic drug, subsequent encounter |
| T43.96XA | Underdosing of unspecified psychotropic drug, initial encounter |
| T43.96XD | Underdosing of unspecified psychotropic drug, subsequent encounter |
| T45.0X1A | Poisoning by antiallergic and antiemetic drugs, accidental (unintentional), initial encounter |
| T45.0X1D | Poisoning by antiallergic and antiemetic drugs, accidental (unintentional), subsequent encounter |
| T45.0X2A | Poisoning by antiallergic and antiemetic drugs, intentional self-harm, initial encounter |
| T45.0X2D | Poisoning by antiallergic and antiemetic drugs, intentional self-harm, subsequent encounter |

| ICD-10 Codes | Description |
|---|---|
| T45.0X3A | Poisoning by antiallergic and antiemetic drugs, assault, initial encounter |
| T45.0X3D | Poisoning by antiallergic and antiemetic drugs, assault, subsequent encounter |
| T45.0X4A | Poisoning by antiallergic and antiemetic drugs, undetermined, initial encounter |
| T45.0X4D | Poisoning by antiallergic and antiemetic drugs, undetermined, subsequent encounter |
| T45.0X5A | Adverse effect of antiallergic and antiemetic drugs, initial encounter |
| T45.0X5D | Adverse effect of antiallergic and antiemetic drugs, subsequent encounter |
| T45.0X6A | Underdosing of antiallergic and antiemetic drugs, initial encounter |
| T45.0X6D | Underdosing of antiallergic and antiemetic drugs, subsequent encounter |
| T46.0X1A | Poisoning by cardiac-stimulant glycosides and drugs of similar action, accidental (unintentional), initial encounter |
| T46.0X1D | Poisoning by cardiac-stimulant glycosides and drugs of similar action, accidental (unintentional), subsequent encounter |
| T46.0X2A | Poisoning by cardiac-stimulant glycosides and drugs of similar action, intentional self-harm, initial encounter |
| T46.0X2D | Poisoning by cardiac-stimulant glycosides and drugs of similar action, intentional self-harm, subsequent encounter |
| T46.0X3A | Poisoning by cardiac-stimulant glycosides and drugs of similar action, assault, initial encounter |
| T46.0X3D | Poisoning by cardiac-stimulant glycosides and drugs of similar action, assault, subsequent encounter |
| T46.0X4A | Poisoning by cardiac-stimulant glycosides and drugs of similar action, undetermined, initial encounter |
| T46.0X4D | Poisoning by cardiac-stimulant glycosides and drugs of similar action, undetermined, subsequent encounter |
| T46.0X5A | Adverse effect of cardiac-stimulant glycosides and drugs of similar action, initial encounter |
| T46.0X5D | Adverse effect of cardiac-stimulant glycosides and drugs of similar action, subsequent encounter |
| T46.0X6A | Underdosing of cardiac-stimulant glycosides and drugs of similar action, initial encounter |
| T46.0X6D | Underdosing of cardiac-stimulant glycosides and drugs of similar action, subsequent encounter |
| T50.901A | Poisoning by unspecified drugs, medicaments and biological substances, accidental (unintentional), initial encounter |
| T50.901D | Poisoning by unspecified drugs, medicaments and biological substances, accidental (unintentional), subsequent encounter |
| T50.902A | Poisoning by unspecified drugs, medicaments and biological substances, intentional self-harm, initial encounter |
| T50.902D | Poisoning by unspecified drugs, medicaments and biological substances, intentional self-harm, subsequent encounter |
| T50.903A | Poisoning by unspecified drugs, medicaments and biological substances, assault, initial encounter |
| T50.903D | Poisoning by unspecified drugs, medicaments and biological substances, assault, subsequent encounter |
| T50.904A | Poisoning by unspecified drugs, medicaments and biological substances, undetermined, initial encounter |
| T50.904D | Poisoning by unspecified drugs, medicaments and biological substances, undetermined, subsequent encounter |
| T50.905A | Adverse effect of unspecified drugs, medicaments and biological substances, initial encounter |
| T50.905D | Adverse effect of unspecified drugs, medicaments and biological substances, subsequent encounter |
| T50.906A | Underdosing of unspecified drugs, medicaments and biological substances, initial encounter |
| T50.906D | Underdosing of unspecified drugs, medicaments and biological substances, subsequent encounter |
| T50.991A | Poisoning by other drugs, medicaments and biological substances, accidental (unintentional), initial encounter |
| T50.991D | Poisoning by other drugs, medicaments and biological substances, accidental (unintentional), subsequent encounter |
| T50.992A | Poisoning by other drugs, medicaments and biological substances, intentional self-harm, initial encounter |
| T50.992D | Poisoning by other drugs, medicaments and biological substances, intentional self-harm, subsequent encounter |
| T50.993A | Poisoning by other drugs, medicaments and biological substances, assault, initial encounter |
| T50.993D | Poisoning by other drugs, medicaments and biological substances, assault, subsequent encounter |
| T50.994A | Poisoning by other drugs, medicaments and biological substances, undetermined, initial encounter |
| T50.994D | Poisoning by other drugs, medicaments and biological substances, undetermined, subsequent encounter |
| T50.995A | Adverse effect of other drugs, medicaments and biological substances, initial encounter |

| ICD-10 Codes | Description |
|---|---|
| T50.995D | Adverse effect of other drugs, medicaments and biological substances, subsequent encounter |
| T50.996A | Underdosing of other drugs, medicaments and biological substances, initial encounter |
| T50.996D | Underdosing of other drugs, medicaments and biological substances, subsequent encounter |
| Z71.51* | Drug abuse counseling and surveillance of drug abuser |
| Z79.891* | Long term (current) use of opiate analgesic |
| Z79.899 | Other long term (current) drug therapy |
| Z91.120 | Patient's intentional underdosing of medication regimen due to financial hardship |
| Z91.128 | Patient's intentional underdosing of medication regimen for other reason |
| Z91.130 | Patient's unintentional underdosing of medication regimen due to age-related debility |
| Z91.138 | Patient's unintentional underdosing of medication regimen for other reason |
| Z91.14 | Patient's other noncompliance with medication regimen |
| Z91.19 | Patient's noncompliance with other medical treatment and regimen |

**Group 2 Medical Necessity ICD-10 Codes Asterisk Explanation: *** Physicians are to select the most appropriate diagnosis code. Labs are not to prepopulate requisition forms with diagnosis codes.

*Use ICD-10- CM code Z71.51 as the primary diagnosis and the specific drug dependence diagnosis as the secondary diagnosis.

*Use ICD-10-M code Z79.891 for COT monitoring.

ICD-10 Codes that DO NOT Support Medical Necessity
**Group 1 Paragraph:** All those not listed under the "ICD-10 Codes that Support Medical Necessity" section of this policy.

**Group 1 Codes:** N/A

ICD-10 Additional Information

Back to Top

# General Information

Associated Information
**Documentation Requirements**

1. All documentation must be maintained in the patient's medical record and made available to the contractor upon request.

2. Every page of the record must be legible and include appropriate patient identification information (e.g., complete name, dates of service(s)). The documentation must include the legible signature of the physician or non-physician practitioner responsible for and providing the care to the patient.

3. The submitted medical record must support the use of the selected ICD-10-CM code(s). The submitted CPT/HCPCS code must describe the service performed.

4. The medical record documentation must support the medical necessity of the services as directed in this policy.

5. Medical record documentation (e.g., history and physical, progress notes) maintained by the ordering physician/treating physician must indicate the medical necessity for performing a qualitative drug test. All tests must be ordered in writing by the treating provider and all drugs/drug classes to be tested must be indicated in the order.

6. When a definitive/quantitative test is performed, the record must show that an inconsistent positive finding was noted on the presumptive testing or that there was no available, commercially or otherwise, presumptive test except when not medically necessary to perform presumptive testing in the COT patient subset.

7. If the provider of the service is other than the ordering/referring physician, that provider must maintain hard copy documentation of the lab results, along with copies of the ordering/referring physician's order for the test. The physician must include the clinical indication/medical necessity in the order for the test.

**Utilization Guidelines**

In accordance with CMS Ruling 95-1 (V), utilization of these services should be consistent with locally acceptable standards of practice.

1. The contractor will consider presumptive UDT testing in excess of 12 per Calendar year not reasonable and necessary.

   **NOTE:** An exception to the above limitation will be made when patients have documented diagnoses consistent with a substance abuse disorder (SUD), for which patients presumptive UDT shall not occur more than 3 times within a seven-day period, based upon the following guidelines for monitoring abstinence.
   a. For patients with 0 to 30 consecutive days of abstinence, presumptive UDT is expected at a frequency of 1 to 3 presumptive UDT per week. More than 3 presumptive panels in one week is not reasonable and necessary and is not covered by Medicare.
   b. For patients with 31 to 90 consecutive days of abstinence, presumptive UDT is expected at a frequency of 1 to 3 UDT per week. More than 3 presumptive UDT in one week is not reasonable and necessary and is not be covered by Medicare.
   c. For patients with > 90 consecutive days of abstinence, presumptive UDT is expected at a frequency of 1 to 3 UDT in one month. More than 3 physician-directed UDT in one month is not reasonable and necessary and is not covered by Medicare.
   d. The contractor will only pay for one presumptive UDT test per patient per date of service regardless of the number of billing providers.

   e. For chronic opioid therapy (COT), the contractor will consider up to 12 definitive tests (i.e., definitive UDT) per Calendar year reasonable and necessary. This would correspond to random testing performed 1-3 times every 3 months for prescribed medications, non-prescribed medications that may pose a safety risk if mixed with prescribed and illicit substances based on patient history, clinical presentation or community usage.

Sources of Information and Basis for Decision
**Contractor is not responsible for the continued viability of websites listed.**

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Other Contractor Policies

Contractor Medical Directors

JL ICD-9 LCD L32050, Qualitative Drug Testing

Original JH ICD-9 Source LCD L34352, Qualitative Drug Testing

Back to Top

# Revision History Information

Please note: Most Revision History entries effective on or before 01/24/2013 display with a Revision History Number of "R1" at the bottom of this table. However, there may be LCDs where these entries will display as a separate and distinct row.

| Revision History Date | Revision History Number | Revision History Explanation | Reason(s) for Change |
|---|---|---|---|
| 01/01/2016 | R8 | LCD revised and published on 02/19/16 effective for dates of service on or after 01/01/2016. New CPT/HCPCS codes added to the LCD on 12/31/15 in response to the 2016 annual CPT/HCPCS update have been placed into the appropriate CPT/HCPCS group 1 and group 2 coding sections. Language in CPT/HCPCS Group 1 Paragraph that was added on 12/31/15 has been deleted. Please refer to revision history R7 for detailed information regarding the code changes. | • Revisions Due To CPT/HCPCS Code Changes |
| 12/31/2015 | R7 | | |

| Revision History Date | Revision History Number | Revision History Explanation | Reason(s) for Change |
|---|---|---|---|
| | | 12/31/15 LCD revised to add the following ICD-10-CM codes to the ICD-10 code group 1 and group 2 as covered diagnoses: Z71.51*; Z91.120; Z91.128; Z91.130; Z91.138; Z91.14; Z91.19; Z79.891; Z79.899 effective for dates of service on and after 12/31/15. The following CPT/HCPCS codes have been added to the CPT/HCPCS code group 1 paragraph and will become group 1 codes effective for dates of service on or after 01/01/2016 to reflect the 2016 annual CPT/HCPCS update; G0477; G0478 and G0479. The following CPT/HCPCS codes will be deleted from the CPT?HCPCS code group 1 effective for dates of service on or after 01/01/2016 as a result of the 2016 annual code update; G0431 and G0434. The following CPT/HCPCS codes have been added to the group 1 paragraph and will become group 2 codes effective for dates of service on or after 01/01/2016 to reflect the 2016 annual CPT/HCPCS update; G04080; G0481; G0482 and G0483. The following CPT/HCPCS codes will be deleted from the CPT/HCPCS group 2 (currently listed in the group 1 paragraph) effective for dates of service on or after 01/01/2016 as a result of the 2016 annual code update; G6030; G6031; G6032; G6034; G6036; G6037; G6040; G6041; G6042; G6043; G6044; G6045; G6046; G6048; G6051; G6052; G6053; G6056; G6057; G6058. | • Revisions Due To CPT/HCPCS Code Changes<br>• Other (Inquiry) |
| 12/31/2015 | R6 | LCD posted for notice on 11/05/2015 to become effective 12/31/2015.<br><br>05/14/2015 Draft LCD posted for comment. | • Creation of Uniform LCDs With Other MAC Jurisdiction |
| 10/01/2015 | R5 | LCD revised and published 10/29/2015 to add additional ICD-10 codes with higher specificity effective for dates of service 10/01/2015 and after. | • Other (Clarification) |
| 10/01/2015 | R4 | LCD published 01/23/2015 to correct the publication date of the annual CPT/HCPCS code updates incorrectly listed as 01/22/2015 in revision history below. The code updates remain as listed in the revision history below. | • Typographical Error |
| 10/01/2015 | R3 | LCD revised and published on 01-22-2015 to reflect the annual CPT/HCPCS code updates. CPT/HCPCS codes 80100, 80101, and 80102 have been deleted and therefore have been removed from the LCD. | • Revisions Due To CPT/HCPCS Code Changes |
| 10/01/2015 | R2 | LCD revised and published on 09/11/2014 to add ICD-10 diagnosis code Z71.51 to the covered diagnosis listing with an asterisk. Asterisks added to diagnosis codes Z79.891 and Z79.899. Asterisk explanation paragraph inserted for the above diagnosis codes. | • Other (Clarification) |
| 10/01/2015 | R1 | LCD revised to accommodate provider commentary on the relationship between qualitative and quantitative methods of urine drug testing effective for dates of service on or after 10/01/2014 (LCD updated 06/06/2014) | • Reconsideration Request |

Back to Top

# Associated Documents

Attachments N/A

Related Local Coverage Documents N/A

Related National Coverage Documents N/A

Public Version(s) Updated on 02/12/2016 with effective dates 01/01/2016 - N/A Updated on 12/23/2015 with effective dates 12/31/2015 - 12/31/2015 Updated on 10/30/2015 with effective dates 12/31/2015 - N/A Updated on 10/23/2015 with effective dates 10/01/2015 - 12/30/2015 Updated on 01/13/2015 with effective dates 10/01/2015 - N/A Updated on 01/12/2015 with effective dates 10/01/2015 - N/A Updated on 09/02/2014 with effective dates 10/01/2015 - N/A Updated on 06/07/2014 with effective dates 10/01/2015 - N/A Updated on

# Keywords

N/A Read the **LCD Disclaimer** Back to Top

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Focused Review

# Prevention of Opioid Abuse in Chronic Non-Cancer Pain: An Algorithmic, Evidence Based Approach

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**Background:** The use of opioids for chronic non-cancer pain has grown exponentially in the last 15 years. Associated with that, dramatic increases in abuse and overdose deaths from opioid use have been noted.

**Objectives:** Most opioid abuse stems from legitimate prescriptions, putting the onus on prescribers to use opioids responsibly for chronic pain. Very little evidence-based guidance exists for those who wish to prescribe opioids for legitimate chronic pain and at the same time prevent opioid abuse.

**Methods:** A review of literature was performed for articles focused on guidelines for opioid use when prescribed for chronic pain, opioid abuse, and overdose, strategies to detect and prevent abuse of opioids, urine drug screens (UDS) in chronic pain settings, prescription monitoring programs (PMP), and the relationship between opioid dosing and abuse.

**Results:** Based on the existing literature, an evidence-based algorithmic approach was developed to decrease opioid abuse in the chronic pain environment. The pillars of prevention are the screening of patients into high, medium, and low risk categories using screening tools; monitoring patients using UDS, PMP, and pill counts, and lastly, dose limitations.

**Conclusion:** This algorithmic approach may enable physicians to prescribe opioids for patients with chronic pain and also to reduce opioid abuse.

**Key words:** Opioids, chronic pain, abuse, prescription, overdose, deaths, overdose deaths, urine drug screens, prescription monitoring programs, opioid dose, screening, monitoring

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The use of opioids has gained universal acceptance in the treatment of acute pain and cancer pain. The use of opioids for chronic non-cancer pain, however, remains controversial. In the last 15 years, there has been a dramatic upsurge in the use of opioids for chronic pain, even though the evidence in support of this practice has not kept up with the increase in the number of prescriptions. Although the use of opioids for chronic non-cancer pain has resulted in an increase in the quality of life and decrease in pain for some, there has been an unacceptable increase in opioid abuse and opioid-related deaths. Most of the abuse and deaths are from legally prescribed opioids. This predicament calls for responsible prescribing by the physician community, and the need for serious and earnest effort to decrease abuse. Prescribers need do this, however, without compromising availability of opioids to those who benefit from them.

## Scope of the Problem

The abuse of prescription opioids has escalated at such an alarming rate that many now consider it an epidemic. It has been reported that the United States consumes 83% of the global supply of oxycodone, and 99% of the hydrocodone supply, despite the fact its population is only 4.6% of the world's population (1-13). In 2010, enough opioids were sold to medicate every American adult with an equivalent dose of 5 mg of hydrocodone every 4 hours for one month (14). In 2008, 2.17 million Americans used pain relievers in an illicit manner; a number close to those using marijuana (2.20 million) and much higher than those using cocaine (722,000) (14). Since 2003, deaths in the United States from drug overdose for whites have exceeded age-adjusted deaths among African Americans. In 2007, the number of deaths involving prescription opioids was 9.3 times the number involving cocaine and 5.38 times the number involving heroin (1). These deaths were more than those from cocaine and heroin combined. It has been shown that from 1997 through 2007, there was a seven fold increase in the number of prescriptions for opioids. This paralleled closely with the increase in deaths due to opioid overdose (15). There were 14,800 opioid overdose deaths in 2008, as compared to less than 2,000, in 1997. In 2008, deaths attributable solely to prescription opioids constituted approximately 73% of all deaths associated with drug-related overdoses (2). This increase in unintentional drug overdose deaths has been directly credited to the increased use of prescription opioids (1,14,15). We must be cognizant that each death represents just the tip of the iceberg and that there is ample abuse lurking beneath it. For every unintentional overdose death related to an opioid analgesic, 9 patients are admitted for substance abuse treatment, 35 visit emergency departments, 161 report drug abuse or dependence, and as many as 461 patients report the nonmedical use of opioid analgesics (2). During the years 1999–2008, prescription opioid sales, emergency department admissions for substance abuse treatment related to prescription opioids, and mortality rates due to opioid overdose all increased at similar rates (14). Sales of prescription opioids in 2010 were 4 times those in 1999 (14). The Treatment Episode Data Set Report (16) found that substance abuse treatment admissions that reported any opioid abuse increased more than fourfold between 1998 and 2008, from 2.2 to 9.8%. A separate report indicated that the substance abuse treatment admission rate in 2009 was almost 6 times the rate in 1999 (14). The nonmedical use of opioids costs insurance companies up to $72.5 billion annually in health care costs (17). According to another report, total US societal costs of prescription opioid abuse were estimated at $55.7 billion in 2007. Workplace costs accounted for $25.6 billion (46%), health care costs accounted for $25 billion (45%), and criminal justice costs accounted for $5.1 billion (9%) (18).

## Source of Opioids Used Illicitly

More than half of those who used opioids illicitly obtained them free of cost either from a relative or a friend; 14% bought the drugs from them and 5% stole the drugs from them. Only 18% got prescriptions from a physician. In other words, about 83% of those who used opioids in an illicit manner had access to them because of a legitimately written prescription. Moreover, 81% of those who obtained the opioids free of cost revealed that their sources had obtained these drugs through a single prescriber. Only 4% paid a drug dealer or a stranger for the medication. Only 5% obtained them by writing a fake prescription, stealing from a doctor's office/clinic/hospital/pharmacy or described their source as "some other way" (1). According to a report by the Centers for Disease Control and Prevention, 76% of nonmedical users report getting drugs that had been prescribed to someone else, while only 20% report that they acquired the drug from their own doctor (2). Furthermore, among persons who died of opioid overdoses, a significant proportion did not have a prescription in their records for the opioid that killed them. In West Virginia, Utah, and Ohio, 25%–66% of those who died of pharmaceutical overdoses used opioids originally prescribed to someone else (2). Hall et al (19) reported that 63% of overdose deaths were from pharmaceutical diversion and 21% were from doctor shopping, meaning that at least 84% of the deaths were from legally prescribed opioids. This data implies that not only is personal abuse a major concern, but that diversion of prescribed opioids deserves equal attention. Drug dealers are no longer the primary source of illicit drugs. It appears that the greatest enemy is now the diversion of drugs from family and friends -- drugs procured from one physician and not from doctor shopping (20).

## How Did It Become An Epidemic?

In the late nineteenth- and early twentieth-century, opioids were used extensively in medicine, even for non-pain conditions such as respiratory problems, anxiety, gynecological conditions, bloating, and many

others. This led to the widespread abuse of opioids and resulted in a public health emergency. Congress in 1912 passed a law severely limiting the use of opioids. Following that, opioids were used very conservatively (21) and perhaps even too cautiously. This changed in the late 1990s with the introduction of long-acting opioid formulations (22). The pharmaceutical industry aggressively marketed long-acting opioids (20-24) for chronic pain relying on 2 erroneous facts:

- That medical management with opioids is the recommended solution for undertreated chronic pain
- That the use of long-acting formulations decreases incidences of prescription opioid abuse.

Aggressive marketing by pharmaceutical companies using "paid consultant" physicians (some of whom did not have formal chronic pain management training and some of whom were non physicians), along with the endorsements of major pain societies, resulted in a reconsideration of then current practices by the state medical boards. The principles of opioid management in acute pain and cancer pain were transferred to the chronic pain arena. This culminated in the embracing of this class of drugs by practicing physicians who wanted to provide relief to their chronic pain patients. According to one study, data from 1990 to 1996 (a phase before the aggressive push for use of opioids for chronic pain), show that during this time period, there was a 22% increase in the medical use of oxycodone and interestingly, a 29% decrease in oxycodone-related emergency department visits (25). The authors concluded that increased opioid use is not associated with deleterious health consequences. The article, in fact, was published in 2000 (during the onset of the epidemic), thus giving the false impression that increased opioid use was not associated with increased abuse. But when similar data were examined by the same group for 1997-2002, there was a 402% increase in the medical use of oxycodone and a 226% increase in fentanyl (26). It is to be noted that during this period, physicians had undergone a significant change in their outlook regarding pain management and were aggressively treating chronic non-cancer pain using opioids. Correspondingly, there was a 1000% and 381% increase in opioid-related emergency department visits; 1,000% for fentanyl and 381% for oxycodone. This group concluded that even though there was an increase in abuse, it did not interfere with legitimate practice (26)! As reported by the Milwaukee Journal Sentinel, this group received funding from the pharmaceutical industry. Approximately two-thirds of the panel responsible for writing guidelines for the use of opioids for chronic pain for the American Academy of Pain Medicine (AAPM) and American Pain Society (APS) had conflicts of interest with the opioid pharmaceutical industry (27-31). These guidelines, while addressing issues like dose escalations, high dose opioid therapy, breakthrough pain, and upward titration of opioids, do not address the issues of dramatic increases in overdoses, deaths, addiction, and costs associated with the increased use of opioids. The investigation announced by the Senate in reference to conflicts of interest in preparation of opioid guidelines and promotion of opioid usage, have resulted in abandonment of the American Pain Foundation on May 10, 2012, which was a pivotal organization in promoting opioid use (32).

## Effectiveness of Opioids in Chronic Pain

The long-term improvement of pain scores and functionality with the use of opioids for chronic pain has been scrutinized by many organizations. A recent review of the literature by Manchikanti et al (33) suggested that, based on the lack of literature supporting the use of opioids for chronic pain, opioids should be used with great restraint and caution. A review of the literature by Kuijpers et al (34) showed that there was poor evidence that opioids were better than a placebo in relieving pain and improving function. They also reported that there was poor evidence that opioids were not superior to nonsteroidal anti-inflammatory drugs (NSAIDS) in relieving pain and improving function. Guidelines by APS and AAPM (27) also suggest that the evidence of effectiveness of opioids for chronic pain is limited, and yet a consensus is provided for the use of opioids. Chou et al (35) also expressed concern that the review of the literature used to formulate the clinical practice guideline for APS and AAPM revealed a lack of effective studies on the long-term benefits and harm of opioids for chronic pain. A Cochrane review (36) of the long-term use of opioids for chronic non-cancer pain showed that there is weak evidence that those who use them long-term experience clinically significant pain relief, and that there was inconclusive evidence that the quality of life or functioning improves. Pinto et al (37) have evaluated the efficacy of opioids for patients with sciatica and concluded that the clinical trials were of low quality and the efficacy and tolerability of these drugs were unclear. An analysis of the literature regarding pharmacological management for low back pain by White et al (38) concluded that opioids have

similar efficacy as NSAIDS, but have more side effects. Franklin et al (39) followed injured workers for one year. They found that despite a 62% increase in opioid doses over a 12 month period (from 26 mg morphine equivalent dose [MED] in the first quarter to 42 mg in the fourth quarter), improvement in pain and function was seen only in 27% and 16% of the patients. In concurrence with Franklin et al (39), multiple other authors have illustrated deleterious consequences of early or continued opioid use for chronic pain, including adverse consequences of dependence, hyperalgesia, and an association between opioid prescribing and overall health status, with increased disability, medical costs, subsequent surgery, and continued or late opioid use (1,39-56).

## Call For Responsible Prescribing

The annual US expenditures related to pain (including direct medical costs and lost wages) are higher than those for cancer, heart disease, and diabetes combined (20). The improvements in the emotional and economic impact of untreated chronic pain are often the criteria by which pain management physicians measure the success of a treatment modality. But the notion that aggressive use of opioids in trying to alleviate chronic non-cancer pain would result in improvement of function (let alone improvement in pain) has been proven erroneous. Despite a cavalier approach to the prescription of opioids in the last decade, numerous studies have shown a consistent lack of evidence that opioids decreased pain, improved function, or decreased health care costs (27,33-39). On the contrary, there is now an abundance of evidence that this aggressive approach has harmed individuals and society and has had a negative economic impact (1,14-18,23,57-87). Gomes et al's study (57) reports that the overall death rate for patients receiving opioids was 10 times higher than those not on opioids, suggesting possible harm. Eriksen et al (23) have shown that patients on opioids report higher pain scores, poor self-rated health, not being engaged in employment, higher use of the health care system, and a negative influence on quality of life. Although pharmacists, state medical boards, and other agencies and professionals play a role in curbing abuse, the primary onus is on the prescribing physician. Since the vast majority of opioid overdose deaths from opioids stem from legitimate prescriptions, calls for responsible prescribing by physicians have been made (88-94). Given that 3% of physicians accounted for 62% of the opioids prescribed in one study (61), the proliferation of high-volume prescribers can have a large impact on the use of opioids and overdose death rates (14).

For controlling acute pain and cancer pain, opioids have been shown to be quite effective. Most of the evidence for prescribing opioids comes from studies of their use in these settings. In such scenarios, other medications, namely NSAIDs, muscle relaxants, antidepressants, and anticonvulsants are not as effective and are used, if at all, in a supplementary role. However, extrapolating these results from acute pain studies to guide managing chronic non-cancer pain may not be a wise step. Opioids have a very important role in chronic pain management and their value should not be underestimated. Unlike other analgesics, opioids do not result in organ toxicity, nor is there any ceiling dose associated with their use. Opioids have, thus, become the mainstay and play a vital role but they are not a panacea for chronic pain. In order to maximize their efficacy, opioids should be used with great restraint and caution and in carefully selected patients as recommended by American Society of Interventional Pain Physicians guidelines (62). According to one study, there is evidence that opioids are being used with the wrong patients (63). We concur with Manchikanti et al (20) that the most underappreciated issue in modern medicine is the adverse consequences of appropriately prescribed opioids, with all the blame diverted to abuses and overuses.

There are 3 types of patients that we should be cautious about: the first is the abuser; the second is the one who is involved in diversion; and, the third is the patient who is a combination of the two. The cornerstones for responsible opioid use for balancing pain relief along with curbing abuse and diversion are:

- Careful patient screening to stratify patients into different risk groups for opioid abuse/diversion
- Monitoring patients to ensure compliance for the responsible use of opioids
- Establishing and adhering to dose limitations.

## Screening Patients

The need for effective screening tools was expressed as early as 2001 (64,65). A decade later we are still looking for a tool that is universally acceptable. Guidelines from AAPM and APS (27) state that risk stratification is an undeveloped skill for many physicians prescribing opioids and that these physicians should be more knowledgeable in this area. There are many screening tools that currently exist which are specifically designed for prescription opioid abuse. Solanki et al (66) reviewed all the available screening tools and con-

cluded that there was no single screening tool that can be applied universally. Chou et al (35) analyzed tools that were specific for prescription opioids and based on their criteria found that most of the studies evaluating the screening tools had methodological flaws. However, screening tools may play an important role in curbing abuse. The failure to utilize existing tools so as to find the perfect tool seems counterproductive in this environment. The question remains: Which is the best existing tool? The tools we find useful are the Screener and Opioid Assessment for Patients with Pain (SOAPP) (67), Pain Medication Questionnaire (PMQ) (68,69), Prescription Drug Use Questionnaire patient version (PDUQP) (70), Addiction Behaviors Checklist (ABC) (71), Diagnosis, Intractability, Risk, Efficacy (DIRE) score (72) and the one by Atluri and Sudarshan (73). The screening tool Current Opioid Misuse Measure (COMM) (74) and Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) (75) were not considered because many of the questions were not related to abuse/diversion and fell under the category of psychological queries. The Pain Assessment and Documentation Tool (PADT) (76) is not a screening tool as it addresses the level of analgesia, adverse events, and activities of daily living along with aberrant drug-related behavior. The section of abuse is a small component of the whole tool. The screening tool by Michna et al (77) addressed only 3 items, and is not comprehensive enough to identify abuse. The Opioid Risk Tool (ORT) (78) is a 5-item tool which is also not comprehensive. The items in this tool are not predictors of abuse. PDUQ and PDUQP tools were developed by the same group. PDUQP (70) is a modified, improved version of PDUQ (69) as all the questions are related to abuse, and questions related to psychopathology were eliminated. Among the tools selected, the first 3 tools are subjective (SOAPP, PMQ and PDUQP) and the last 3 are objective tools (DIRE score, ABC checklist and the tool by Atluri and Sudarshan). Although there has been a call for the use of these subjective tools (79-82), abusers tend not be truthful in subjective questionnaires (83-87). The screening tool developed by Wu et al (71), the DIRE Score (72), and the screening tool created by Atluri and Sudarshan (73) may have more value since they incorporate objective measures. These tools can be used singularly or in combination. Generic screening tools for drug and alcohol abuse are not as useful as those specifically designed for prescription opioid abuse. Guidelines developed for opioid use for chronic pain (27,87,88) include recommendations for using screening tools, but with the reservation that risk stratification is currently underutilized (89,90). Classifying patients into high and low risk groups helps tremendously with opioid management and might possibly be one of the cornerstones in abuse prevention. As described below, screening patients into different risk categories determines the frequency of monitoring, aggressiveness of dosage, and frequency of follow-up visits.

## Urine Drug Screens

Currently, urine drug screens (UDS) remain one of the most important tools for detecting inappropriate use of opioids. Although Starrels et al (91) concluded in their review that the evidence in support of the effectiveness of UDS for reducing opioid misuse in chronic pain is relatively weak, they have also noted that based on cross-sectional studies and case series, UDS is a valuable tool for detecting the use of unprescribed drugs and for confirming adherence to prescribed medications with a higher degree of accuracy than when identified by patient self-report or the impression of the treating physician. Starrels et al (91) also suggested that UDS might improve the provider-patient relationship and clinic morale. After a review of the literature regarding the role of UDS and opioids, Christo et al (92) concluded that, "UDS is one of the major tools of adherence monitoring in the assessment of the patient's predisposition to, and patterns of, drug misuse/abuse – a vital first step towards establishing and maintaining the safe and effective use of opioid analgesics in the treatment of chronic pain." Katz et al (93) have shown that using UDS along with monitoring aberrant behaviors enhances abuse detection. In Manchikanti et al's study (94), random UDS reduced illicit drug use in the chronic pain population. In a separate study, Manchikanti et al (95) have shown that by using UDS they could identify a combined use of illicit drugs and the misuse of prescription drugs in 24% of patients on hydrocodone and in 33% of patients receiving methadone (96). The Federation of State Medical Boards has formally included UDS in current guidelines for using opioids in the management of chronic noncancer pain (97). Since there is evidence that UDS have not been universally adopted by physicians treating chronic pain (98,99), the use of UDS must be encouraged. Random UDS may have more value in detecting abuse as patients may change their behavior when expected to be tested (27).

## Prescription Monitoring Programs

Prescription monitoring programs (PMPs) serve as a means of data collection for opioid prescriptions, providing physicians with information about who wrote the prescriptions and the pharmacies that dispensed them. Physicians have access to this data to check if patients are getting opioid prescriptions from more than one physician at the same time. This information becomes extremely useful especially if the patient signs an opioid contract agreeing to obtain the prescription from only one physician and to fill it in only one pharmacy. Currently, there are 38 states with this program (66). A national program would be invaluable in curbing abuse and doctor shopping (100). The National All Schedule Prescription Electronic Reporting Act (NASPER) was enacted by Congress in 2005 but has not yet been fully implemented (101). Calls for immediate funding and rapid implementation of NASPER have been made. This law requires states to collect prescription information for Schedule II, III, and IV medications. It also requires states to have the capability to share this information with one another. This would potentially decrease cross-border opioid trafficking and would be invaluable in curbing abuse and doctor shopping (15,102,103). Paulozzi et al's study (104) recommends using PMP to curb overuse, noting that the rate of overdose deaths is higher in those who use multiple pharmacies and doctors. This assertion is also expressed by White et al (105). In one study, 21% of overdose deaths resulted from doctor shopping (106). In response to the epidemic of prescription drug abuse, the White House Office of National Drug Control Policy issued a document in which it recommended enhanced use of prescription drug monitoring programs (106). The National Alliance for Model State Drug Laws indicates that these databases foster the legitimate medical use of controlled substances while limiting drug abuse and diversion (102). Access to PMP can help clinicians curb diversion and abuse and to decrease the number of unnecessary prescriptions while still providing analgesia to those who need it (102). Manchikanti et al (107) have recently shown that the Kentucky's PMP, KASPER (Kentucky All Schedule Prescription Electronic Reporting Program) has led to a decrease in doctor shopping from 18% in 2001 to 2.1% in 2011. Baehren et al (108) showed that in an emergency department setting, the use of PMP positively influenced the opioid prescribing pattern. Based on the PMP results, 61% of their study patients were prescribed less opioid medication than originally planned, whereas 39% received more opioid medication than previously planned. Paulozzi et al (109) reported that PMPs were not significantly associated with lower rates of drug overdose or opioid overdose mortality or lower rates of consumption of opioid drugs. An accompanying editorial (110) clarified that the lack of impact of PMPs is due to their underutilization.

## A Case for Dose Limitation

The evidence in favor of long-term opioid use for chronic pain is at best problematic. Considering the irrefutable evidence showing widespread abuse and diversion, the rationale for high dose opioids should be reexamined. Patients who do not respond to a low/medium dose of opioids generally would not find their pain alleviated by larger doses. In 2007, the state of Washington issued guidelines that in general, the daily dose should not exceed 120 mg of MED (87). The guidelines by APS and AAPM in 2009 defined high dose as 200 mg MED (27). The Canadian guidelines in 2010 identified 200 mg MED as a watchful dose (88). Until recently, however, there was only limited data verifying the safety of these recommended doses, especially in high risk patients. Five recent studies showed that the rate of overdose was directly proportional to the prescribed opioid dose (57,104,111-113). Bohnert et al's study (111) in a national sample of Veterans Health Administration patients revealed that there was a dose-response relationship between the maximum daily prescribed dose of opioid and the risk of opioid overdose death. The overdose death rate for patients receiving a dose of less than 20 mg MED was 0.11 per 1,000 compared to those getting more than 100 mg MED, for whom the death rate was 1.24/1,000. This difference was even higher in those with a history of substance abuse (0.54 versus 2.97). Since the death rates were higher in patients receiving doses of 50 mg MED versus those getting less than 50 mg MED, the authors concluded that that the risk of opioid overdose increased when the opioid dose was equivalent to 50 mg MED.

Dunn et al (112) reported that in a population from a health maintenance organization in Washington State , there was a 9-fold increase in opioid overdose in patients receiving high dose opioids (more than 100 mg MED) to those getting low dose (less than 20 mg). There was a 3.7-fold increase in overdose events in patients receiving doses between 50-99 mg MED versus those getting less than 20 mg MED. Paulozzi et al (104) found that compared to patients receiving lower opioid doses or no opioid prescriptions, the risk of overdose was greatest at daily opioid doses above 40 mg

MED. Braden et al (113) found that patients (Arkansas Medicaid and HealthCore commercially insured enrollees) receiving MEDs of more than 120 mg/d are more likely to have drug-related encounters than those getting lower doses. There were no differences between these 2 groups regarding emergency department visits. Gomes et al (57) found that patients from Ontario's public drug plan receiving "very high" doses (> 400 mg MED) and "high" doses (200-400 mg MED) had a much higher overdose death than those getting "moderate" doses (< 200 mg MED). In "very high" and "high" dose patients the opioid-related mortality rates were 9.94/1,000 for "very high" and 7.92/1,000 for "high." Comparatively, the opioid-related mortality rate was 1.63/1,000 in those with "moderate" doses. Also, the overall death rate (from any cause) was much higher in patients receiving opioids (20.05/1,000) when compared to those who were not getting any opioids (4.00/1,000).

In the above 5 studies, the doses which are related to an emergency department admission for overdoses or death are 40 mg MED (104), 50 mg MED (111,112), 120 mg MED (113), and 200 mg MED (57). We did not find any study in which a higher dose did not correlate with increased mortality and only one study where there was no correlation between higher opioid dose and emergency department visits. Moreover, Paulozzi et al (15) reported that in 80% of all patients receiving opioids, the dose was less than 100 mg MED and was obtained from one physician. This patient pool constituted 20% of the overall overdose deaths. Even though only 10% of all patients were receiving a dose of greater than 100 mg MED from a single prescriber, the overdose death rate in this population was as high as 40%. Patients receiving more than 100 mg MED from multiple physicians constituted the rest of the 10%. The percentage of overdose deaths was 40% in this segment. In other words, patients receiving more than 100 mg MED (from single or multiple prescribers), contributed to 80% of all the overdose deaths, whereas patients on doses of less than 100 mg MED contributed to only 20% of the overall overdose deaths, implying that 100 mg MED is a dangerous dose. There has been a call for establishing a maximum daily dose in order to guide physicians treating patients with chronic pain (114). Based on the current available evidence presented above, defining 50 mg MED/d as a high dose does not seem unreasonable. The dose limits recommended earlier by Washington State (120 mg MED) (109) and the Canadian guideline (200 mg MED) (110) seem excessive. Defining 200 mg MED by APS and AAPM as a high dose also appears to be harmful. We agree with Katz (114) that having dose limits will provide a guide for practicing physicians, reduce harm by eliminating high doses, assist in the negotiation process between physicians and patients pressing for higher doses and finally, impel high dose prescribers to exercise more caution. We concur with Manchikanti et al (20) that commencing long-acting opioid therapy is often the starting point for high dose opioid therapy, a practice that growing evidence suggests is harmful to patients and increases the black market availability of opioids through diversion. Many argue that chronic pain is undertreated and opioids must be used more liberally. We agree that chronic pain is undertreated, but we completely disagree, based on evidence, that aggressive opioid use is the answer to alleviating undertreated chronic pain. Given our awareness of the inadequacy and adverse effects of using opioids for the treatment of chronic pain, the failure to set dose limits is irresponsible and hazardous both to the individual and to society.

## Algorithmic Approach to Prevent Opioid Abuse

Opioids play an important but limited role in treating chronic pain. The challenge for the physician is to make opioids available for those who are truly in need, and to withhold them from those who are either abusing or diverting. Although difficult, this can be achieved in most cases. If all nonopioid measures fail in alleviating pain, and if opioids are being used, the following steps would be very helpful. The 3 cornerstones for responsible prescribing are stratifying patients by using screening tools into high, medium and low risk groups; monitoring patients by using UDS, PMPs and pill counts; and lastly, establishing dose limits (Fig. 1).

Stratification of patients into different risk categories is the first step. This requires the use of existing screening tools designed specifically to screen for opioid misuse (subjective tools like SOAPP (67), PMQ (68), PUDQP (70) or objective tools like ABC checklist (71), DIRE Score (72) and the tool by Atluri and Sudarshan (73) to classify patients as high risk, medium risk and low risk. As mentioned earlier, objective tools may be better than subjective tools. Those who are categorized as "high risk" should be monitored closely by performing UDS every 3 to 6 months and PMP every 2-4 months. Opioids should be either avoided or prescribed in low doses. Doses of more than 50 mg MED should be very rarely used and only under specialized settings in conjunction, when available, with addiction specialists. Pa-

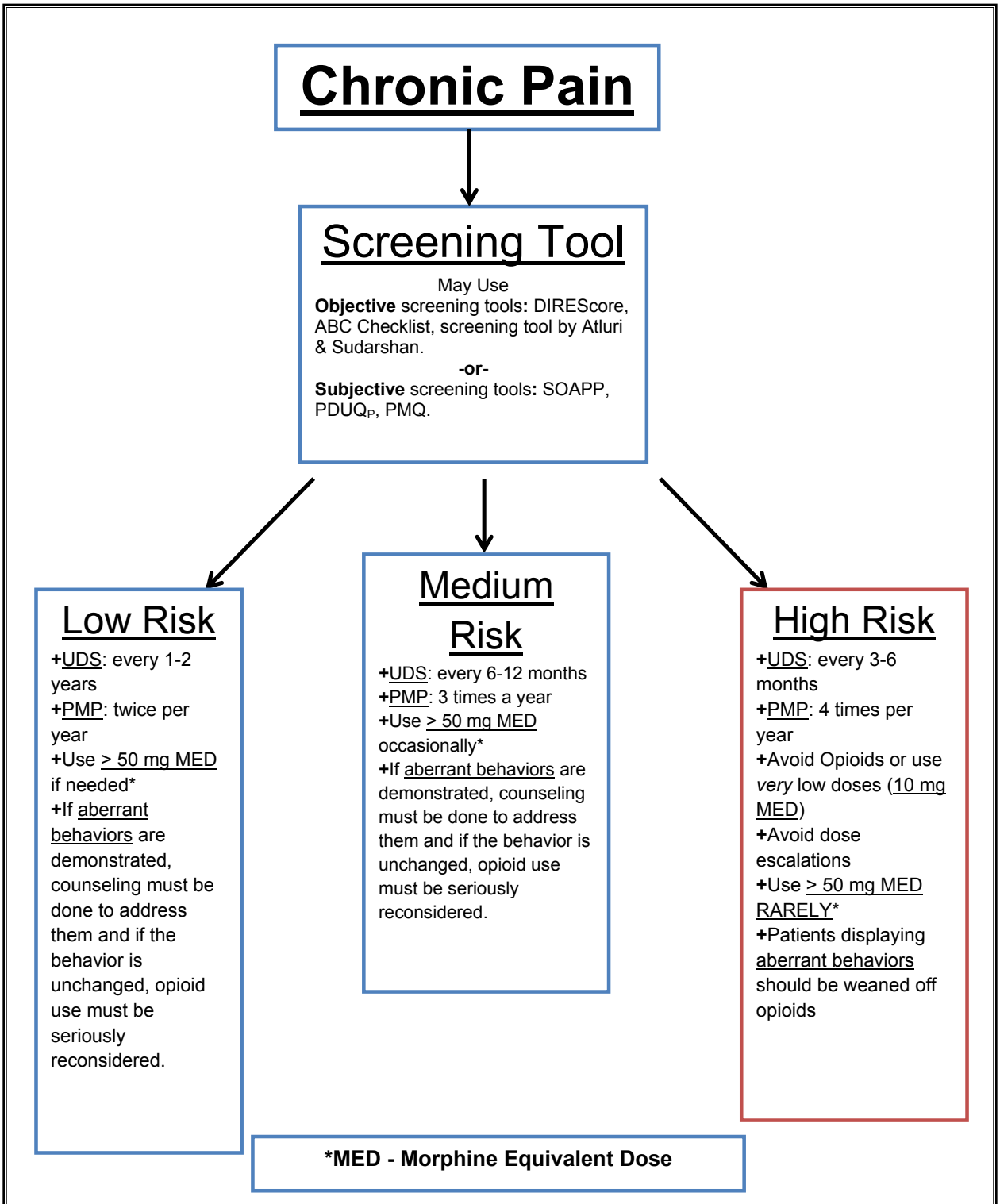


Fig. 1. *Illustration of the 3 cornerstones for responsible prescribing are stratifying patients by using screening tools into high, medium and low risk groups; monitoring patients by using UDS, PMPs and pill counts; and lastly, establishing dose limits*

tients displaying aberrant behaviors (asking for early refills, frequent visits to an emergency department for opioids, doctor shopping, taking opioids from others, etc.) should be weaned off opioids. Patients falling into the "low risk" category should be subjected to UDS every 1-2 years and PMP every 6 months to 1 year. Dose escalations can be done more liberally if required, keeping in mind that doses more than 50 mg MED/d should be an exception rather than the rule. If aberrant behaviors are present, counseling must commence. If counseling does not alter the behavior, opioid use must be seriously reconsidered. Those who are deemed as "medium risk" should be monitored with UDS every 6-12 months and PMP every 3-6 months. Opioid doses and their escalations should be guarded. Doses more than 50 mg MED/d can be used occasionally in carefully selected patients. If aberrant behaviors are present, counseling must commence, with a reconsideration of opioid use if the behavior does not change. These measures, along with an opioid agreement requiring patients to use a single prescriber and a single pharmacy, discouraging self dose escalations, giving limited refills, establishing regular office follow-ups, explaining the risks and benefits of opioids along with insisting on compliance with the opioid agreement should be useful in curbing inappropriate use of opioids.

## Conclusion

To tackle the epidemic of prescription opioid abuse, the following is suggested by Paulozzi et al (15).

1. Improving legislation and enforcement of existing laws regarding doctor shopping, diversion, and unscrupulous physicians.
2. Improving medical practice in prescribing opioids through proper education. In our opinion, and in order to encourage proper prescribing, this education should be based on evidence and not influenced by pharmaceutical companies. Currently, most of the education in this field is sponsored by pharmaceutical companies. Not surprisingly, there has been an escalation of abuse despite "voluntary" education (14). There is some evidence that the risk reduction strategies are not employed by primary care physicians, even in high risk patients (115). Mandatory education for those prescribing opioids for chronic pain may be helpful.
3. Pain organizations and societies should establish guidelines based on sound science without conflict of interest. Opioid management should be based on evidence and not on consensus of experts, no matter how learned they may be (116).

Opioids have an important but limited role in chronic pain. Their use should not be curtailed. The aim of this article is to encourage opioid use for patients who need it and at the same time deny it to those who abuse it. Unless the medical community takes an active role in curbing abuse, opioid use will be subject to excessive regulation by the government, making it difficult for us to prescribe. Responsible opioid prescribing, entails employing screening tools, monitoring patients, and establishing dose limits, and is required to prevent harm and preserve access to those who need it. Lest, we should forget, "first do no harm."

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# Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office-Based Setting

*Note: These guidelines do not replace clinical judgment in the appropriate care of patients. They are not intended as standards of care or as templates for legislation, nor are they meant for patients in palliative care programs or with cancer pain. The recommendations are an educational tool based on the expert opinion of numerous physicians and other health care providers, medical/nursing boards, mental and public health officials, and law enforcement personnel in Oklahoma and throughout the United States. The guidelines are available at* http://poison.health.ok.gov.

## Opioid Treatment for Acute Pain

1. Opioids should only be used for treatment of acute pain when the severity of the pain warrants that choice and after determining that other non-opioid pain medications or therapies will not provide adequate pain relief.
2. Providers should query the Oklahoma Prescription Monitoring Program (PMP) for patients presenting with acute pain, prior to prescribing an opioid medication. In circumstances where a patient's pain is resulting from an objectively diagnosed disease process or injury, a provider may prudently opt not to review the Oklahoma PMP.
3. When opioids are prescribed for treatment of acute pain, the number of doses dispensed should be no more than the number of doses needed based on the usual duration of pain severe enough to require opioids for that condition.
4. When opioids are prescribed for treatment of acute pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.
5. Long duration-of-action opioids (e.g., methadone, buprenorphine, fentanyl, extended release oxycodone, and morphine) are rarely indicated for treatment of acute pain.
6. The use of opioids should be re-evaluated carefully, including assessing the potential for abuse, if persistent pain suggests the need to continue opioids beyond the anticipated time period of acute pain treatment for that condition. Health care providers should query the Oklahoma PMP as part of this re-evaluation process.
7. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.

## Opioid Treatment for Chronic Pain

1. Alternatives to opioid treatment should be tried, or previous attempts documented, before initiating opioid treatment.
2. A comprehensive evaluation should be performed before initiating opioid treatment for chronic pain. For chronic pain patients transferring their care to new health care providers, new opioid prescriptions should generally not be written until the previous provider's records have been reviewed or the previous health care provider has been notified of the transfer of care.
3. The health care provider should screen for risk of abuse or addiction before initiating opioid treatment.
4. Prior to the initial prescribing of opioid medications, health care providers should query the Oklahoma Prescription Monitoring Program (PMP).
5. When opioids are used for the treatment of chronic pain, a written treatment plan should be established that includes measurable goals for reduction of pain and improvement of function. One health care provider should coordinate a patient's comprehensive pain care plan and provide all opioid prescriptions required for the plan.

6. The patient should be informed of the risks, benefits, and terms for continuation of opioid treatment, ideally using a written and signed treatment agreement.
7. Opioids should be initiated as a short-term trial to assess the effects of opioid treatment on pain intensity, function, and quality of life. In most instances, the trial should begin with a short-acting opioid medication.
8. Regular visits for evaluation of progress toward goals should be scheduled during the period when the dose of opioids is being adjusted (titration period). During the titration period, and until the patient is clinically stable and judged to be compliant with therapy, it is recommended that the health care provider check the Oklahoma PMP more frequently.
9. Once a stable dose has been established (maintenance period), regular monitoring should be conducted at face-to-face visits during which treatment goals, analgesia, activity, adverse effects, and aberrant behaviors are monitored. The Oklahoma PMP should be queried at least once per year for patients receiving opioid treatment for chronic pain.
10. Continuing opioid treatment should be a deliberate decision that takes into consideration the risks and benefits of chronic opioid treatment for that patient. Patients and health care providers should periodically reassess the need for continued opioid treatment, weaning whenever possible, as part of the comprehensive pain care plan. A second opinion or consultation may be useful in making that decision.
11. Opioid treatment should be discontinued if adverse effects outweigh benefits or if aberrant, dangerous, or illegal behaviors are demonstrated.
12. Health care providers treating chronic pain patients with opioids should maintain records, in accordance with state and federal law, documenting patient evaluation, treatment plan, discussion of risks and benefits, informed consent, treatments prescribed, results of treatment, and any aberrant behavior observed.
13. Health care providers should consider consultation for patients with complex pain conditions, serious co-morbidities and mental illness, a history or evidence of current drug addiction or abuse, or when the provider is not confident of his/her ability to manage the treatment.
14. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.
15. The administration of intravenous and intramuscular opioids for the relief of exacerbations of chronic pain is discouraged, except in special circumstances.
16. Long-acting opioids are associated with an increased risk of overdose death, and should only be prescribed by health care providers familiar with their indications, risks, and need for careful monitoring.
17. When opioids are prescribed for treatment of chronic pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.

**Oklahoma Society of Interventional Pain Physicians**

## Background

Prescription drug abuse is Oklahoma's fastest growing drug problem. Of the nearly 3,200 unintentional poisoning deaths in Oklahoma from 2007-2011, 81% involved at least one prescription drug.[1] In 2010, Oklahoma had the fourth highest unintentional poisoning death rate in the nation (17.9 deaths per 100,000 population).[2] Prescription painkillers (opioids) are now the most common class of drug involved in overdose deaths in Oklahoma (involved in 87% of prescription drug-related deaths, with 417 opioid-involved overdose deaths in 2011).1 In a 2010 National Survey on Drug Use and Health report, Oklahoma led the nation in non-medical use of painkillers, with more than 8% of the population age 12 and older abusing/misusing painkillers.[3] Oklahoma is also one of the leading states in prescription painkiller sales per capita.[4]

These guidelines were primarily adapted from the Utah Clinical Guidelines on Prescribing Opioids.[5] The Opioid Prescribing Guidelines for Oklahoma Workgroup also studied other state and national recommendations in an effort to prepare guidelines most relevant to the practice of medicine in Oklahoma. The Workgroup created these guidelines in an effort to help reduce the misuse of prescription opioid analgesics while preserving patient access to needed medical treatment.

## Guidelines for Acute Pain

### 1. Opioids should only be used for treatment of acute pain when the severity of the pain warrants that choice and after determining that other non-opioid pain medications or therapies will not provide adequate pain relief.[6]

Most acute pain is better treated with non-opioid medications [e.g., acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs)] or physical modalities such as therapeutic exercises or stretching. Opioid medications have less desirable adverse effect profiles in acute pain patients. Care should be taken to assure that opioid treatment does not interfere with early implementation of functional restoration programs such as exercise and physical therapy. Non-medical use of opioids is more common among younger people, and these risks should be considered when prescribing to an adolescent.

### 2. Providers should query the Oklahoma Prescription Monitoring Program (PMP) for patients presenting with acute pain, prior to prescribing an opioid medication. In circumstances where a patient's pain is resulting from an objectively diagnosed disease process or injury, a provider may prudently opt not to review the Oklahoma PMP.

The Oklahoma PMP is a real-time database of scheduled prescriptions written to persons who filled a prescription in Oklahoma. The Oklahoma PMP can be accessed at: http://www.ok.gov/obndd/Prescription_Monitoring_Program/.

Patients with a history of or current substance abuse are at increased risk of misusing opioids when prescribed.[7,8] Medical providers should ask the patient about a history of substance abuse prior to prescribing an opioid medication for the treatment of acute pain. A non-opioid regimen is preferred for patients presenting with a history of substance abuse who have acute pain. Although this should not exclude a patient from being prescribed opioids for acute pain, it should prompt a discussion with the patient about the potential for addiction. When a patient with a history of opioid addiction presents with acute pain due to an objectively diagnosed clinical or traumatic condition requiring the use of opioids for pain control, very close follow-up is indicated.

### 3. When opioids are prescribed for treatment of acute pain, the number of doses dispensed should be no more than the number of doses needed based on the usual duration of pain severe enough to require opioids for that condition.

Prescribing more medications than necessary can lead to non-medical use, abuse, and diversion of unused

medications. Opioid pain medications should be discontinued when the pain severity no longer requires opioid medications.

### 4. When opioids are prescribed for treatment of acute pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.

It is important that patients understand the need to store medications securely. Health care providers should encourage patients to keep medications in a locked environment rather than in easily accessible locations, such as the bathroom or kitchen cabinet, where medications are accessible to children and can be a target for theft. After recovery from pain, leftover medications should be properly disposed of immediately to help protect the medications from being diverted.

Tools to accompany *Recommendation 4:*

- United States Food and Drug Administration (FDA) Guidelines on Proper Disposal of Prescription Drugs http://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingOver-the-CounterMedicines/ucm107163.pdf
- Oklahoma Bureau of Narcotics and Dangerous Drugs Take Back Container Locations http://www.ok.gov/obndd/documents/TakeBackBoxes.pdf

### 5. Long duration-of-action opioids (e.g., methadone, buprenorphine, fentanyl, extended release oxycodone, and morphine) are rarely indicated for treatment of acute pain.

Given the epidemiological data showing a significant increase in mortality associated with long-acting opioids, the inherent difficulty in titrating these medications, and the availability of alternative medications and/or treatment modalities, health care providers are advised to refrain from the routine use of long-acting opioids in the acute pain setting.[5,9]

### 6. The use of opioids should be re-evaluated carefully, including assessing the potential for abuse, if persistent pain suggests the need to continue opioids beyond the anticipated time period of acute pain treatment for that condition. Health care providers should query the Oklahoma PMP as part of this re-evaluation process.

Patients with acute pain who fail to recover in a usual timeframe or otherwise deviate from the expected clinical course for their diagnosis should be carefully re-evaluated. The continuation of opioid treatment for acute pain in this setting may represent the initiation of opioid treatment for a chronic pain condition without being recognized as such. At this time, the diagnosis and appropriateness of the treatment plan should be re-evaluated and the patient's medical history should be reviewed for factors that could interfere with treatment and pose a risk for complications during opioid treatment, including substance abuse or history of substance abuse.

Tools to accompany *Recommendation 6:*

- Oklahoma Prescription Monitoring Program http://www.ok.gov/obndd/Prescription_Monitoring_Program/

### 7. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.

Patients misusing controlled substances frequently report their opioid medications as having been lost or stolen. Pain specialists routinely stipulate in pain agreements with patients that lost or stolen controlled substances will not be replaced. Most written agreements between chronic pain patients and pain management physicians, including the Health Resources and Services Administration (HRSA) toolkit sample pain agreement, state that prescriptions for opioids will not be replaced.[10]

The diversion of prescribed opioids is common. One study looked at completed patient surveys, and found that 45% of respondents reported some form of drug diversion at least once. Stolen medication was the most prevalent method of drug diversion, with 30% of respondents reporting at least one incident of stolen medication.[11] In another survey study, among persons 12 years and older who abused opioid pain medications (2009-2010), 71.2% came from friends or relatives; 55% were given to the abuser, 11.4% were purchased, and 4.8% were stolen.[12,13]

## Guidelines for Chronic Pain

### 1. Alternatives to opioid treatment should be tried, or previous attempts documented, before initiating opioid treatment.[6,9,13,14,15]

Opioid medications are usually not the most appropriate first line of treatment for patients with chronic pain. Other measures, such as non-opioid pain medications, non-steroidal anti-inflammatory drugs (NSAIDs), antidepressants, antiepileptic drugs, and non-pharmacologic therapies (e.g., therapeutic exercise, physical therapy), should be tried first and the outcomes of those therapies documented. Opioid therapy should be considered only when other potentially safer and more effective therapies prove inadequate. This approach is consistent with the World Health Organization's (WHO) *Pain Relief Ladder*.[16]

**1.1** Clinicians should refer to disease-specific guidelines for recommendations for treatment of chronic pain related to specific diseases or conditions.

Tools to accompany *Recommendation 1:*

- Non-opioid Pain Management Tool
  http://health.utah.gov/prescription/tools.html (see *Informational Tools* on website)

### 2. A comprehensive evaluation should be performed before initiating opioid treatment for chronic pain. For chronic pain patients transferring their care to new health care providers, new opioid prescriptions should generally not be written until the previous provider's records have been reviewed or the previous health care provider has been notified of the transfer of care.[13,14,15,17]

There are many reasons to prescribe cautiously when initiating opioid therapy; therefore a comprehensive initial evaluation is necessary to identify patients at high risk for adverse outcomes. The major goal should be to provide the greatest functional benefit while minimizing the potential for harm to patients. The potential for serious harm, including death, exists due either to overdose or to dangerous behaviors that may occur while taking opioids. The patient may be directly harmed, but others may also be harmed through diversion or by acts performed by a person taking opioids.

Initiating opioid treatment often results in short-term relief, which may not be sustainable. Safe long-term use of opioid medications requires the commitment of adequate resources. Patients need to be monitored regularly to evaluate outcomes and identify aberrant behavior or adverse side effects.

The goal of the comprehensive evaluation is to determine the nature of the patient's pain, and to evaluate how the pain is affecting the patient's function and quality of life. The provider should attempt to identify other conditions or circumstances that could adversely affect the treatment plan or the approach to managing the patient's treatment plan. The provider should also re-assess and re-evaluate prior approaches to the patient's pain management to provide a basis for establishing an effective ongoing plan of care.

The evaluation should specifically assess:

A. The character and potential cause(s) of pain, as well as prior treatments.

- The duration of the pain should be considered.
- The character of the pain should be considered. Since certain types of pain, such as neuropathic pain,

might not be best treated with opioids. It is important for the clinician to consider the type and character of pain when prescribing a medication.

B. Social factors and medical or mental health conditions might influence treatment, especially those that might interfere with appropriate and safe use of opioid therapy.[14]

- Obtain a history of substance use, addiction, or dependence. (If present, refer to *Recommendations 13.2 and 13.3*.)
- Consider potential psychiatric conditions, including personality disorders that may affect pain or the treatment of pain. (If present, refer to *Recommendation 13.4*.)
- Identify use of alcohol and other medications that might interact with opioid medications used to treat pain. Particular attention and caution should be given to alcohol, benzodiazepines, and other sedative medications.
- Assess the presence of medical conditions that might complicate the treatment of pain, including medication allergy, cardiac or respiratory disease, and sleep apnea or risk factors for sleep apnea.
- Central sleep apnea is common among persons treated with methadone and other opioid medications, especially at higher dosages. Some experts recommend that all patients who are considered for long-term opioid treatment receive a sleep study prior to therapy or when higher dosages are considered.[14]

C. Effects of pain on the patient's life and function.

- Assess the patient's baseline severity of pain, functional status, and quality of life using a valid, reliable method/instrument that can be used later to evaluate treatment effectiveness.

Tools to accompany *Recommendation 2:*

- Sheehan Disability Tool
  http://health.utah.gov/prescription/pdf/guidelines/SheehanDisabilityScale.pdf
- Pain Management Evaluation Tool
  http://health.utah.gov/prescription/pdf/guidelines/PainManagementWorksheet.pdf

## 3. The health care provider should screen for risk of abuse or addiction before initiating opioid treatment.

**3.1** Use a screening tool to assess the patient's risk of misuse prior to prescribing an opioid medication for chronic pain.[6]

A number of screening tools have been developed for assessing a patient's risk of misuse of medications. The screening tools are intended to assist the health care provider in determining whether opioid treatment is appropriate and in determining the level of monitoring appropriate for the patient's level of risk.

**3.2** Consider performing drug screening before initiating long term opioid treatment for chronic pain.

Drug testing can identify problems, such as use of undisclosed medications, non-use of reported medications (i.e., potential diversion), undisclosed use of alcohol, or the use of illicit substances, not identified without testing.

Health care providers should use a urine drug screen or another laboratory test that can detect the presence of illegal drugs, unreported prescription medications, and/or unreported alcohol use. It is recommended that drug testing be strongly considered and conducted, especially when other factors suggest caution. When screening is limited to situations when there is suspicion of substance misuse, some opportunities may be missed. In one study, testing results upon first admission to a pain clinic did not correlate with reported medication use for nearly one-fourth of patients. Most discrepancies involved substances not reported by the patient; a small minority reported taking medications that were not found on testing.[18]

A positive drug screen indicates the need for caution, but does not preclude opioid use for the treatment of pain. However, consideration should be given to referral for substance abuse counseling and/or a pain management specialist. If an opioid medication is subsequently prescribed, the patient should be more carefully monitored and the conditions under which opioids are being prescribed should be well documented in the treatment plan. (See *Recommendations 5, 6, 8, 12*.)

Inexpensive immunoassays can be performed in the office. These tests can rapidly determine if opioids are present but they do not identify specific substances. When necessary, specific substances can be identified by ordering confirmatory laboratory testing. However, in many cases, candidly going over the results of the initial in-office test with the patient can eliminate the need for confirmatory testing. It is extremely important to keep in mind that immunoassays have both false-positive and false-negative results. Certain over-the-counter medications may cause a positive result. The prescriber should consider confirmatory gas chromatography or mass spectrometry testing or consultation with a certified Medical Review Officer if drug test results are unclear or confirmation is clinically necessary.[9]

Tools to accompany *Recommendation 3:*

- Urine Drug Testing Devices
  http://health.utah.gov/prescription/pdf/guidelines/CLIADrugTestlist.pdf
- Current Opioid Misuse Measure
  http://health.utah.gov/prescription/tools.html (see *Tools to Screen for Risk of Complications* on website)
- SOAPP-R
  http://health.utah.gov/prescription/tools.html (see *Tools to Screen for Risk of Complications* on website)
- Opioid Risk Tool
  http://health.utah.gov/prescription/pdf/guidelines/ORTwithout_scoring.pdf
- Signs of Substance Misuse
  http://health.utah.gov/prescription/pdf/guidelines/signs_substance_misuse.pdf
- Checklist for Adverse Effects, Function, and Opioid Dependence
  http://health.utah.gov/prescription/pdf/guidelines/checklist%20for%20adverse%20effects.pdf

## 4. Prior to the initial prescribing of opioid medications, health care providers should query the Oklahoma Prescription Monitoring Program (PMP).

Most patients who request treatment for pain are legitimately seeking relief of pain. However, subsets of patients seeking treatment for pain are seeking drugs for recreational use, to support an established addiction, or for profit. Information about past patterns of controlled substance prescriptions filled by the patient, such as obtaining medications from multiple providers or obtaining concurrent prescriptions, can alert the provider to potential problems.

The Oklahoma Bureau of Narcotics and Dangerous Drugs Control (OBNDDC) maintains the Oklahoma Prescription Monitoring Program, a real time, searchable database of all controlled substance prescriptions filled in the state. The PMP is used to track and collect data on the dispensing of Schedule II-V drugs by all retail, institutional, and outpatient hospital pharmacies, and in-state/out-of-state mail order pharmacies. Access to the data is provided to authorized individuals and used to identify potential cases of drug over-utilization, misuse, and potential abuse of controlled substances throughout the state. This database is accessible online to all controlled substance prescribers.

Tools to accompany *Recommendation 4:*

- Oklahoma Prescription Monitoring Program
  http://www.ok.gov/obndd/Prescription_Monitoring_Program/

## 5. When opioids are used for the treatment of chronic pain, a written treatment plan should be established that includes measurable goals for reduction of pain and improvement of function. One health care provider should coordinate a patient's comprehensive pain care plan and provide all opioid prescriptions required for the plan.

**5.1** The treatment plan should be tailored to the patient's circumstances and the characteristics and pathophysiology of the pain. The pathophysiology helps to predict whether opioid medication is likely to help reduce pain or to improve function, and should be considered when establishing treatment goals. Non-opioid treatment modalities should be included in the treatment plan, whenever possible, to maximize the likelihood of achieving treatment goals.

**5.2** Goals for the treatment of chronic pain should be measurable and should include improved function and quality of life as well as improved control of pain.[6,9,14]

For most chronic pain conditions, complete elimination of pain is an unreasonable goal. Goals for treatment of chronic pain should include improvement in the tolerability of pain and function.[15] The clinician should counsel the patient on reasonable expectations for treatment outcomes so that agreement is achieved on the goals of addressing pain, function, and quality of life.

The pathophysiologic basis of the pain can help establish a prognosis for future improvement (or worsening) in function and pain and should influence the goals of treatment. Goals for functional improvement and measures to track progress against those goals should be established and documented to serve as a basis of evaluating treatment outcomes.[6,14] These include:

- Objective physical findings obtained by the examining health care provider (e.g., improved strength, range of motion, aerobic capacity);
- Functional status at work (e.g., increase in physical output, endurance, or ability to perform job functions); and
- Functional status at home (e.g., increased ability to perform instrumental activities of daily living, and frequency and intensity of conditioning).

Targets for improved quality of life should also be identified and documented to serve as a basis for evaluating treatment outcomes. These may include:

- Patient rating of quality of life on a measurement scale;
- Psychosocial status (e.g., increased social engagement or decreased emotional distress);
- Familial status (e.g., improved relationships with, or decreased burden, on family members); and
- Physical status (e.g., increased ability to exercise, perform chores, or participate in hobbies).

Health care providers should consider cultural differences in assessing function, quality of life, and pain intensity (see http://prc.coh.org/culture.asp for examples). These measures of improvement could be reported by the patient, family members, and/or the employer. Permission to discuss the patient's condition with these persons should have been previously obtained and documented.

**5.3** Treatment goals should be developed jointly by the patient and health care provider.[15]

Engage patients in their own health care. Health care providers have observed that when patients assume a significant portion of the responsibility for their rehabilitation they are more likely to improve and that when they participate in goal setting they are more likely to achieve the goals. As with any other chronic illness (such as diabetes or heart disease), the health care provider should focus not just on pain control, but also on treating the patient's underlying diseases and encouraging them to engage in ownership of their own health.

Tools to accompany *Recommendation 5:*

- Pain Management Evaluation Tool
  http://health.utah.gov/prescription/pdf/guidelines/PainManagementWorksheet.pdf
- Patient Pain and Medication Tracking Chart
  http://health.utah.gov/prescription/pdf/guidelines/PatientPain-FunctionTracking.pdf
- Sheehan Disability Scale
  http://health.utah.gov/prescription/pdf/guidelines/SheehanDisabilityScale.pdf
- Brief Pain Inventory Form
  http://health.utah.gov/prescription/pdf/guidelines/BriefPainInvNPEC.pdf
- Sample Treatment Plan for Prescription Opioids
  http://health.utah.gov/prescription/pdf/guidelines/treatment_plan.pdf
- Cultural considerations in assessing function, quality of life, and pain intensity
  http://prc.coh.org/culture.asp

## 6. The patient should be informed of the risks, benefits, and terms for continuation of opioid treatment, ideally using a written and signed treatment agreement.[13]

**6.1** Patients should be informed not to expect complete relief from pain. The excitement and euphoria of initial pain relief that may occur with a potent opioid can lead the patient to expect long-term complete pain relief. Without careful guidance, this may lead the patient to disappointment and to seek excessive doses of opioids.

The patient should be counseled about the appropriate use of opioid medications, possible adverse effects, and the risks of developing tolerance, physical and/or psychological dependence, and withdrawal symptoms.[9,19] Adverse effects can include opioid-induced hyperalgesia, allodynia, abnormal pain sensitivity, and depression.[6,9,20]

Sedation and cognitive impairment may occur when patients are taking opioid medications. Therefore, discuss with patients the need for caution in operating motor vehicles or equipment or performing other tasks where impairment would put them or others at risk.[11]

Ensure the patient does not have any absolute contraindications, and review risks and benefits related to any relative contraindications with the patient.

Absolute contraindications for opioid prescribing:

- Allergy to an opioid agent (may be addressed by using an alternative agent);
- Co-administration of a drug capable of inducing life-threatening drug-drug interaction; and
- Active diversion of controlled substances (providing medication to someone for whom it was not prescribed).

More detail about absolute contraindications is contained in the *Guidelines Tools* section.

Consider co-prescribing naloxone for high risk patients, and providing training to family/caregivers to reverse potential life-threatening depression of the respiratory and central nervous system. Educate patients and family/caregivers about the danger signs of respiratory depression. Everyone in the household should know to summon medical help immediately if a person demonstrates any of the following signs while on opioids:

- Snoring heavily and cannot be awakened;
- Periods of ataxic (irregular) or other sleep disordered breathing;
- Trouble breathing;

- Exhibiting extreme drowsiness and slow breathing;
- Slow, shallow breathing with little chest movement;
- Increased or decreased heartbeat; and
- Feeling faint, very dizzy, confused or has heart palpitations.

**6.2** The patient and, when applicable, the family or caregiver should be involved in the education process.[14]

Educational material should be provided in written form and discussed in person with the patient and, when applicable, the family or caregiver.[14] Educating the family or caregiver about the signs of opioid overdose may help detect problems before they lead to a serious complication.

It is important to act within the constraints of the Health Insurance Portability and Accountability Act (HIPAA). HIPAA regulates the conditions under which information about the patient can be disclosed to others, such as family members, and under what conditions discussions about the patient with others are allowed.

**6.3** The treatment plan, which defines the responsibilities of both the patient and health care provider, should be documented.[6,9,13,14,15]

Patient responsibilities include properly obtaining, filling, and using prescriptions, and adherence to the treatment plan. Patient responsibilities also include instructions to keep a pain diary, a diary or log of daily activities and accomplishments, and/or instructions on how and when to give feedback to the prescriber.[14]

The prescribing health care provider may consider requiring that the treatment plan be documented in the form of a treatment agreement signed by the patient. Patients should be encouraged to store opioid medications in a secure location to keep the medication away from others who should not have access to them.

**6.4** The treatment plan should contain goals of treatment, guidelines for prescription refills, agreement to submit to urine or serum screening upon request, and reasons for possible discontinuation of drug therapy.[9,13,14,15,17]

The treatment plan (sometimes referred to as a treatment agreement) should contain the items developed jointly by the patient and health care provider, such as follow-up appointments, the pharmacy and health care provider to be used, as well as any non-negotiable demands or limitations the health care provider wishes to make, such as the prohibition of sharing or trading the medication or getting refills early. Specific grounds for immediate termination of the agreement and cessation of prescribing may also be specified, such as forgery or selling of prescriptions or medications or obtaining them from multiple providers as documented by Oklahoma's Prescription Monitoring Program.[14,20]

Optional inclusions in the agreement:

- Pill counts may be required as a means to gauge proper medication use;[14,19]
- Prohibition of use with alcohol or certain other medications;[14]
- Documentation of counseling regarding driving or operating heavy machinery; and [6,14]
- Specific frequencies of urine testing.

Ideally, the patient should be receiving prescriptions from one prescriber only and filling those prescriptions at one pharmacy only.[14,17,19]

It is not necessary to include specific consequences for specific non-compliant behaviors, but it should be documented in the treatment agreement that continuing failure by the patient to adhere to the treatment plan will result in escalating consequences, up to and including termination of the clinician-patient relationship and of opioid prescribing by that clinician.

**6.5** Discuss involvement of family members in the patient's care and request that the patient give written permission to talk with family members about the patient's care.

This is best done before starting to treat the patient because it can be more difficult to obtain consent after an issue occurs. Prior to initiating treatment with opioids, the health care provider may want to consider a family conference to help assess the patient's integrity.[19] Consultation with others, however, must be done within the constraints of HIPAA, as noted above. (See *Recommendation 6.2*.)

Tools to accompany *Recommendation 6:*

- Absolute Contraindications to Opioid Prescribing
  http://health.utah.gov/prescription/pdf/guidelines/absolute_contraindications.pdf
- Sample Treatment Plan for Prescribing Opioids
  http://health.utah.gov/prescription/pdf/guidelines/treatment_plan.pdf
- Signs of Substance Misuse
  http://health.utah.gov/prescription/pdf/guidelines/signs_substance_misuse.pdf
- Guidance on HIPAA
  http://www.hhs.gov/ocr/privacy/hipaa/understanding/coveredentities/provider_ffg.pdf
- Prescription Drug Overdose in Oklahoma Brochure
  http://www.ok.gov/health2/documents/DrugOverDoseBrochure_2013.pdf

## Initiating, Monitoring, and Discontinuing Opioid Treatment

### 7. Opioids should be initiated as a short-term trial to assess the effects of opioid treatment on pain intensity, function, and quality of life. In most instances, the trial should begin with a short-acting opioid medication.

**7.1** The health care provider should clearly explain to the patient that initiation of opioid treatment is not a commitment to long-term opioid treatment and that treatment will be stopped if the trial is determined to be unsuccessful. The trial should be for a specific time period with pre-determined evaluation points. The decision to continue opioid medication treatment beyond the trial period should be based on the balance between benefits, including function and quality of life, and adverse effects experienced. Criteria for cessation should be considered before treatment begins. Refer to *Recommendation 11* for more information on discontinuation of treatment.

**7.2** Short-acting opioid medications are, in general, safer and easier to titrate to an effective dose. If the treatment trial proves successful in achieving the goals established in the treatment plan, the health care provider may consider switching the patient to a long-acting or sustained-release formulation. The patient's individual situation should influence whether the patient is switched from a short-acting medication. Treatment with a long-acting opioid medication before a trial using a short-acting medication has been performed is an option that should be prescribed only by those with considerable expertise in chronic pain management.

Tools to accompany *Recommendation 7:*

- Dosing Guidelines
  http://health.utah.gov/prescription/pdf/guidelines/dosing_guidelines.pdf
- Current Opioid Misuse Measure (COMM)
  http://health.utah.gov/prescription/tools.html (see *Tools to Screen for Risk of Complications* on website)

## Titration Phase of Opioid Treatment

### 8. Regular visits for evaluation of progress toward goals should be scheduled during the period when the dose of opioids is being adjusted (titration period). During the titration period, and until the patient is clinically stable and judged to be compliant with therapy, it is recommended that the health care provider check the Oklahoma PMP more frequently.[14]

**8.1** Face-to-face follow-up visits should occur at least every 2-4 weeks during the titration period. More frequent follow-up visits may be advisable and caution should be used when prescribing an opioid medication if the patient has a known addiction problem, suspected drug-behavior problems, or co-existing psychiatric or medical problems. Frequency of visits should also be based on risk stratification (e.g., as determined by a screening tool) and the clinician's judgment (taking into account the volume of the drug being prescribed and how likely it is to be abused).[15]

**8.2** When pain and function have not sufficiently improved on a current opioid dose, a trial of a slightly higher dose could be considered.[14,15]

The rate at which the dosing is increased should balance the risk of leaving the patient in a painful state longer than necessary by increasing too slowly with the risk of causing harm, including fatal overdose, by increasing too fast. Ideally, only one drug at a time should be titrated in an opioid-naïve patient.[14] Age, health, and severity of pain should be taken into consideration when deciding on increments and rates of titration. Particular caution should be used in titrating dosing of methadone.

Evidence and other guidelines are not in agreement regarding the risks and benefits of high daily doses of opioid measured in morphine milligram equivalents (MMEs). It is likely that the risk-benefit ratio is less favorable at higher doses. Clinical vigilance is needed at all dosage levels of opioids, but is even more important at higher doses. Health care providers who are not experienced in prescribing high doses of opioids should consider either referring the patient or obtaining a consultation from a qualified provider for patients receiving high dosages. No clear threshold for a high dose has been established based on evidence. The Washington State guidelines suggest a threshold of 120 MME per day. It is important to increase clinical vigilance at doses exceeding 120 MME per day. Patients receiving 100 MME or more per day had a 9-fold increase in overdose risk. Most overdoses were medically serious, 12% were fatal.[9]

During titration, all patients should be seen frequently until dosing requirements have stabilized. Patients should be instructed to use medication only as directed, that is, not to change doses or frequency of administration without specific instructions from the health care provider.

**8.3** During the titration period, and until the patient is clinically stable and judged to be compliant with therapy, it is recommended that the health care provider check the Oklahoma Prescription Monitoring Program more frequently, such as monthly or quarterly.

Tools to accompany *Recommendation 8:*

- Dosing Guidelines
  http://health.utah.gov/prescription/pdf/guidelines/dosing_guidelines.pdf
- Electronic MME Dosing Calculator
  http://agencymeddirectors.wa.gov/mobile.html
- Prescription Monitoring Program
  http://www.ok.gov/obndd/Prescription_Monitoring_Program/

## Maintenance of Opioid Treatment

### 9. Once a stable dose has been established (maintenance period), regular monitoring should be conducted at face-to-face visits during which treatment goals, analgesia, activity, adverse effects, and aberrant behaviors are monitored. The Oklahoma PMP should be queried at least once per year for patients receiving opioid treatment for chronic pain.[13,15]

**9.1** The health care provider is advised to consider baseline drug testing at the initiation of opioid treatment, compliance monitoring one to three months later, and random monitoring every 6-12 months. In the event of unexpected drug screens or suspicious patient behavior, additional monitoring can be performed. Health care

providers may consider each of the following four areas of concern at each visit: Analgesia, Activity, Adverse effects, and Aberrant behavior. These assessments can be remembered as the "four A's": [21]

- Analgesia: inquire about level of pain (current, recent, trends, etc.)
- Activity: assess the patient's function and overall quality of life
- Adverse events: determine whether the patient is having medication side effects
- Aberrant behavior: evaluate for possible drug abuse-related behavior

**9.2** During the maintenance period, the Oklahoma Prescription Monitoring Program should be checked at least annually.

After the titration period is complete and the maintenance period is underway, the frequency of checks of the Oklahoma PMP can be based on clinical judgment, but should be done no less than annually. The Oklahoma PMP should be checked more often for high risk patients and patients exhibiting aberrant behavior.

**9.3** Continuation or modification of treatment should depend on the health care provider's evaluation of progress towards stated treatment goals.[13]

Treatment goals include reduction in a patient's pain scores and improved physical, psychological, and social function. If patient compliance with agreed-upon activity levels, are not being achieved despite medication adjustments, the health care provider should re-evaluate the appropriateness of continued treatment with the current medications.[9,17]

A frequent need for dose adjustments after a reasonable time interval of titration is an indication to re-evaluate the underlying condition and consider the possibility the patient has developed opioid hyperalgesia, substantial tolerance, or psychological/physical dependence.

**9.4** Adjustments to previously stable maintenance treatment may be considered if the patient develops tolerance, a new pain-producing medical condition arises or an existing one worsens, or if a new adverse effect emerges or becomes more clinically significant.[14]

Options for adjustment include reducing the medication or rotating opioid medications. If it is documented that the patient is compliant with agreed-upon recommendations such as exercise, working, etc., the addition of supplemental short-acting medications for control of break-through pain (e.g., as related to an increase in activity, end-of-dose pain, weather-related pain exacerbation, or specific medical conditions) can be considered as well. If patients do not achieve effective pain relief with one opioid, rotation to another frequently produces greater success.[22] If rotating among different opioid medications, refer to a standard dosing equivalence table, taking into account the current drug's half-life and potency.

If the patient's situation has changed permanently and consideration is given to the increased risk of adverse events, it is reasonable to consider an ongoing increase in maintenance dosing. In general, if the patient's underlying medical condition is chronic and unchanging, and if opioid-associated problems (hyperalgesia, substantial tolerance, important adverse effects) have not developed, it is recommended that the effective dose achieved through titration not be lowered once the patient has reached a plateau of adequate pain relief and functional level.[14]

**9.5** Dosing changes should generally be made during a clinic visit.[14]

If the patient's underlying, pain-producing, chronic medical condition improves, it is expected that the health care provider will begin tapering the patient off the opioid medication. (See *Recommendation 11* for guidelines on discontinuation.)

Tapering an opioid medication with or without the goal of discontinuation may be performed as described below (*Recommendation 11*) or as described in the *Strategies for Tapering and Weaning Tool*.

Tools to accompany *Recommendation 9:*

- Checklist for Adverse Effects, Function, and Opioid Dependence
  http://health.utah.gov/prescription/pdf/guidelines/checklist%20for%20adverse%20effects.pdf
- Signs of Substance Misuse
  http://health.utah.gov/prescription/pdf/guidelines/signs_substance_misuse.pdf
- Pain Management Evaluation Tool
  http://health.utah.gov/prescription/pdf/guidelines/PainManagementWorksheet.pdf
- Dosing Guidelines
  http://health.utah.gov/prescription/pdf/guidelines/dosing_guidelines.pdf
- Strategies for Tapering and Weaning
  http://health.utah.gov/prescription/pdf/guidelines/Strategies_tapering_weaning.pdf

## Evaluating the Opioid Treatment Trial

### 10. Continuing opioid treatment should be a deliberate decision that takes into consideration the risks and benefits of chronic opioid treatment for that patient. Patients and health care providers should periodically reassess the need for continued opioid treatment, weaning whenever possible, as part of the comprehensive pain care plan. A second opinion or consultation may be useful in making that decision.

The health care provider should clearly explain to the patient that initiation of opioid treatment is not a commitment to long-term opioid treatment and that treatment will be stopped if the trial is determined to be unsuccessful. The trial should be for a specific time period with pre-determined evaluation points. The decision to continue opioid treatment beyond the trial period should be based on the balance between benefits, including function and quality of life, and adverse effects experienced. A second opinion or consult may be useful in making the decision to continue or discontinue opioids after the treatment trial.

## Discontinuing Opioid Treatment

### 11. Opioid treatment should be discontinued if adverse effects outweigh benefits, or if aberrant, dangerous, or illegal behaviors are demonstrated.[9]

**11.1** Discontinuation of opioid treatment is recommended if any of the following occurs:

- Dangerous or illegal behaviors are identified;
- Patient claims or exhibits a lack of effectiveness;
- Pain problem resolves;
- Patient expresses a desire to discontinue therapy; and
- Opioid treatment appears to be causing harm to the patient, particularly if harm exceeds benefit.[14]

The decision to discontinue opioid treatment should ideally be made jointly with the patient and, if appropriate, the family/caregiver.[17] This decision should include careful consideration of the outcomes of ongoing monitoring.

**11.2** When possible, offer to assist patients in safely discontinuing medications, even if they have withdrawn from treatment or been discharged for agreement violations.[14]

The goal is to taper all patients off opioid medications safely. If the patient is discharged, the health care provider is obliged to offer continued monitoring for 30 days post-discharge. Possible complications of opioid

withdrawal should be taken into consideration when discontinuing or tapering opioid medications.

Tools to accompany *Recommendation 11:*

- Strategies for Tapering and Weaning
  http://health.utah.gov/prescription/pdf/guidelines/Strategies_tapering_weaning.pdf

## Documentation and Medical Records

### 12. Health care providers treating chronic pain patients with opioids should maintain records, in accordance with state and federal law, documenting patient evaluation, treatment plan, discussion of risks and benefits, informed consent, treatments prescribed, results of treatment, and any aberrant behavior observed. [9,13,14,15,17]

**12.1** A written treatment plan should document objectives that will be used to evaluate treatment success.[9,13,14,15,17]

**12.2** Opioid prescriptions should be written on tamper-resistant prescription paper to help reduce the likelihood of prescription fraud or misuse.[15]

To reduce the chance of tampering with the prescription, write legibly, and keep a copy.[15]

**12.3** Assessment of treatment effectiveness should be documented in the medical record.[9,13,15]

Both the underlying medical condition responsible for the pain, if known, and other medical conditions that may affect the efficacy of treatment or risks of adverse events should be assessed and documented at every visit.

Health care providers should consider utilizing a standardized approach such as "The Four A's" or "The SAFE Tool" for medical documentation. The Four A's considers four areas of concern: Analgesia, Activity, Adverse effects, and Aberrant behavior.[21] The SAFE Tool is a numerical five point scoring system that helps to guide the health care provider toward broader views of treatment options.[23] It considers four areas of concern: social functioning (S), analgesia (A), physical function (F), and emotional functioning (E).

The Four A's can be remembered as:

- Analgesia: inquire about level of pain (current, recent, trends, etc.);
- Activity: assess both the patient's function and overall quality of life;
- Adverse events: determine whether the patient is having medication side effects; and
- Aberrant behavior: regularly evaluate for possible drug abuse-related behavior.

The SAFE Tool can be remembered as:

- Social functioning: inquire about family and employment relationships;
- Analgesia: inquire about level of pain (current, recent, trends, etc.);
- Physical functioning: inquire about how well the patient is meeting goals; and
- Emotional functioning: ask about changes in the patient's mental health status.

**12.4** Adherence to the treatment plan, including any evidence of aberrant behavior, should be documented in the medical record.[14]

Specific components of the treatment plan for which adherence should be assessed include:

- Use of opioid analgesics; and
- Follow-up referrals, tests, and other therapies.

Health care providers are encouraged to make use of resources designed to assist them in managing the care of patients with aberrant behavior. Serious non-adherence issues (e.g., illegal, criminal, or dangerous behaviors, including altering of prescriptions) may also warrant immediate discontinuation of opioid treatment.

Tools to accompany *Recommendation 12:*

- Checklist for Adverse Effects, Function, and Opioid Dependence
  http://health.utah.gov/prescription/pdf/guidelines/checklist%20for%20adverse%20effects.pdf
- Signs of Substance Misuse
  http://health.utah.gov/prescription/pdf/guidelines/signs_substance_misuse.pdf
- Federal Laws on Prescribing Controlled Substances (21 CFR 1306 et. seq.)
  http://www.deadiversion.usdoj.gov/21cfr/cfr/
- Osteopathic Rules on Prescribing for Intractable Pain (OAC 510:5-9-1 et. seq.)
  http://www.ok.gov/osboe/documents/RULES.pdf
- Medical Board Rules on Prescribing for Intractable Pain (OAC 435:10-7-11 et. seq.)
  http://www.okmedicalboard.org/download/457/MDRULES.pdf

## Consultation and Management of Complex Patients

### 13. Health care providers should consider consultation for patients with complex pain conditions, serious co-morbidities and mental illness, a history or evidence of current drug addiction or abuse, or when the provider is not confident of his or her ability to manage the treatment.[9,13]

**13.1** Prescribers may wish to consider referring patients if any of the following conditions or situations are present, or if other concerns arise during treatment:

- The patient has a complex pain condition and the clinician wishes verification of diagnosis;
- The patient has significant co-morbidities, including psychiatric illness;
- The patient is at high risk of aberrant behavior or addiction; or
- The clinician suspects the development of significant tolerance, particularly at higher doses.

The main goal of a consultation is for the prescribing clinician to receive recommendations for ongoing treatment.

**13.2** Patients with a history of addiction or substance use disorder or who have positive drug screens indicative of a problem should be closely monitored (e.g., more frequent random drug screens, random pill counts) or considered for referral to an addiction specialist for evaluation of recurrent risk and for assistance with treatment.[9,13,14]

Although this is a desirable approach, it is recognized that following this recommendation may not be feasible in parts of Oklahoma where there is a shortage of readily available addiction specialists.

**13.3** Pain patients addicted to medications/drugs should be referred to a pain management and/or mental health/substance use disorder specialist, if available, for recommendations on the treatment plan and assistance in management.

The health care provider may consider prescribing opioid medications for pain even if the patient has a self-reported or documented previous opioid abuse problem, as long as monitoring is performed during the titration and maintenance phase.

**13.4** Patients with a coexisting psychiatric disorder should receive ongoing mental health support and treatment while receiving an opioid medication for pain control.

Management of patients with a coexisting psychiatric condition may require extra care, monitoring, or documentation.[17,19] Consultation can be obtained to assist in formulating the treatment plan and establishing a

plan for coordinated care of both the chronic pain and psychiatric condition(s).

Tools to accompany *Recommendation 13:*

- Strategies for Tapering and Weaning
  http://health.utah.gov/prescription/pdf/guidelines/Strategies_tapering_weaning.pdf

### 14. Health care providers should generally not provide replacement prescriptions for opioids that have been lost, stolen, or destroyed.

Patients misusing controlled substances frequently report their opioid medications as having been lost or stolen. Pain specialists routinely stipulate in pain agreements with patients that lost or stolen controlled substances will not be replaced. Most written agreements between chronic pain patients and pain management physicians, including the Health Resources and Services Administration (HRSA) toolkit sample pain agreement, state that prescriptions for opioids will not be replaced.[10]

The diversion of prescribed opioids is common. One study looked at completed patient surveys and determined that 45% of respondents reported some form of drug diversion at least once. Stolen medication was the most prevalent method of drug diversion, and 30% of respondents reported at least one incident of stolen medication.[11] Another survey study found that among persons 12 years and older who abused opioid pain medications (2009-2010), 71.2% came from friends or relatives; 55% were given to the abuser, while 11.4% were purchased, and 4.8% were stolen.[12,13]

### 15. The administration of intravenous and intramuscular opioids for the relief of exacerbations of chronic pain is discouraged, except in special circumstances.

Parenteral opioids should be generally avoided for the treatment of chronic pain because of their short duration and potential for addictive euphoria. For chronic pain, oral opioids are superior to parenteral opioids in duration of action and provide a gradual decrease in the level of pain control. When there is evidence or reasonable suspicion of an acute pathological process causing the acute exacerbation of chronic pain, parenteral opioids may be appropriate.

Tools to accompany *Recommendation 15:*

- Dosing Guidelines
  http://health.utah.gov/prescription/pdf/guidelines/dosing_guidelines.pdf
- Current Opioid Misuse Measure (COMM)
  http://health.utah.gov/prescription/tools.html (see *Tools to Screen for Risk of Complications*)

## Methadone and Extended Release/Long-Acting Opioids

### 16. Long-acting opioids are associated with an increased risk of overdose death, and should only be prescribed by health care providers familiar with their indications, risks, and need for careful monitoring.

**16.1** The prescription use of methadone remains controversial due to concerns about its efficacy and safety. During the past two decades methadone-related death rates increased in Oklahoma and the U.S. From 2007-2011, methadone was listed in the cause of death in 21% of prescription drug-related unintentional poisoning deaths in Oklahoma.[1]

The half-life of methadone is long and unpredictable, increasing the risk of inadvertent overdose. The peak respiratory depressant effect of methadone occurs later and lasts longer after treatment initiation or dosage change than does the peak analgesic effect. Conversion tables that have been established to assist with converting a patient from another opioid medication to methadone are considered by many experts to be unreliable.

Methadone metabolism is complicated and varies among individuals. Methadone interacts with several other medications that can alter its metabolism, changing the effects of a given dose on pain and on respiratory depression. Potential for interactions should be considered before starting methadone in a patient taking other medications, and before starting any medication in a patient taking methadone.

Methadone can prolong the rate-corrected QT interval (QTc), increase the risk of Torsades de Pointe, and sudden cardiac death. Caution should be used in prescribing methadone to any patient at risk for prolonged QTc interval, including those with structural cardiac disease, cardiac arrhythmias or cardiac conduction abnormalities and in patients taking another medication associated with QTc interval prolongation.[24] An online reference of such medications is available at: http://www.azcert.org/medical-pros/drug-lists/drug-lists.cfm.

Health care providers should consider obtaining an electrocardiogram (ECG) to measure the QTc interval in patients treated with methadone, especially at higher doses. A recently published consensus guideline recommended that an ECG be performed before prescribing methadone, within the first 30 days, and annually. Additional ECG examinations were recommended if the methadone dose exceeds 100 mg per day or if a patient on methadone has unexplained syncope or seizure. Guidance was provided for actions to be taken at two levels of QTc prolongation (450-500 ms and greater than 500 ms).[25]

Methadone and other opioids have been associated with worsening obstructive sleep apnea and new onset of central sleep apnea. Clinicians should question patients about symptoms and signs of sleep apnea and consider obtaining a sleep study in patients treated with opioids if they develop any signs of sleep-disordered breathing or respiratory depression. This is particularly important for patients receiving higher doses of opioid medications. In a recent study, 92% of patients on opioid doses at or above 200 MMEs had developed ataxic or irregular breathing.[25]

**16.2** If extended release/long-acting opioids are prescribed, consideration should be given to the increased risk of overdose with these medications. Prescribers should consider the current risk evaluation and implement mitigation strategies and close monitoring to reduce the possibility of adverse events.

Tools to accompany *Recommendation 16:*

- Dosing Guidelines
  http://health.utah.gov/prescription/pdf/guidelines/dosing_guidelines.pdf
- The Role of Methadone in the Management of Chronic Non-Malignant Pain
  http://health.utah.gov/prescription/pdf/guidelines/role_of_methadone.pdf
- Electronic MME Dosing Calculator
  http://agencymeddirectors.wa.gov/mobile.html

## Education of Chronic Pain Patients on Using Opioids

### 17. When opioids are prescribed for treatment of chronic pain, the patient should be counseled to store the medications securely and never to share with others. In order to prevent non-medical use of the medications, it is also recommended that patients dispose of medications when the pain has resolved.

It is important that patients understand the need to store medications securely. Health care providers should encourage patients to keep medications in a locked environment rather than in easily accessible locations, such as the bathroom or kitchen cabinet, where they are accessible to unsuspecting children, curious teenagers, and can be a target for theft. Tell the patient that if they have leftover medications after they have recovered, they should dispose of their medications immediately to help protect them from being a target for theft as well as protect others from getting into the medications.

Tools to accompany *Recommendation 17:*

- United States Food and Drug Administration (FDA) Guidelines on Proper Disposal of Prescription Drugs http://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingOver-the-CounterMedicines/ucm107163.pdf
- Oklahoma Bureau of Narcotics and Dangerous Drugs Take Back Container Locations http://www.ok.gov/obndd/documents/TakeBackBoxes.pdf

## Guidelines Tools

**Tools to use in evaluation and monitoring:**

- Pain Management Evaluation Tool
  http://health.utah.gov/prescription/pdf/guidelines/PainManagementWorksheet.pdf
- Patient Pain and Medication Tracking
  http://health.utah.gov/prescription/pdf/guidelines/PatientPain-FunctionTracking.pdf
- Sheehan Disability Scale
  http://health.utah.gov/prescription/pdf/guidelines/SheehanDisabilityScale.pdf
- Brief Pain Inventory Form
  http://health.utah.gov/prescription/pdf/guidelines/BriefPainInvNPEC.pdf
- Treatment Plan for Prescribing
  http://health.utah.gov/prescription/pdf/guidelines/treatment_plan.pdf
- SF-12
  http://health.utah.gov/prescription/pdf/guidelines/SF-12v2Standard-Sample.pdf

**Tools to screen for risk of complications:**

- Oklahoma Prescription Monitoring Program
  http://www.ok.gov/obndd/Prescription_Monitoring_Program/
- Current Opioid Misuse Measure (COMM)
  http://health.utah.gov/prescription/tools.html
- SOAPP-R
  http://health.utah.gov/prescription/tools.html
- Opioid Risk Tool
  http://health.utah.gov/prescription/pdf/guidelines/ORTwithout_scoring.pdf
- Urine Drug Testing Devices
  http://health.utah.gov/prescription/pdf/guidelines/CLIADrugTestlist.pdf
- Signs of Substance Misuse
  http://health.utah.gov/prescription/pdf/guidelines/signs_substance_misuse.pdf
- Checklist for Adverse Effects, Function, and Opioid Dependence
  http://health.utah.gov/prescription/pdf/guidelines/checklist%20for%20adverse%20effects.pdf

**Informational tools:**

- United States Food and Drug Administration (FDA) Guidelines on Proper Disposal of Prescription Drugs
  http://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingOver-the-CounterMedicines/ucm107163.pdf
- Non-opioid Pain Management Tool
  http://health.utah.gov/prescription/tools.html
- Absolute Contraindications to Opioid Prescribing
  http://health.utah.gov/prescription/pdf/guidelines/absolute_contraindications.pdf
- Strategies for Tapering and Weaning
  http://health.utah.gov/prescription/pdf/guidelines/Strategies_tapering_weaning.pdf
- Information for Patients-Opioid Analgesics for Non-cancer Pain
  http://health.utah.gov/prescription/pdf/guidelines/Information_for_patients.Opioid_analgesics_for_non-cancer_pain.pdf
- The Role of Methadone in the Management of Chronic Non-Malignant Pain
  http://health.utah.gov/prescription/pdf/guidelines/role_of_methadone.pdf
- Dosing Guidelines
  http://health.utah.gov/prescription/pdf/guidelines/dosing_guidelines.pdf

- Prescription Drug Overdose in Oklahoma Brochure
  http://www.ok.gov/health2/documents/DrugOverDoseBrochure_2013.pdf
- Oklahoma Bureau of Narcotics and Dangerous Drugs Take Back Container Locations
  http://www.ok.gov/obndd/documents/TakeBackBoxes.pdf
- Electronic MME Dosing Calculator
  http://agencymeddirectors.wa.gov/mobile.html
- Federal Laws on Prescribing Controlled Substances (21 CFR 1306 et. seq.)
  http://www.deadiversion.usdoj.gov/21cfr/cfr/
- Osteopathic Rules on Prescribing for Intractable Pain (OAC 510:5-9-1 et. seq.)
  http://www.ok.gov/osboe/documents/RULES.pdf
- Medical Board Rules on Prescribing for Intractable Pain (OAC 435:10-7-11 et. seq.)
  http://www.okmedicalboard.org/download/457/MDRULES.pdf

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