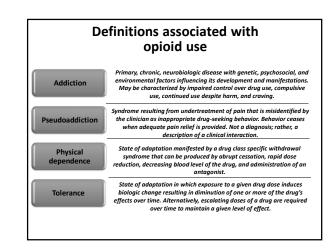
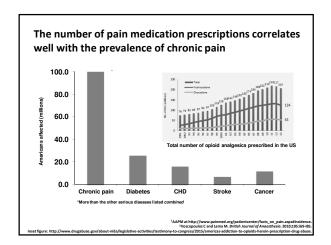
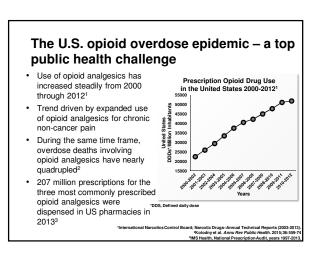
Definitions: Misuse and Abuse

- Misuse: Intentional or unintentional use of medication for medical purpose other than as directed.
- Abuse: Use of illegal drug or intentional self-administration of medication for nonmedical purpose.

American College of Preventive Medicine. http://www.acpm.org/?UseAbuseRxClinRef#Prevalence. Passik SE, et al. Pallative Care and Supportive Oncology, 2002

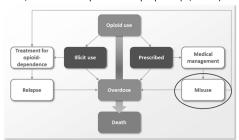


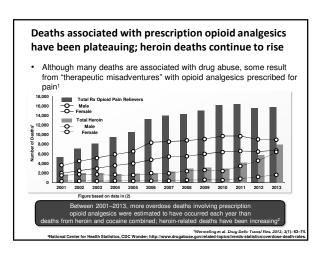




Opioid harm is not limited to non-medical users: the Opioid Continuum

• Misuse can include use with other CNS depressant drugs, dosing errors, or use for non-pain-related purposes (ie, abuse)





Pain Management Goal: Define most appropriate treatment regimen for each person in pain, which could include opioids therapy Fine PG, et al. J. Support Oncol. 2004;2(suppl 4):5-22.
Portenoy RK, et al. in: Lowinson JH, et al, eds. Substance Abuse: A Comprehensive Textbook. 4th ed. Philadelphia, PA: Lippincott, Williams & Wilkins; 2005:863-903.

Rational use of opioid analgesics for chronic cancer and non-cancer pain

- Dichotomy of "pro-opioid" and "anti-opioid" is false, and does not serve healthcare professionals, patients, or society well
 - Ethical healthcare providers are "pro-health" and make treatment decisions within that context
- Clinicians must
 - Learn how to <u>select</u> patients for opioid therapy, when indicated
 - Manage patients on opioid therapy as safely and effectively as possible

Opioid Receptors

- Administered opioids bind to the same three receptor subtypes that normally bind endogenous opioid peptides1
 - $-\ \mu$ (MOP): Analgesia, sedation, respiratory depression, bradycardia, nausea, vomiting, reduced gastric motility
 - δ (DOP): Spinal/supraspinal analgesia, reduced gastric motility
- κ (KOP): Spinal analgesia, diuresis, dysphoria
- Opioids can be classified according to their effect at opioid receptors¹
 - Agonists: act at a receptor to produce maximal receptor-mediated responses; eg, morphine and analgesia
 - Antagonists: bind to a receptor but do not cause a functional response; binding prevents an agonist from binding to that receptor, however, eg, naloxone
 - Partial agonists: can bind to a receptor but result in only partial functional response, independent of the amount of drug administered, eg, buprenorphine
- Most clinically administered opioid analgesics bind to μ (MOP)

Opioids have benefits for many patients with chronic pain

- · Not all patients become dependent or addicted
- Most patients do not experience overdose
- Many patients respond well if not at first to one opioid, then to an alternative opioid(s) and at doses within recommended ranges¹
- But not all types of chronic pain are optimally
 - treated with opioid therapy
 - Headache - Fibromyalgia
- Chronic abdominal pain
- However, there may be more than one pain type in a given patient

180-120 mg/day, MED, in Franklin G. Neurology. 2014. 83:1277-

Drug

Fentanyl transdermal

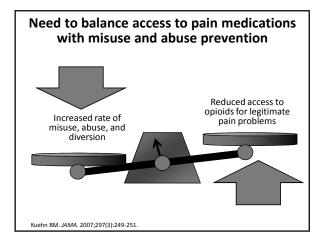
Hydromorphone

Oxymorphone

30 mg

7.5

10



What can we clinicians do?

Proposed critical thinking model for chronic opioid therapy Patient selection Initial patient assessment Comprehensive pain management plan Alternatives to opioid therapy Patient reassessment Continue opioid therapy Implement exit strategy

Goals of clinical assessment

- Achieve diagnosis of pain
- Identify and treat underlying causes of pain
- Identify and treat comorbid conditions
- Evaluate psychosocial factors
- Evaluate functional status (activity levels)
- Set goals
- Develop a targeted treatment plan
- Determine whether a consultation is needed

Evaluation of the patient

- Medical history
- Physical exam including pain assessment
- Review of prior work up, diagnostic tests, prior treatment
- Document the nature, intensity, location of pain, effect of pain on physical and psychological function
- History of substance abuse

Risk stratification

10 Principles of universal precautions

- 1. Diagnosis with appropriate differential
- 2. Psychological assessment including risk of addictive disorders
- Informed consent (verbal or written/signed)
- 4. Treatment agreement (verbal or written/signed)
- 5. Pre-/post-intervention assessment of pain level and function
- 6. Appropriate trial of opioid therapy adjunctive medication
- 7. Reassessment of pain score and level of function
- 8. Regularly assess the "Four A's" of pain medicine: Analgesia, Activity, Adverse Reactions, and Aberrant Behavior
- Periodically review pain and comorbidity diagnoses, including addictive disorders
- 10. Documentation

Gourlay DL, Heit HA. *Pain Med*. 2009;10(Suppl 2):S115-123. Gourlay DL, et al. *Pain Med*. 2005;6(2):107-112.

Risk factors for aberrant behaviors/harm

Age ≤ 45 years Gender Family history of prescription drug or alcohol abuse

Biological

Substance use disorder Preadolescent sexual abuse (in women) Major psychiatric disorder (eg, personality disorder, anxiety or depressive disorder, bipolar

Prior legal problems
History of motor
vehicle accidents
Poor family support
Involvement in a

subculture

Katz NP, et al. Clin J Pain. 2007;23(2):103-118. Manchikanti L, et al. J Opioid Manag. 2007;3(2): 89-100. Webster LR, Webster RM. Pain Med. 2005;6(6):432-442.

disorder)

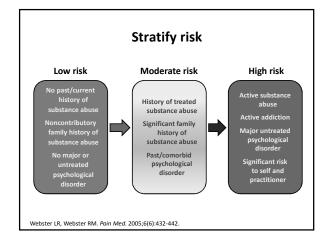
Opioid risk assessment and guidance

- Questionnaires
 - Current Opioid Misuse Measure (COMM)
 - Diagnosis, Intractability, Risk, and Efficacy (DIRE)
 - Opioid Risk Tool (ORT)
 - Screener and Opioid Assessment for Patients in Pain–Revised (SOAPP-R)
 - Screening Instrument for Substance Abuse Potential (SISAP)
- Opioid treatment agreement
- Reviewing PDMP information
- Urine drug testing (UDT)
- Abuse deterrent opioid formulations
- Ongoing patient monitoring

Butler SF, et al. *J Pain*. 2008;9(4):360-372. Katz NP, et al. *Clin J Pain*. 2007;23(2):103-118. Webster LR, Webster RM. *Pain Med*. 2005;6(6):432-442. Manchikanti L, et al. *J Opioid Manag*. 2007;3(2):89-100.

Opioid Risk Tool Mark each box that applies 1. Family history of substance abuse **□** 3 Alcohol Administration Illegal drugs **3** Initial visit Prescription drugs Prior to opioid therapy 2. Personal history of substance abuse **D** 3 **D**3 Alcohol 0-3 (6%): low risk Illegal drugs 4 4 4-7 (28%): moderate risk Prescription drugs **1**5 **1**5 ☐ ≥8 (91%): high risk 3. Age (mark box if between 16 and 45 years) 🗖 1 Percentages indicate proportion of classified patients who exhibited an 4. History of preadolescent sexual abuse **□** 3 **0**0 5. Psychological disease ADD, OCD, bipolar, schizophrenia **D**2 **D**2 Depression **1 1** Scoring totals ADD, attention-deficit disorder; OCD, obsessive-compulsive disorder. Webster LR, Webster RM. Pain Med. 2005;6(6):432-442.

Screener and Opioid Assessment for Patients with Pain (SOAPP®) Short Form Please answer the questions below using the following scale: $0=\mbox{Never}, 1=\mbox{Seldom}, 2=\mbox{Sometimes}, 3=\mbox{Often}, 4=\mbox{Very Often}$ 1. How often do you have mood swings? ratings of all questions. A score of 4 or higher on this 5-question version of the How often do you smoke a cigarette within an hour after you wake up? 0 1 2 3 SOAPP-SF is considered high How often have you taken medication other than the way that it was prescribed? 01234 Score = 3 How often have you used illegal drugs (for example, marijuana, cocaine, etc.) in the past five years? ① 1 2 3 How often, in your lifetime, have you had legal problems or been arrested? Please include any additional information you wish about the above answers. Multiple versions of the SOAPP are available at PainEDU.org © 2012 Inflexxion, Inc. Permission granted solely for use in published format by individual practitioners in clinical practice. No other uses or alterations are authorized or permitted by copyright holder. Permissions questions: painEDU@inflexcion.com. The SOAPP* was developed with grants from the National Institutes of Health and an educational grant from Endo Pharmaceuticals.



Principles for responsible prescribing

- I have resolved key points before initiating opioid therapy
 - Diagnosis established and opioid treatment plan developed
 - · Established level of risk
 - I can treat this patient alone/I need to enlist other consultants to comanage this patient (pain or addiction specialists)
- I have considered nonopioid modalities
 - Pain rehabilitation program
 - · Behavioral strategies
 - Non-invasive and interventional techniques

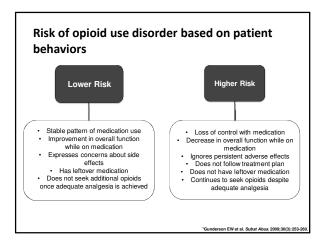
Patient background and personal history influences risk of death from overdose with prescription opioid analgesics

Category	Risk Factor
Demographics ¹	Gender (male?) Between the ages of 45-54 years White or Native American
Socioeconomics ¹	Residing in a rural area Low income Covered by Medicaid
Substance abuse ²	Alcohol consumption Long-term oploid use Recent medical care for opioid poisoning or intoxication Recent released prison or from a mandatory abstinence or drug detox program History of substance abuses*
Prescription drug use	 Filling of multiple prescriptions (doctor shopping)¹ Concomitant use of CNS depressants such as benzodiazepines and tricyclic antidepressants ³
Other	Military veteran ⁴ Mental health problem ¹
	CDC policy document; Overdose and ER Interventions F SAMHSA Opioid Overdose Toolkit. HHS Publication No. (SMA) 13-4742. Rockville, MD: SAMHSA

"CDC policy document; Overdose and ER Interventions Payers MMHSA Opioid Overdose Tooikit. HHS Publication No. (SMA) 13-4742. Rockville, MD: SAMHSA, 2013 "Webster I.R, et al. *Pain Med.* 2011; 12 Suppl 2::258-253 "Seal KH, et al. *J. Am Med.* 2305.2012; 307-340-947

Medical history influences risk of overdose

- · The diagnosis of any of the following medical conditions increases the risk of overdose1
 - Sleep apnea
 - Chronic obstructive pulmonary disease
 - Asthma
 - Chronic kidney disease
 - Liver function abnormalities
 - HIV infection²
- · Risk is also influenced by
 - Post traumatic stress syndrome
 - Other psychological or psychiatric conditions



Risk of overdose for bystanders: children and teenagers

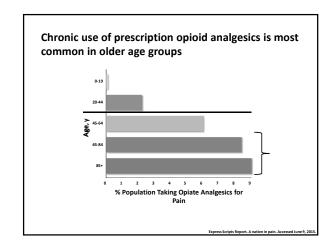
- Young children and teenagers are exposed to prescription opioids that are prescribed for others, most commonly at home1
- A RADARS* study (2003-2006) found that nearly all exposures to prescription opioids in children <6 years old involved ingestion (99%) and occurred in the home (92%)1
 - In 9.179 children, exposures were associated with 8 deaths
- A 10-year study of pediatric poisonings compared against adult prescriptions found adult medications significantly associated with exposures and poisonings in children of all ages with the strongest association for opioids²
 - Across medications, the greatest risk was among children <5 years old, then 13–19 year-olds
 - Rates of ED visits were highest for hypoglycemics (60.1%) but serious injuries and hospitalizations occurred most frequently with opioids (26.8%, 35.2%, respectively)
- Every day, 2,500 US adolescents, aged 12–17, abuse a prescription pain reliever for the
 - Past-month non-medical use of opioid pain relievers highest in 15–24 year-olds⁴

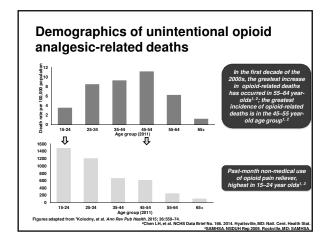
 **Balley II, et al. Ann. Imerg

 **Burghand; et al. Pada

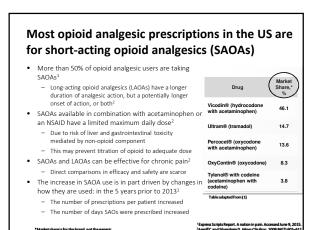
 **Researched Abuse, Diversion and

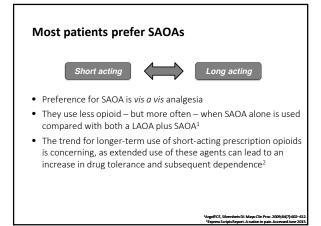
 **Thirty/www.asam.ora/docs/defaults-source/abuse/conjoined addition.in

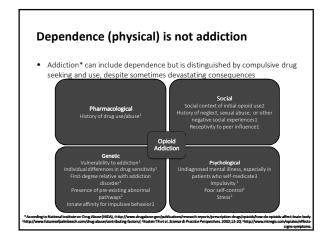


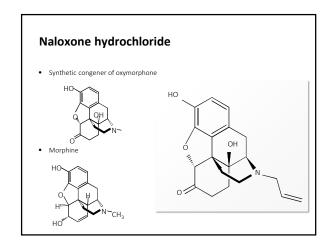


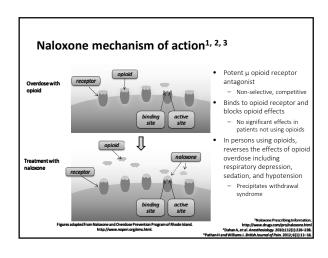


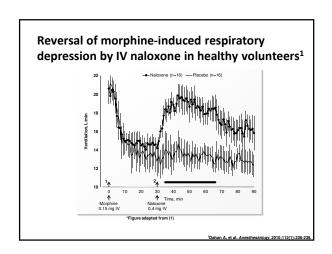


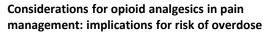












- · Variability in dose requirements
- · Variation in susceptibility to side effects
- · Varying potency among opioids (opioid equivalence)
 - Can result in differences in side effect profiles
 - These differences can be genetic in origin
- · Presence of co-morbidities
 - Depression, may be underdiagnosed
 - Insomnia, very common in patients with chronic pain
- · Dose regimens and tolerance
- Variability in outcomes (starting pain intensity and degree of relief with opioid) measurements

Naloxone in clinical practice

Naloxone has been approved in the US for reversal of the effects of opioid overdose since 1971 Injection indicated for complete Well tolerated but can p

or partial reversal of opioid depression¹

Dosing initiated at 0.4-2 mg and repeated at 2-3 min intervals until patient responds with adequate spontaneous breathing.1

Rapidly distributed throughout the body1:

 C_{max} : 1.07 ng/mL² T_{max}: 20 min²

Duration of effect 30-90 min; further doses may be required if patient has taken long-acting opioids.

t_{1/2}: 30-81 min

Well tolerated but can precipitate opioid withdrawal syndrome in patients with opioid dependence Body aches

Runny nose

Diarrhea Shaking

 Sneezing Irritability

Increased blood

• Sweating pressure Tachycardia

Nausea/vomiting • Yawning Piloerection Weakness

2-3 criteria, mild

4-5 criteria, moderat

6-7 criteria, sever

Clinical interface between pain and addiction

- Pain and addiction are complex; both have strong behavioral components¹
- Both the addiction and pain systems are dependent on opioid agonist activity at the mu-receptor2
- Both the treatment of pain with opioid analgesics and abuse of opioids interact at the brain-reward center in the limbic system, which leads to feelings of pleasure or reward³
- Genetic data suggest that pain, opioid analgesia, and opioid addiction may share similar patterns of gene expression1
- The goals of pain treatment are to reduce pain and suffering, enhance quality of life, and increase the ability to function, which requires achieving a balance between treating the pain and avoiding diversion and abuse⁴
- Developing and following a treatment plan, and monitoring behaviors of patients treated with opioid analgesics can help achieve treatment goals^{4,5}

'ASAM Essentials of Addiction Medicine. 2015. (Chapter ss). "Trescot AM, et al. Pair Physician. 2008;11:5133-515. "Edwards S, Koob GF. Future Neurol. 2010;5(3):339-40. "Passik SD, Krah K. L. pp. Cin Pypriopham. 2008;16(3):400-40. "Gunderson EW et al. Subst Abus. 2009;00:253-26

Criteria for substance use disorder diagnosis:1 patient must meet at least 2 criteria

- Repeatedly unable to carry out major obligations at work, school, or home due to opioid use
- Recurrent use of opioids in physically hazardous situations
- Continued use despite persistent or recurring social or interpersonal problems caused or made worse by opioid use
- Tolerance as defined by either a need for markedly increased amounts tachieve intoxication or desired effect or markedly diminished effect with continued use of the same amount
- Withdrawal manifesting as either characteristic syndrome or the substance is used to avoid withdrawal
- Using greater amounts or using over a longer time period than intended Persistent desire or unsuccessful efforts to cut down or control opioid use Spending a lot of time obtaining, using, or recovering from using opioids
- Stopping or reducing important social, occupational, or recreational activitie due to opioid use
- Consistent use of opioids despite acknowledgment of persistent or recurrent physical or psychological difficulties from using opioids

Craving or a strong desire to use opioids

¹American Psychiatric Association (2013). Diagnostic and Statistical Manual of Mental Dis

Opioid overmedication and potential for overdose1

OVERMEDICATION

Unusual sleepiness or drowsiness Mental confusion Slurred speech Slow or shallow breathing

OVERDOSE

Face clammy and pale Body is limp Fingernails and lips tinged blue or purple

slow or stopped Cannot be awakened Death rattle

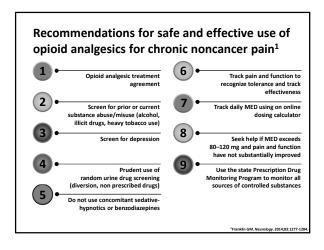
HHS Publication No. (SMA) 13-4742. Rockville, MD: Substance Abuse and Mental Health Services Administration

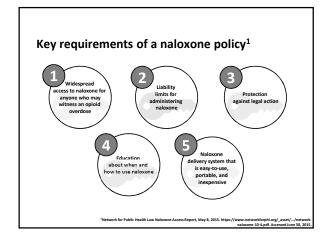
Strategies for prevention of overdose

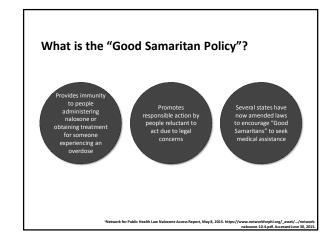
- Education of drug users¹
- Family support groups¹
- Motivational post-overdose interviews¹
- Supervised injecting rooms¹
- Provide naloxone for home use¹
- Encourage prescribers to use state Prescription Drug Monitoring Program (PDMPs)²
- Assessment of patient: Obtain history of the patient's past drug use²
- In emergency situations, the physician should prescribe the smallest possible quantity (typically not exceeding 3 days' supply) and arrange for return visit the next day2

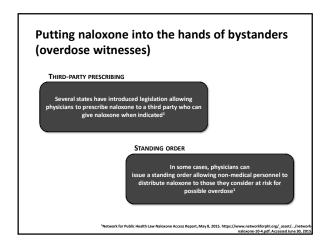
¹Sporer KA. Brit. Med Journal. 2003; 326:4 loid Overdose Toolkit. HHS Publication No. (SMA) 13-4742, Rockville, MD: Substance Abuse and Mental Health Services Administration

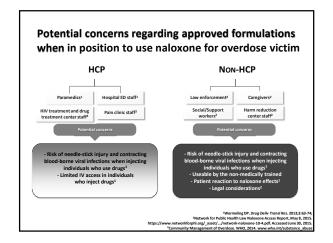
Mitigation of overdose risk in people with pain Risk exists for both people with pain, and people with substance use disorders And, of course, in those with both There is a recent trend toward increased prescribing of naloxone for use in case of unintentional overdose Much of the focus in this area has been for people without a legitimate medical need for opioids as part of a pain care plan When should naloxone prescribing be considered for people with pain who use opioids for pain relief? Take special precautions with new patients Educate patients and obtain informed consent Monitor patient's response to treatment Decide when and whether to end opioid Consider prescribing naloxone for patients "SAMMA Opioid Overdose Toolikit Hist Publication No. (SIMA) 13-1742. Rockville, MD. Salvatance Above and Mental Health Services Administration, 2013











All Prescribers Play an Active Role in Reducing the Risks Associated With Opioids

- When opioids are being considered as part of a chronic pain treatment plan:
 - Establish diagnosis
 - · History and physical
 - · Relevant diagnostic tests
 - Complete an appropriate risk assessment PRIOR to prescribing
 - · Monitor the patient regularly on an ongoing basis
 - · Recognize that all patients are at risk
 - Prescribe opioids as part of a multimodal treatment regimen

McCarberg BH. Postgrad Med. 2011;123(2):119-130; Brennan MJ, et al. PM R. 2010;2(6):544-558.

Conclusions

- Opioid analgesics remain among the most commonly prescribed medications for people experiencing chronic pain.
- Among the many adverse effects of chronic opioid therapy is the potential for misuse, abuse and unintentional overdose resulting in significant morbidity including death.
- Multiple practical steps can be instituted by the prescriber to help reduce the risk of misuse and abuse as well as reduce the risk of unintentional overdose.