# **Pain and Addiction**

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Name	Commercial Interests	Relevant Financial Relationships: What Was Received	Relevant Financial Relationships: For What Role	No Relevant Financial Relationships with Any Commercial Interests
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## **Pain and Addiction-Outline**

- Definitions
- Statistics/Epidemiology
- "PRINCIPLES" Overview
- Key Issues in Treatment Management
- Intersection: Pain/Opioids/Addiction The "ASAM Niche"
- PCSS-O.org and PCSS-MAT.org



## Definitions

- Medication Misuse: +Rx, Not following prescriber instructions or taking for other indications.
- Non-Medical Use: -Rx, May use for appropriate medical indications, or not.
- Prescription Medication Abuse: Less specific term.
  Generally results in negative consequences.
- Focus of this presentation on prescription opioids.
- Sedative-hypnotics overlap, especially in ODs



### Alleviating Suffering 101 Pain Relief in the USA

- 2011 IOM Report: 116 Million Americans have pain which persists for weeks to years
- \$560---\$635 Billion per year
- Some physicians overprescribe opioids, while others refuse to prescribe
- Lack of education: Providers and Patients headache, LBP, Neck Pain, Joint Pain, Fibromyalgia

NEJM 366:3 Jan 19,2012



## **Prescription Drug Abuse**



USA utilizes 80% of global opioid medication supply; >90% Hydrocodone



### Drug Overdose Deaths by Major Drug Type, United States, 1999–2010



CDC, National Center for Health Statistics, National Vital Statistics System, CDC Wonder. Updated with 2010 mortality data.



### Rates of Opioid Overdose Deaths, Sales, and Treatment Admissions, United States, 1999–2010



CDC. MMWR 2011. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6oe1101a1.htm?s\_cid=mm6oe1101a1\_w. Updated with 2009 mortality and 2010 treatment admission data.



### Drug Overdose Death Rate, 2008, and Opioid Pain Reliever Sales Rate, 2010



National Vital Statistics System, 2008; Automated Reports Consolidated Orders System, 2010.



### **Rx Opioid Dose and Overdose Risk**



Overdose defined as death, hospitalization, unconsciousness, or respiratory failure.

**OD** Deaths

Dunn et al. Opioid prescriptions for chronic pain and overdose. *Ann Int Med* 2010;152:85-92. Gomes et al, Opioid dose and drug-related mortality in patients with nonmalignant pain. *Ann Int Med* 2011;17197):686-691



### In 2010, 2 million people reported using prescription painkillers non-medically for the first time within the last year—nearly 5,500 a day.



### "Principles"

### **Comprehensive, Complete, Clear, References**

- Chap.34: Misuse All Controlled Medications
- Chap.93: Basic Science and Overlap P & A
- Chap.94: Psychological Issues
  "If life is empty, pain will fill it up"
- Chap.95: Rehabilitation Modalities
- Chap. 96: Non-Opioid Pharmacotherapy
- Chap.97: Opioid Therapy
- Chap.98: Co-morbid Pain and Addiction
- Chap.99: Legal & Regulatory Issues in Opioid Prescribing



# **Non-Opioid Pharmacotherapy**

- Acetominophen, NSAIDS: Somatic, Inflamm.
- Adjuvants: Anti-depressants: TCAs, SSRIs, SNRIs Neuropathic Pain, Fibromyalgia
   Anti-Convulsants: Neuropathic Pain, Migraine Pro
- Alpha Agonists: clonidine, tizanidine
- Topicals: Capsaicin, Lidocaine patch, NSAID
- Muscle Relaxants: Baclofen, cyclobenzadrine
  Ø-- B/Z, carisoprodol
- Interventional Rx: Epidurals, Nerve Blocks, etc



# Non-Pharmacologic Therapy

- Physical Therapy
- CBT
- Meditation, Mindfulness
- Exercise
- Biofeedback
- Massage
- Aquatic Therapy
- TENS



# Opioids

- Acute Pain: e.g. Post-Operative
- Cancer Pain
- Palliative Care, Hospice
- End of Life Care
- Chronic Opioid Therapy (COT) for Chronic Non-Cancer Pain (CNCP) Effectiveness, Safety, Adverse Effects, Hyperalgesia, IR vs. ER



## Long Term(>16wks.) COT for CNCP

Long-term Opioid Treatment of Chronic Nonmalignant Pain: Unproven Efficacy and Neglected Safety. Kissin, Igor *Journal of Pain Research*, 2013:6 513-529

 "..No high quality evidence on the efficacy of COT for CNCP." no RCT lasting >3mos

\* "Until 2003, opioid addiction associated with the treatment of CNCP was clearly a neglected topic of publication."



### Assess Each Patient's Risk of Abuse, Including Substance Use & Psychiatric Hx

- Obtain a complete Hx of current & past substance misuse
  - Prescription drugs, Illegal substances
  - Alcohol & tobacco
    - Substance abuse Hx does not prohibit treatment with opioids but may require additional monitoring & expert consultation/referral
  - Family Hx of substance abuse & psychiatric disorders
  - Hx of sexual abuse, Younger Age
- Social history also relevant
  - Employment, cultural background, social network, marital history, legal history, & other behavioral patterns

Chou R, et al. J Pain. 2009;10:113-30. SAMHSA. Managing Chronic Pain in Adults With or in Recovery From Substance Use Disorders. Treatment Improvement Protocol (TIP) Series 54. HHS Publication No. (SMA) 12-4671. 2011. Department of Veterans Affairs, Department of Defense. VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain. 2010.



### **Risk Assessment Tools: Examples**

Tool	# of items	Administered			
Patients considered for long-term opioid therapy:					
ORT Opioid Risk Tool	5	By patient			
<b>SOAPP</b> <sup>®</sup> Screener & Opioid Assessment for Patients w/ Pain	24, 14, & 5	By patient			
<b>DIRE</b> Diagnosis, Intractability, Risk, & Efficacy Score	7	By clinician			
Characterize misuse once opioid treatments begins:					
PMQ Pain Medication Questionnaire	26	By patient			
<b>COMM</b> Current Opioid Misuse Measure	17	By patient			
PDUQ Prescription Drug Use Questionnaire	40	By clinician			
Not specific to pain populations:					
<b>CAGE-AID</b> Cut Down, Annoyed, Guilty, Eye-Opener Tool, Adjusted to Include Drugs	4	By clinician			
<b>RAFFT</b> Relax, Alone, Friends, Family, Trouble	5	By patient			
DAST Drug Abuse Screening Test	28	By patient			
SBIRT Screening, Brief Intervention, & Referral to Treatment	Varies	By clinician			



# **Opioid Risk Tool (ORT)**

Mark each box that applies		Female	Male	
1.	Family Hx of substance abuse			Administer
	Alcohol	1	3	
	Illegal drugs	2	3	On initial visit
	Prescription drugs	4	4	
2.	Personal Hx of substance abuse			Prior to opioid therapy
	Alcohol	3	3	
	Illegal drugs	4	4	Cooring (rick)
	Prescription drugs	5	5	Scoring ( <i>risk</i> )
3.	Age between 16 & 45 yrs		1	o-3: low
4.	Hx of preadolescent sexual abuse	3	0	4-7: moderate
5٠	Psychologic disease			
	ADD, OCD, bipolar, schizophrenia	2	2	≥8: high
	Depression	1	1	

Webster LR, Webster RM. Pain Med. 2005;6:432-42.

Scoring Totals:



# **Initiating Opioid Treatment**

 Prescribers should regard initial treatment as a therapeutic trial

- May last from several wks to several months
- Decision to proceed w/ long-term treatment should be intentional & based on careful consideration of outcomes during the trial
  - Progress toward meeting therapeutic goals
  - Functional Improvement
  - Presence of opioid-related AEs
  - Changes in underlying pain condition
  - Changes in psychiatric or medical comorbidities
  - Identification of aberrant drug-related behavior, addiction, or diversion

#### Chou R, et al. J Pain. 2009;10:113-30. 21/25 Fair to Poor Evidence



## **Opioid Rotation**

### Definition

- Change from an existing opioid regimen to another opioid w/ the goal of improving therapeutic outcomes
- Rationale
  - Differences in pharmacologic or other effects make it likely that a switch will improve outcomes
    - Effectiveness & AEs of different mu opioids vary among patients
    - Patients show incomplete cross-tolerance to new opioid
      - Patient tolerant to 1<sup>st</sup> opioid can have improved analgesia from 2<sup>nd</sup> opioid at a dose lower than calculated from an EDT

Fine PG, et al. J Pain Symptom Manage. 2009;38:418-25. Knotkova H, et al. J Pain Symptom Manage. 2009;38:426-39. Pasternak GW. Neuropharmacol. 2004;47(suppl 1):312-23.



### **Equianalgesic Dose Table**

Drug	Oral	Parenteral	Conversion ratio to oral morphine
Morphine	30 mg	10 mg	Parenteral morphine: 3 times as potent as oral morphine
Oxycodone	20 mg	NA	Oral oxycodone: ~1.5 times as potent as oral morphine
Hydrocodone	20 mg	NA	Oral hydrocodone: ~1.5 times as potent as oral morphine
Hydromorphone	7.5 mg	1.5 mg	Oral hydromorphone: ~4-7 times as potent as oral morphine Parenteral hydromorphone: 20 times as potent as oral morphine
Fentanyl	NA	15 mcg/hr	Transdermal fentanyl: ~80 times as potent as morphine (based on studies converting from morphine to fentanyl)

Periyakoil V. End of Life Online Curriculum. *Pain control: opioid conversion module*. <u>http://endoflife.stanford.edu/M11\_pain\_control/intro\_mo1.html</u>. 2008.



# **Guidelines for Opioid Rotation**

Calculate equianalgesic dose of new opioid from EDT
 Reduce calculated equianalgesic dose by 25%-50%
 Methadone: Decrease by 90%
 Start Low, Go Slow
 30% of Overdose Deaths: Pain, not OTPs

Fine PG, et al. J Pain Symptom Manage. 2009;38:418-25.



### **Taper Dose When Discontinuing**

- Taper dose to avoid opioid withdrawal in physically dependent patient
- Outpatient setting in patients without severe medical or psychiatric comorbidities
  - Rehabilitation setting if patient unable to reduce opioid dose in a less structured setting
  - When aberrant drug-related behaviors continue, may need to enforce tapering efforts
- Approaches range from slow 10% dose reduction/wk to more rapid 25%-50% reduction every few days

Chou R, et al. J Pain. 2009;10:113-30. Department of Veterans Affairs, Department of Defense. VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain. 2010.







Chang and Compton Addiction Science & Clinical Practice 2013, 8:21 http://www.ascpjournal.org/content/8/1/21

#### +Random UDT

#### Table 3 Ten steps of universal precautions

- 1. Make a diagnosis with appropriate differential.
- Perform a psychological assessment, including risk of addictive disorders.
- 3. Obtain informed consent.
- 4. Use a treatment agreement.
- Conduct assessment of pain level and function before and after the intervention.
- Begin an appropriate trial of opioid therapy with or without adjunctive medications and therapies.
- 7. Reassess pain score and level of function.
- Regularly assess the 4 "As" of pain medication: Analgesia, Activity, Adverse effects, and Aberrant behavior.
- Periodically review pain diagnosis and co-occurring conditions, including addictive disorders.
- 10. Document initial evaluation and follow visits.

Adopted from Gourlay DL et al [41].



### Urine Tox Results in Chronic Pain Patients on Opioid Therapy



Source: Couto JE, Goldfarb NI, Leider HL, Romney MC, Sharma S. High rates of inappropriate drug use in the chronic pain population. *Popul Health Manag.* 2009;12(4):185–190.



### **PDMPs**

- Almost All States are Operational
- Some States Mandatory at time of Rx, e.g. N.Y.
- Some States Include Bordering States
- OTPs are exempt: both methadone and bupe
- OBOT Bupe included in PDMPs
- $\checkmark$  Doctor Shopping and Rx Opioid Prescribed
- No evidence of  $\psi$  OD deaths as of yet (6/14)
- ◆ Unintentional Consequences: ?↑Heroin, ↑Pain



## **Examples of Metabolism of Opioids**



Oxycodone -> Oxymorphone

Methadone, Fentanyl, Oxymorphone, Hydromorphone Do Not Metabolize to other Opioid Analgesics

Gourlay DL, et al. Urine Drug Testing in Clinical Practice. The Art & Science of Patient Care. Ed 4. 2010.



# **Prescription Opioid Cautions**

- Do Not Tamper with Tablets or Capsules, especially ER/LA, which become IR with high potency by IN or IV route
  - Tamper resistant Oxycodone>Heroin
- Avoid Other CNS Depressants: Benzodiazepines, Alcohol, Carisoprodol
  - COT: No SUD hx: 29% sedatives; SUD hx: 39% ; Alcohol=12%

Saunders, et al, The Journal of Pain, 2012 266-275



# **Opioid Rx Disposal**

- DEA Take Back Programs
- Some Pharmacies, Some Police Stations
- Mix with cat litter/coffee grounds, then seal in plastic bag, and throw out in trash
- Flush down toilet: ?environmental issues
  Fentanyl Patch
- DO NOT Throw out in trash in Rx bottle



## **Complex Interactions**





# **Pain and Addiction: Definitions**

 "Pain is viewed as a biopsychosocial phenomenon that includes sensory, emotional, cognitive, developmental, behavioral, spiritual and cultural components." (IASP website)  Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic **biological**, psychological, social and spiritual manifestations. (ASAM 2011)



## Pain and Addiction No Objective Measurements







# **Physical Dependence**

- "Physical dependence is the physiological adaptation of the body to the presence of an opioid. It is defined by the development of withdrawal symptoms when opioids are discontinued.
- "Physical dependence is a normal and expected response to continuous opioid therapy. Physical dependence may occur within a few days of dosing with opioids, although it varies among patients. Physical dependence (indicated by withdrawal symptoms) does not mean that the patient is addicted."

O'Brien CP. Drug addiction and drug abuse. In: Goodman and Gilman's The pharmacological basis of therapeutics. 9th edition.



## **Opioid Sites of Action in the Brain**




## **Hedonic Tone**

- Sense of well being, happiness, pleasure, contentment
- "Set" by/in the mesolimbic dopaminergic circuitry(Pleasure/Reward/Survival Center)
- Range: Euphoria  $\leftarrow \rightarrow$  Dysphoria
- Altered by Psychoactive Activities
- A Delicate Balance
- Human Condition
- (?abnormal tone in the vulnerable to addiction)



## **Hedonic Tone Demonstration**







## Pain and Addiction—Hedonic Tone





## Pain and Addiction and Opioids

- The usual DSM criteria for opioid addiction (dependence) have been misleading in the context of the opioids being prescribed by a HCP for the treatment of pain. The usual problematic behaviors involved in obtaining an ongoing supply of opioids is obviated by the prescribing paradigm.
- The usual illegal, illicit issues do not pertain.
- Harm may be masked under these conditions.



## Substance Use Disorder DSM V

- \* Tolerance\*
- Withdrawal\*
- More use than intended
- Craving for the substance
- Unsuccessful efforts to cut down
- Spends excessive time in acquisition

- Activities given up because of use
- Uses despite negative effects
- Failure to fulfill major role obligations
- Recurrent use in hazardous situations
- Continued use despite consistent social or interpersonal problems

\*not counted if prescribed by a physician

Severity measured by number of symptoms, 2-3 mild, 4-6 moderate, 7-11 severe



## **Pain and Addiction**



Ann Quinlan-Colwell, PhD, PCSS-O Webinar 2011



## Pain and Addiction-Psychiatric Co-morbidity

- Association Between Mental Health Disorders, Problem Drug Use, and Regular Prescription Opioid Use Sullivan M.D., Arch Intern Med 2006;166:2087-2093
- Healthcare for Communities waves 1998 and 2001
- N=6430 telephone survey
- Association of common mental health disorders in 1998 with regular Opioid Rx. Use in 2001 Odds Ratios

Major Depression—3.43 Dysthymia—6.51 Panic—5.37 GAD—2.56 Problem Drugs—3.57 Problem Alcohol—.73

**Concl:** Common mental health and drug disorders are associated with initiation and use of prescribed opioids. Attention to psychiatric disorders is important when considering opioid therapy



## **latrogenic** Addiction

 latrogenic addiction occurs when a patient, with a negative personal or family history for alcohol or drug addiction or abuse, is appropriately prescribed a controlled substance & subsequently in the therapeutic course meets the diagnostic criteria for addiction to that substance

Heit HA, Gourlay DL. Treatment of Pain in Substance Abuse Disordered Population. Ballantyne JC, Rathmell JP, Fishman SM (eds). Bonica's Management of Pain. 4<sup>th</sup> ed. Lippincott Williams & Wilkins. In Press.



## Opioid Treatment for Pain: Risk of Addiction

- Voluminous literature including multiple systematic reviews
- Rates vary widely o%-50%-- higher in those with addiction hx.
- Often not clear how the diagnosis of addiction is confirmed
- Aberrant and Problematic Behaviors often considered to make a diagnosis of addiction
- Diagnosis is often not clear when opioids are prescribed for pain by HCP—lack of education in addictive disease
- "Easy" cases involve non-prescribed or illicit prescription opioids or heroin, with no history of pain
- Often a challenge to differentiate between addiction and a "pain case gone bad"
- Clinical expertise and individualization required. ASAM members uniquely qualified



## Opioid Treatment for Pain: Risk of Addiction

What Percentage of CNCP Patients Exposed to COT develop Addiction and/or Aberrant drug-Related Behaviors? A Structured Evidence-Based Review. Fishbain et al *Pain Med* 2008

- <sup>1</sup>. 24 studies COT, 26.2 mos. (n=2,507), average % addiction= 3.27%
- 2. 17% of studies pre-selected for no current/past hx. of addiction/abuse addiction in preselected 0.19% vs. 5.0% in non-selected
- Average % ADRBs =11.5% , pre-selected= 0.59%
- UDS, 5 studies, ADRBs = 20% no opioid/other non-Rx opioid
- 5. UDS, illicit drugs non-opioid, 14.5%

Conclusions: The results of this evidence-based structured review indicate that COT exposure will lead to abuse/addiction in a very small % of patients. This % can be dramatically decreased by preselecting CPPs for no previous/ current hx of drug/alcohol abuse/addiction



### Systematic Review: Opioid Treatment for Chronic Back Pain: Prevalence, Efficacy, and Addiction

Martell, B. Ann Intern Med. 2007;146:116-127

 Conclusion: Opioids are commonly prescribed for chronic back pain and may be efficacious for shortterm pain relief. Long-term efficacy (>16 weeks) is unclear. Substance use disorders are common in patients taking opioids for back pain, and aberrant medication-taking behaviors occur in up to 24%.



## **Aberrant/Problematic Behaviors**

#### Probably more predictive

- Selling prescription drugs
- Prescription forgery
- Stealing or borrowing another patient's drugs
- Injecting oral formulation
- Obtaining prescription drugs from non-medical sources
- Concurrent abuse of related illicit drugs
- Multiple unsanctioned dose escalations
- Recurrent prescription losses

- Probably less predictive
  - Aggressive complaining about need for higher doses
  - Drug hoarding during periods of reduced symptoms
  - Requesting specific drugs
  - Acquisition of similar drugs from other medical sources
  - Unsanctioned dose escalation 1-2 times
  - Unapproved use of the drug to treat another symptom
  - Reporting psychic effects not intended by the clinician



## **Treating Pain in the Addicted Patient**

- "Pain Patients with a coexisting SUD are among the most challenging patients in medicine."
- Universal Precautions
- ?? "Real Pain" may make opioids less rewarding/euphorogenic
- Addicted Patients Have Pain: Trauma, Lower Thresholds, Medical
- Screening Tests: ORT, SOAPP, others
- Untreated Pain is a trigger for relapse
- Address both pain and addiction
- Significant other to secure and dispense opioid meds
- Psychiatric Co-morbidity
- Active Addiction recovery program
- UDS, pill counts, agreements, etc.
- Multidisciplinary Pain Program

Bailey, et al. Pain Medicine 2010; 11: 1803-1818



## **Pain and Addiction**





# Dependence

Opioid Dependence vs Addiction A Distinction Without a Difference? Ballantyne J, Sullivan M, Kolodny A, Arch Intern Med, 2012

"Dependence on opioid pain treatment is not, as we once believed, easily reversible; it is a complex physical and psychological state that may require therapy similar to addiction treatment, consisting of structure, monitoring, and counseling, and possibly continued prescription of opioid agonists. Whether or not it is called addiction, complex persistent opioid dependence is a serious consequence of long term pain treatment that requires consideration when deciding whether to embark on long term opioid pain therapy as well as during the course of such therapy.



## **Pain and Addiction**





## **Pain and Addiction**





## **The Clinical Conundrum**



"...as we know, there are known knowns, there are things we know we know. We also know there are known unknowns; that is to say we know there are some things we do not know. But there are also unknown unknowns – the ones we don't know we don't know."

the Pentagon.

– Donald Rumsfeld



## Conclusions: Known Knowns & Unknowns

- De Novo latrogenic addiction: o—50%
- Aberrant/Problematic Behaviors are common: ~20%
- Risks are highest in those with current/past history of addiction/psychiatric disorder– Multidisciplinary Team
- Monitoring patients, using Universal Precautions is helpful
- Follow the FSMBs guidelines to avoid any regulatory problems
- Is it a "Pain Case Gone Bad" or Addiction—often Grey Zone
- Suffering is common: "Terribly Sad Life Syndrome"
- Challenging Clinical Cases—Requires Individualization Tx
- Buprenorphine: Therapeutic Option-- Pain and Addiction Roux, et al. Pain, 154 (2013) 1442-1448



## Opioid Therapy for Chronic Pain in the United States: Promises and Perils

Sullivan, Howe: Pain, 154 (2013) S94-S100

- 12 week studies: pain reduced 30% vs placebo
- Functional Improvement ±
- Majority of patients stop opioids: -efficacy + Aes
- COT : Less likely to return to work
- Patients with SUD or Mental Health Disorders are More likely to receive Long Term COT
- >90 days COT> long term: >120mgME> misuse
- "Adverse Selection:" The likelihood of a patient receiving COT increases as the associated risks increase





## **Baby Boomers**

