

# Regulatory Issues and Opioids

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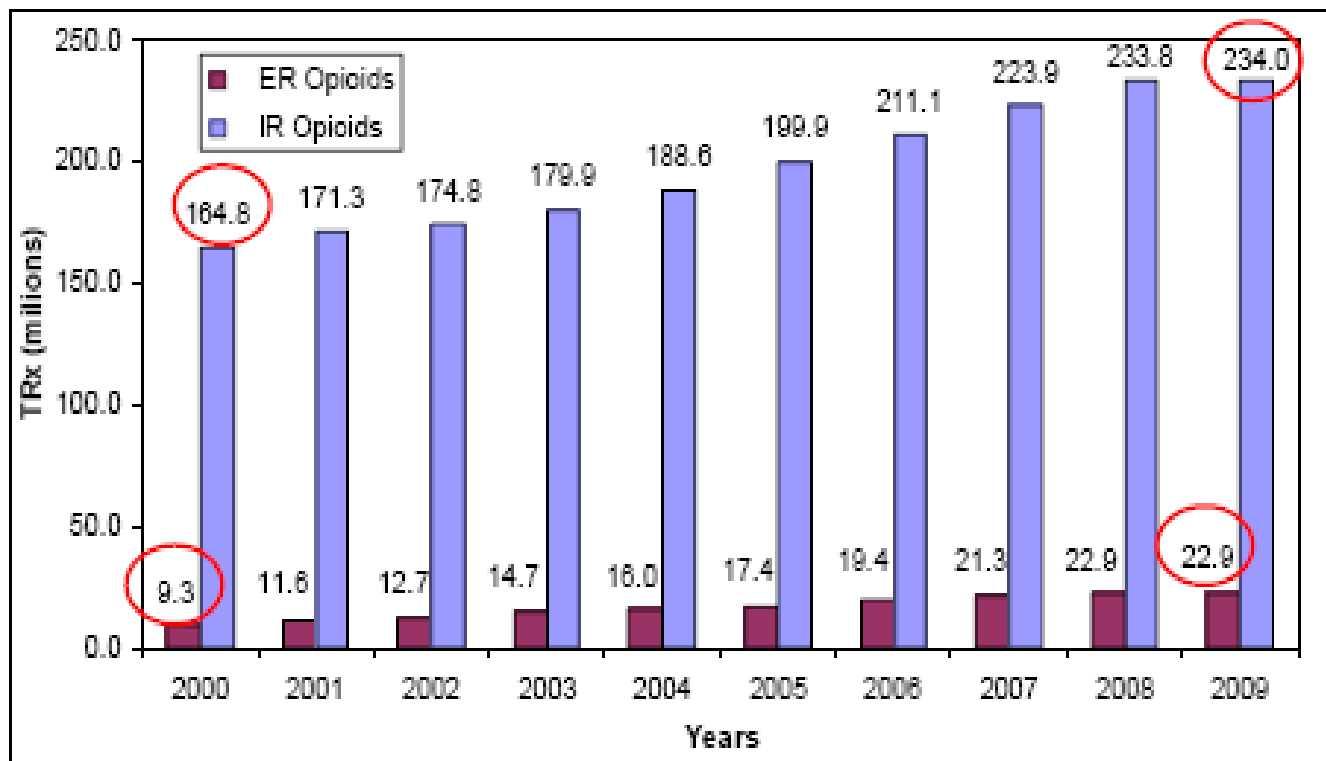
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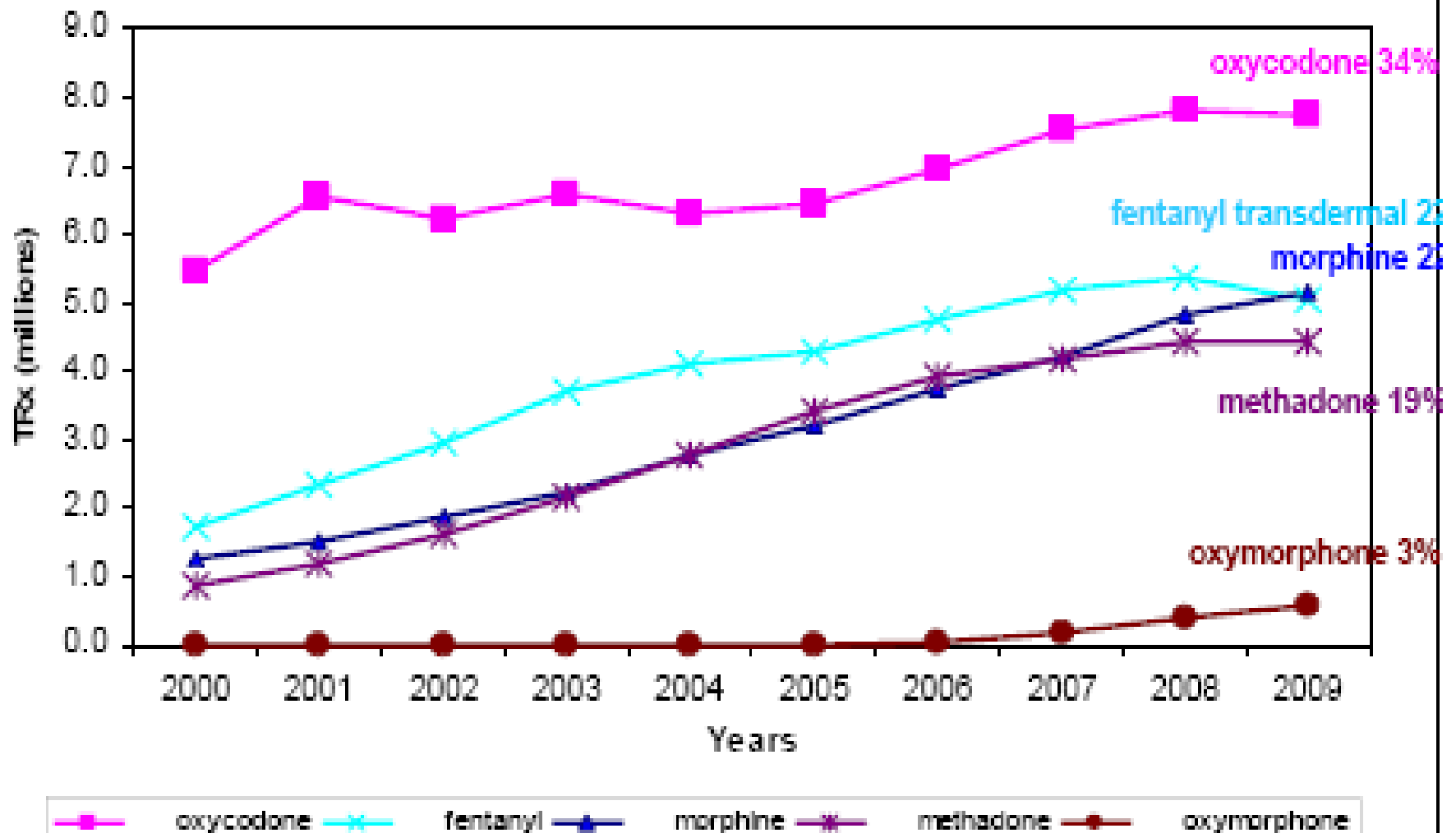
# Learning Objectives

- Incorporate recent regulatory changes in regard to the prescription of opioid medications into practice
- Learn evidence-based approach to use of pain management agreements
- Learn psychosocial factors that are important in the assessment and management of pain

## Total number of prescriptions dispensed for ER/LA and IR opioids from U.S. outpatient retail pharmacies, Year 2000 - 2009

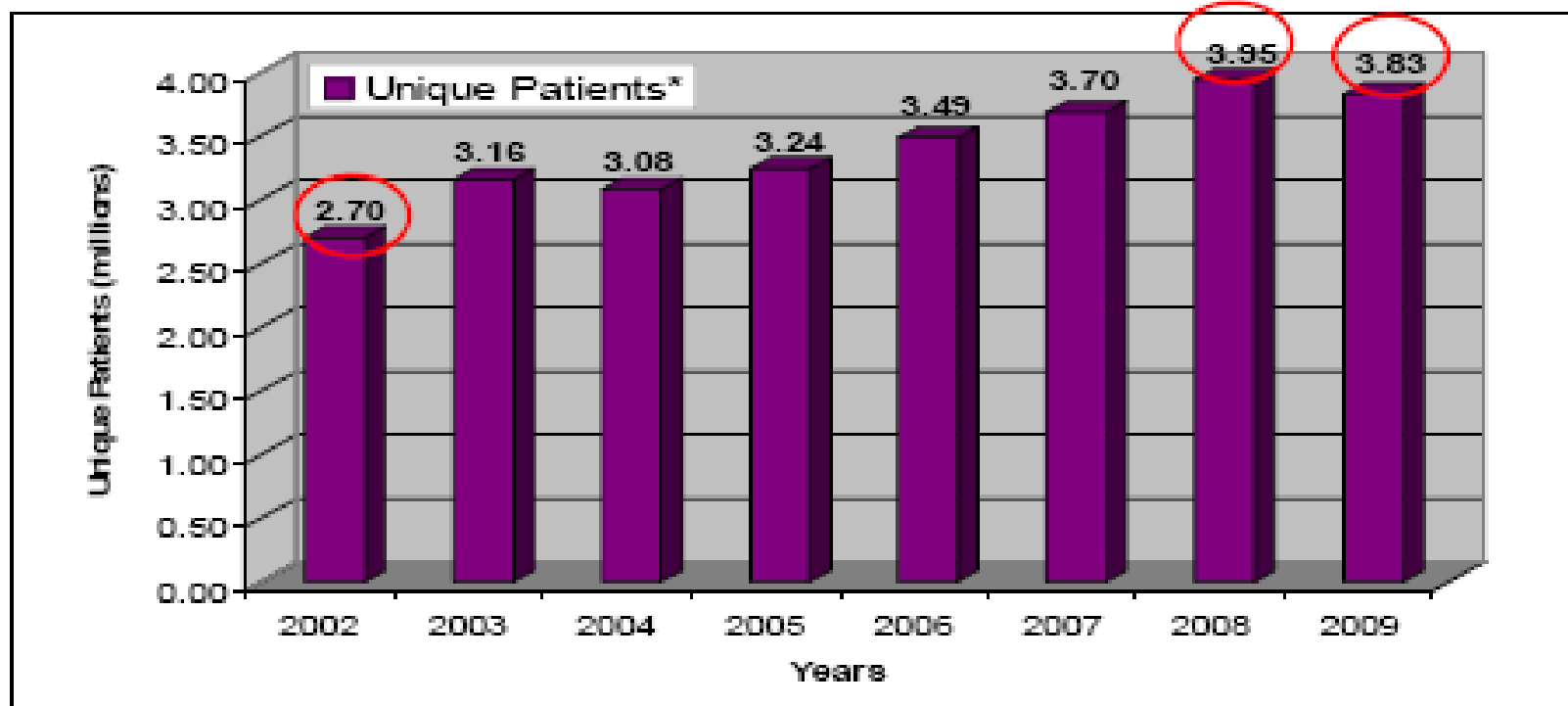
SDI, Vector One®: National. Extracted June 2010.





## Total number of unique patients receiving a dispensed prescription for a ER/LA opioid product from U.S. outpatient retail pharmacies, Years 2002 – 2009

SDI, Total Patient Tracker. Extracted June 2010.



# CDC Per Capita opioid consumption (2010) by state and drug overdose rates by state (2008)

**Figure 1:** Amount of prescription painkillers sold by state per 10,000 people (2010)



Kilograms of prescription painkillers per 10,000 people  
3.7-5.9    □ 6.0-7.2    ■ 7.3-8.4    ■ 8.5-12.6

**Figure 2:** Drug overdose death rates by state per 100,000 people (2008)



Rate per 100,000 people (adjusted for age)  
5.5-9.4    ■ 9.5-12.3    ■ 12.4-14.8    ■ 14.0-27.0

# CDC Drug Mortality Data

- In 2009 almost 425,000 visits to the Emergency Department involved non medical or inappropriate use of opioid medications and 15,600 deaths were attributed to opioid medications and account for >70% of prescription medication overdose related deaths and exceed overdose associated deaths from cocaine and heroin combined
- This number has increased more than fivefold in the last 10 years.

# Opioid Use and Adverse Events

- In the United States in 2010, there were 5.4 opioid-related deaths per 100,000 people and 5.4 admissions for treatment of opioid addiction per 10,000 people.

Source National Vital Statistics

In 1999 there were ~2KG/10,000 persons of opioids prescribed in 2010 that increased to 7.1KG/10,000



# Prescription Drug Use Free Act reauthorization (PDUFA)

- An amendment offered by Joe Manchin and passed by senate would have rescheduled hydrocodone combination products from class III to class II.
- The amendment was subsequently removed following input from specialty groups including the AAHPM with the proviso that the FDA would hold hearings on this
- FDA panel endorsed this in February 2013 by a majority vote

- Citizen's petitions such as a petition by 37 "Physicians for Responsible Prescribing (PROP) to the FDA in 2012 recommending restricting opioid use in non cancer pain to "severe" pain and for only 90 days or less and at a limit of 100MG. For ambulatory patients.

- The need to balance access for relief of suffering needs to be balanced by patient safety education and safeguards
- 2012 FDA and the DEA released its final Risk Evaluation and Mitigation strategy for extended release opioids (REMS)
- Prescription Drug Monitoring Programs (PDMPs)

- <http://Opioids911.org>

**Updated Medication Guides and patient counseling document:** *These materials will contain consumer-friendly information on the safe use, storage, and disposal of ER/LA opioid analgesics.*

# Continuing Education for Prescribers of ER/ LA opioids

- **Training for prescribers:** *Based on the FDA's Blueprint, continuing education (CE) programs are being developed for prescribers of ER/LA opioids and are expected to contain 3 hours of core content. This education will be voluntary and accessible at no charge to practitioners.*

<http://www.ER-LA-opioidREMS.com>

# The reality on the ground

Seventy Four percent of 2015 medical interns at Rush attending a lecture on opioid safety could recollect receiving prior didactic training on this topic

In 2016 84% had no prior didactic training on this topic.

# State Regulatory Requirements

- States with highest rates of adverse events have enacted strictest legislation
- 2012 Washington state tightest to date
- Medicaid and Workers' compensation program require that any patient on >120MG oral morphine equivalent/day must see a pain specialist
- Subsequent waiver for hospice and palliative medicine
- In response to these programs deaths and per capita opioid consumption are dropping but many chronic pain patients report being terminated from their PCPs practices
- Many other states are considering enacting it.

# PDMPs

- All states except Missouri have passed legislation establishing PDMPs
- Although they have been shown to reduce opioid prescription rates they have not been shown to reduce prescription opioid abuse or overdoses



# Schedule II Drugs

- **Schedule II Substances**
- Substances in this schedule have a high potential for abuse with severe psychological or physical dependence.
- Examples of single entity Schedule II narcotics include morphine,
- codeine, and opium. Other Schedule II narcotic substances and their common name
- brand products include: hydromorphone (Dilaudid<sup>®</sup>), methadone (Dolophine<sup>®</sup>),
- meperidine (Demerol<sup>®</sup>), oxycodone (OxyContin<sup>®</sup>), and fentanyl (Sublimaze<sup>®</sup> or
- Duragesic<sup>®</sup>).

- **Schedule III Substances**

- Substances in this schedule have a potential for abuse less than substances in Schedules I or II.
- Examples of Schedule III narcotics include combination products containing less than 15 milligrams of hydrocodone per dosage unit (i.e., Vicodin<sup>®</sup>) and products containing not more than 90 milligrams of codeine per dosage unit (i.e., Tylenol with codeine<sup>®</sup>).
- Examples of Schedule III non-narcotics include benzphetamine (Didrex<sup>®</sup>), phendimetrazine, dronabinol (Marinol<sup>®</sup>), ketamine, and anabolic steroids such as oxandrolone (Oxandrin<sup>®</sup>).

- **Schedule IV Substances**

- Substances in this schedule have a lower potential for abuse relative to substances in Schedule III.
- Examples of a Schedule IV narcotics include propoxyphene (Darvon<sup>®</sup> and Darvocet-N 100<sup>®</sup>).
- Other Schedule IV substances include alprazolam (Xanax<sup>®</sup>), clonazepam (Klonopin<sup>®</sup>), clorazepate (Tranxene<sup>®</sup>), diazepam (Valium<sup>®</sup>), lorazepam (Ativan<sup>®</sup>), midazolam (Versed<sup>®</sup>), temazepam (Restoril<sup>®</sup>), and triazolam (Halcion<sup>®</sup>).

- **Schedule V Substances**
- Substances in this schedule have a lower potential for abuse relative to substances listed in Schedule IV and consist primarily of preparations containing limited quantities of certain narcotic and stimulant drugs. These are generally used for antitussive, antidiarrheal and analgesic purposes.
- Examples include cough preparations containing not more than 200 milligrams of codeine per 100 milliliters or per 100 grams (Robitussin AC<sup>®</sup>, and Phenergan with Codeine<sup>®</sup>).

- U.S. FDA – TIRF-REMS ACCESS Program (IR Fentanyl Products)
- *In March 2012, the Transmucosal Immediate Release Fentanyl (TIRF) Risk Evaluation and Mitigation Strategy (REMS) ACCESS program was instituted. This is an FDA-required program designed to ensure informed risk-benefit decisions before initiating treatment, and during treatment to ensure appropriate use of TIRF medicines. The purpose of TIRF-REMS ACCESS is to mitigate risks of misuse, abuse, addiction, overdose, and serious complications due to errors in the use of TIRF medicines.*

<http://www.tirfremaccess.com/>

- DEA - Announcements
- **From:** US Department of Justice, Drug Enforcement Administration.
- *Effective December 19, 2007 the DEA's Notice of Proposed Rulemaking to permit an individual practitioner to issue multiple prescriptions to be filled sequentially and authorizing a patient to receive a total of up to a 90-day supply of a Schedule II controlled substance (e.g., opioids) became finalized.*

# DEA Guidelines 2006

- **Safeguards for Prescribers**
- In addition to the required security controls, practitioners can utilize additional measures to ensure security. These include:
  - 1. Keep all prescription blanks in a safe place where they cannot be stolen; minimize the number of prescription pads in use.
  - 2. Write out the actual amount prescribed in addition to giving a number to discourage alterations of the prescription order.
  - 3. Use prescription blanks only for writing a prescription order and not for notes.
  - 4. Never sign prescription blanks in advance.
  - 5. Assist the pharmacist when they telephone to verify information about a prescription order; a corresponding responsibility rests with the pharmacist who dispenses the prescription order to ensure the accuracy of the prescription.
  - 6. Contact the nearest DEA field office (see Appendix E) to obtain or to furnish information regarding suspicious prescription activities.
  - 7. Use tamper-resistant prescription pads.

# Disposal of opioids

- **Disposal of Controlled Substances**
- A practitioner may dispose of out-of-date, damaged, or otherwise unusable or unwanted controlled substances, including samples, by transferring them to a registrant who is authorized to receive such materials. These registrants are referred to as “Reverse Distributors.” The practitioner should contact the local DEA field office (See Appendix E) for a list of authorized Reverse Distributors. Schedule I and II controlled substances should be transferred via the DEA Form 222, while Schedule III–V compounds may be transferred via invoice. The practitioner should maintain copies of the records documenting the transfer and disposal of controlled substances for a period of two years.



# Faxed prescriptions for class II controlled substances

- In order to expedite the filling of a prescription, a prescriber may transmit a Schedule II prescription to the pharmacy by facsimile. The original Schedule II prescription must be presented to the pharmacist for review prior to the actual dispensing of the controlled substance.
- Parenteral (IV or intraspinal) and oral (for resident of a long term care facility or hospice patient)
- In an emergency, a practitioner may call-in a prescription for a Schedule II controlled substance by telephone to the pharmacy, and the pharmacist may dispense the prescription provided that the quantity prescribed and dispensed is limited to the amount adequate to treat the patient during the emergency period.
- The prescribing practitioner must provide a written and signed prescription to the pharmacist postmarked within seven days. Further, the pharmacist must notify DEA if the prescription is not received. There is no regulation specifying how many days or doses constitute an emergency supply

# Exceptions for Schedule II Faxed Prescriptions

- 1. A practitioner prescribing Schedule II narcotic controlled substances to be compounded for the direct administration to a patient by parenteral, intravenous, intramuscular, subcutaneous or intraspinal infusion may transmit the prescription by facsimile. The pharmacy will consider the facsimile prescription a “written prescription” and no further prescription verification is required. All normal requirements of a legal prescription must be followed.
- 2. Practitioners prescribing Schedule II controlled substances for residents of Long Term Care Facilities (LTCF) may transmit a prescription by facsimile to the dispensing pharmacy. The practitioner’s agent may also transmit the prescription to the pharmacy. The facsimile prescription serves as the original written prescription for the pharmacy.
- 3. A practitioner prescribing a Schedule II narcotic controlled substance for a patient enrolled in a hospice care program certified and/or paid for by Medicare under Title XVIII or a hospice program which is licensed by the state may transmit a prescription to the dispensing pharmacy by facsimile. The practitioner or the practitioner’s agent may transmit the prescription to the pharmacy. The practitioner or agent will note on the prescription that it is for a hospice patient. The facsimile serves as the original written prescription

- **Schedule III-V Substances**
- A prescription for controlled substances in Schedules III, IV, and V issued by a practitioner, may be communicated either orally, in writing, or by facsimile to the pharmacist, and may be refilled if so authorized on the prescription or by call-in.
- **Refills**
- Schedule III and IV controlled substances may be refilled if authorized on the prescription. However, the prescription may only be refilled up to five times within six months after the date on which the prescription was issued. After five refills or after six months, whichever occurs first, a new prescription is required.
- **Facsimile Prescriptions for Schedule III-V Substances**
- Prescriptions for Schedules III-V controlled substances may be transmitted by facsimile from the practitioner or an employee or agent of the individual practitioner to the dispensing pharmacy. The facsimile is considered to be equivalent to an original prescription.
- **Telephone Authorization**
- A pharmacist may dispense a controlled substance listed in Schedule III, IV, or V
- pursuant to an oral prescription made by an individual practitioner and promptly
- reduced to writing by the pharmacist containing all information required for a valid
- prescription, except for the signature of the practitioner.

# Prescription Information, Refills and Prescription Series

- Prescriptions for Schedule II opioids must be written, dated and signed on the day issued
- It is permissible to write a prescription series for up to a 90 day supply of medication e.g. patient can be given 3 prescriptions each for 30 days worth of the same drug, with two of the prescriptions noting: “Do not fill until [1 or 2 months, respectively, from the issue date.]”

# Partial dispensing

- Permissible if the pharmacist can't supply the full quantity at one time. The remaining portion of the prescription must be filled within 72 hours.
- For LTCF patients or patients with a terminal diagnosis partial quantities up to 60 days can be filled. The script must specify if the patient is “terminally ill” or in a LTCF

# Delivery of a Controlled Substance to Persons Outside the U.S.

- Controlled substances that are dispensed pursuant to a legitimate prescription may not be delivered or shipped to individuals in another country. Any such delivery or shipment is a prohibited export under the CSA.

# Illinois Department of Professional Regulation

- The Illinois Department of Human Services Prescription Monitoring Program – Prescription Information
- Library (PIL) can be accessed at [www.ilpmp.org](http://www.ilpmp.org). The program can also be reached by phone at 217- 685-0426 or by fax at 217-557-7975.
- IDFPR and the DEA strongly encourage practitioners and pharmacists to utilize their state Prescription Monitoring Program. Title 21, Code of Federal Regulations section 1306.04 (a) states that the
- responsibility for the proper prescribing and dispensing of controlled substances is on the prescribing practitioner, but a corresponding responsibility rests with the pharmacist who fills the prescription

# Pharmacist changes to prescriptions

- Pharmacists may independently add or change the patient's address
- After consultation with the prescriber the pharmacist may add or change the dosage form, drug strength, drug quantity, directions for use and issue date



# Patients with addictive disease or in a drug treatment program

- Clinicians approved for Schedule II prescribing can prescribe any Schedule II drug including methadone and buprenorphine for pain.
- They are strongly recommended to obtain a pain management and addictionology consultation

# Recommended elements of an agreement for pain management

- Potential risks and benefits of long term opioid therapy
- Potential side effects (short and long term e.g. nausea, constipation, libido loss, hypogonadism and secondary osteoporosis)
- Cognitive side effects
- Likelihood of tolerance and dependence
- Risk of drug interactions and over sedation
- Risk of impaired motor skills (and risk of driving)
- Limited evidence of benefit of long term opioid therapy
- Responsibilities for safe storage

# SFHP PAIN MANAGEMENT PROGRAM: GUIDELINES FOR USE OF OPIOIDS IN CHRONIC NON-CANCER PAIN

Consider use of validated screening tools to assess effectiveness of opioid therapy and objectively assess risk. The PEG tool is simple, quick and easily administered, and consists of three questions related to Pain, Enjoyment of Activities, and General Functioning

. The Opioid Risk Tool is a validated self-assessment tool, and the DIRE tool is a validated clinician assessment.

# SFHP PAIN MANAGEMENT PROGRAM: GUIDELINES FOR USE OF OPIOIDS IN CHRONIC NON-CANCER PAIN

Clinicians should screen all chronic patients for depression and other mental illness, and refer for cognitive behavioral therapy and other appropriate behavioral health interventions. CBT has been proven to be effective in improving pain and function for patients with chronic non-cancer pain.

In one study, 40% of fatal opioid overdoses were in patients with mental illness.

*Hall et al. Patterns of Abuse Among Unintentional Pharmaceutical Overdose Fatalities, JAMA 2008; 300 (22); 2613-2620*

# SFHP PAIN MANAGEMENT PROGRAM: GUIDELINES FOR USE OF OPIOIDS IN CHRONIC NON-CANCER PAIN

Clinicians should order a random urine drug screen for all patients at initiation of treatment, and at least once a year, to detect prescribed and non-prescribed opioids and other controlled or illicit drugs. Monitoring should increase in frequency in the presence of behaviors concerning for substance abuse. Rationale: physicians are extremely inaccurate in predicting substance use based on clinical judgment alone

*Vijayaraghavan M, Penko J, Guzman D, Miaskowski C, Kushel MB. Primary Care Providers' Judgments of Opioid Analgesic Misuse in a Community-Based Cohort of HIV-Infected Indigent Adults. J Gen Intern Med. 2011;26(4):412–8.*

# SFHP PAIN MANAGEMENT PROGRAM: GUIDELINES FOR USE OF OPIOIDS IN CHRONIC NON-CANCER PAIN

- Practices should develop standardized policies ensuring consistent practices by prescribers for common challenges in pain management: new patients, early refill requests, management of unexpected urine drug screens, and management of concerning behaviors, including guidelines on when discontinuation or weaning of opioids is required. Practices could consider a tiered approach, depending on the behavior. Examples of successive tiers include: warning/concerned discussion, increased monitoring, decreased dosage of medication, or cessation of medication. Rationale: wide variation in the management of concerning behaviors by prescribers at a clinic or practice site contributes to doctor-shopping and has a negative impact on patient safety, provider morale and staff morale.

# Driving

- Patient agreement should stipulate that patient agrees not to drive while under the influence of a narcotic medication

# Pill counts

- Confirm adherence, minimize diversion
- 28 days instead of 30
- Prescribe so patient has residual medications at appointments
- Patient brings in medications at each visit
- If concerned, can do random pill counts





# Outpatient management of the chemically-dependent pain patient

- Maximally structured approach includes:
  - Frequent visits
  - Pain agreement
  - Limited supply of medications (weekly, monthly)
  - **Rotate from short acting agents to primarily long-acting opioids with low street value**
  - Ask pharmacy to run a profile of recently filled medications.
  - Urine Point of Service toxicology and Mass Spectroscopy (MS)/Gas Chromatography (GC)
  - Recovery program/psychotherapy
  - Referral to addiction specialist

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# CAM – other

- Integration of cognitive behavioral therapies into management of pain targeted to specific symptoms such as pain and fatigue can significantly reduce pain severity **Level of Evidence I**

Given B 2002, Anderson KO 2007

- Art Therapy and Music Therapy have been shown to be helpful for procedural pain in pediatric cancer patients
- J of Pediatric Oncol Nursing 2010 May-Jun;27(3):146-55

- RCTs have also shown benefits for hypnosis on procedural and peri-operative pain

J of the National Cancer Institute 99:17 2007

# Mindfulness based stress reduction

- Systematic review of 3 RCTs with 119 adults effective for short and long term relief of chronic low back pain in younger adults
- Negative results in older adults

Cramer H BMC Complement Altern Med. 2012

- 8 week RCT trial of MBSR vs. a multidisciplinary pain clinic

-MBSR was as effective at reducing pain intensity and lessening pain distress at 6months

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# PTSD and pain management

- PTSD rates higher than average in Chicago (as high as 43%, per 2011 Stroger Hospital study)
- Approximately 1/3 of patients seen in non-malignant palliative clinic with PTSD/trauma history
- PTSD and chronic pain symptom overlap: anxiety, hypervigilance, emotional lability, and elevated somatic focus



# Psychosocial factors

- Community violence
  - Higher PTSD rates
  - Lack of safety for utilization of public transit (more frequent missed appointments as a result)
- Impact of poverty on access to medical care
  - Food deserts- limited access to healthy living choices
  - Medicaid/insurance challenges with opioid coverage

# Practice limitations

- Group practice model
- Variations among providers regarding expertise in non-malignant pain management
- Provider self-awareness of implicit bias
- Ancillary/support staff limitations
- Insurance issues
- Lack of referral sources (i.e., addiction specialists)
- Co-managing pain with methadone clinics

# Implicit Bias

- Study by Dr. Knox Todd, MD, MPH, uncovered differences in treatment and opioid management for African-American patients compared with white and Hispanic patients
- Implicit Association Test (IAT)  
(<https://implicit.harvard.edu/implicit/>)
  - measures subjects' reaction times in making connections between words or images with positive or negative associations and faces or names of people representing different races, nationalities, ages, sexes, body types, and other categories, along with other objects of interest such as religious symbols and US presidents.

# Clinic Practice Models

- Opioid risk survey tool screening
  - Family history of substance abuse
  - Personal history of substance abuse
  - Pre-adolescent sexual abuse (female)
  - Psychological risk factors
- LCSW for psychosocial assessment of all new chronic (non-malignant pain patients)
  - AUDIT-C, DAST 10, CAGE
- LCSW vs psychosocial oncology assessment for cancer pain patients with identified substance abuse histories
- Standardization of opioid agreement completion
- Outpatient weekly team meetings
- Algorithm for patients who need longitudinal provider
- Smaller quantities of opioid medications- more frequent follow up

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# Conclusions

- Opioid prescriptions and misuse are on the rise
- Universal precautions and safe opioid prescribing should be integrated into everyday palliative medicine practices
- Consider additional non-pharmacological modalities (i.e. CAM) for patients with pain syndromes