

Welcome to Virtual Colorado MAT Forum

- *As you join you will be promoted to presenter.*
- *You will be muted.*
- *Please unmute yourself by clicking on the microphone icon for asking questions and participation in discussions.*
- *You may also put your questions and comments in the Chat box.*
- *We encourage active participation!*

Monthly Webinars

- ***Virtual CO MAT Learning Forum***

1st Thursday 12:30pm-1:30pm

[REGISTER](#)

- ***Induction Basics: Tips from the Trenches****

2nd Tuesday 7:30am-8:30am

[REGISTER](#)

* *same topic each month*

- ***Denver Health Learning Collaborative***

3rd Wednesday 12:15pm-1:15pm

[REGISTER](#)

Denver Health Addiction Journal Club

Scheduled dates for 2020

- *Every fourth Tuesday January-October*
- *November 10th*
- *December 8th*

Time; noon to 1 pm

To join; email ITMATTTRs2@UCDENVER.EDU

- See our website for previous presentations & resources as well as upcoming topics
 - <https://www.practiceinnovationco.org/itmatttrs2/mat-forum/>

Webinars

See our website for previous presentations & resources as well as upcoming topics

<https://www.practiceinnovationco.org/opioids/mat-forum/>

<https://nccc.ucsf.edu/clinician-consultation/substance-use-management/>

Clinician Consultation

Clinical Resources

About the Center

You are here: [Home](#) > [Clinician Consultation](#) > [Substance Use Management](#)

Substance Use Management



Clinically supported advice on substance use management for healthcare providers

Peer-to-peer consultation from physicians, clinical pharmacists, and nurses with special expertise in substance use evaluation and management.

Submit a Case for Consultation

Send a CCC clinician your case online.

[SUBMIT](#)

Call for a Phone Consultation

(855) 300-3595

Monday – Friday, 9 a.m. – 8 p.m. ET

[CALL](#)

California-based clinicians, please visit our [California Substance Use Line](#).

ADDICTION AND CHRONIC PAIN
WHAT TO DO
WHEN THEY RUN TOGETHER ?

NORTHERN COLORADO LEARNING FORUM
JUNE 4, 2020

STEVEN WRIGHT, MD
FAMILY MEDICINE 1982
ADDICTION MEDICINE 1987
MEDICAL PAIN MANAGEMENT 2003

Disclosures

Alliance for Benzodiazepine Best Practices

NEMA Research

The Schreiber Research Group

BioDelivery Sciences, Inc (BDSI)

Benzodiazepines

Benzodiazepines, Opioid induced constipation

Benzodiazepines, Opioids – Public Health

Belbuca

Objectives

- 1) Outline the general principles of pain management
- 2) Outline opioid risks and risk management approaches in pain management
- 3) Describe how to address opioid-related aberrancies in pain management



CLASOWNE
BOLD | FULL
BOLD | BOLD
BOLD | BOLD
BOLD | BOLD
BOLD | BOLD



PAIN



A more terrible lord over mankind
Than even death itself - Schweitzer

If Pain is not Reversible

- Non – medication approaches
- Non – opioid medications
- Opioids

Multi – Modal ¹⁻⁶

What is Necessary for Good Function?

¹ Arden. ESI for sciatica RCT. *Rheum (Oxford)*. 2005;44(11):1399-406

² Sinatra. Causes, consequences of inadequate acute pain Rx. *Pain Med*. 2010;11(12):1859-71

³ Guzmán. Multidisciplinary rehab for chronic LBP review. *BMJ*. 2001;322(7301):1511-6

⁴ van Middelkoop. Physical, rehab interventions for chronic LBP. *Eur Spine J*. 2011;20(1):19-39

⁵ McCarthy. Myalgias & myopathies: FM. *FP Essent*. 2016;440:11-5

⁶ Arnold. FM management for 1st care. *Mayo Clin Proc*. 2012;87(5):488-96



“ Hul Gil ”

Sumerian for “Plant of Joy” 3400 BCE

“Opos” Greek for “Juice”

1890s
Sears and Robuck
Heroin and Works
\$1.50



**She forgot where she was
and fell among the poppies, fast asleep.**

“ What shall we do? ” asked the Tin Woodman.

“ If we leave her here she will die ” said the Lion.

- The Wonderful Wizard of Oz

General Skills for Medical (Pain Management) Providers

Knowledge¹⁻⁴

Application of Knowledge^{5,6} Including Guidelines⁷⁻⁹

Documentation¹⁰⁻¹²

¹ Argyra. Undergrad pain course, physician pain concept awareness. *Pain Med.* 2015;16(2):301-11

² Geneen. Chronic pain education meta-analysis. *Syst Rev.* 2015;4:132

³ Meier. Improving palliative care. *Ann Int Med.* 1997;127(3):225-30

⁴ Watt-Watson. Prelicensure pain curricula. *Pain Res Manag.* 2009;14:439-44

⁵ McKinlay. Patient med requests & physician prescribing. *Med Care.* 2014;52(4):294-9

⁶ Darlow. Acute LBP management in general practice. *Fam Pract.* 2014;31(6):723-32

⁷ Williams. LBP best practice care survey. *Arch Int Med.* 2010;170(3):271-7

⁸ Jackson. LBP guideline impact on practice. *South Med J.* 2005;98(2):139-43

⁹ González-Urzelai. Acute LBP 1st care guideline adherence. *Eur Spine J.* 2003;12(6):589-9

¹⁰ Center for Medicare & Medicaid Services: Documentation Guidelines. 2015. Accessed 11/14/16

¹¹ Manchikanti. E&M in interventional pain. *Pain Phys.* 2000;3(3):322-41

¹² Manchikanti. Chronic spinal pain management documentation. *Pain Phys.* 2009;12(4):E199-224

Structured Approach

Equal and Interactive attention to both domains

- **Pain Management**
- **Risk Management**

Documentation

	Pain	Function
Subjective	✓	✓
Objective	✓	✓
Assessment	✓	✓
Plan	✓	✓

Documentation

	Pain	Function	Risk
Subjective	✓	✓	✓
Objective	✓	✓	✓
Assessment	✓	✓	✓
Plan	✓	✓	✓

Treatment Principles

- Chronic care model ¹
- Stepped care: WHO analgesic ladder ^{2,3}
- Multimodal: ≥ 2 treatments with different mechanisms ⁴⁻⁶
- Multi-disciplinary ⁷ Team
Family-inclusive ⁸ Peer coaching ⁹ Integrated
Pharmacy ¹⁰
- Person-centered ¹¹ Trauma-informed ¹²

¹ Institute for Healthcare Improvement: Changes to Improve Chronic Care

² Jadad. WHO analgesic ladder, cancer. *JAMA*. 1995;274:1870-3

³ Azevedo. WHO analgesic ladder, cancer. *Support Care Cancer*. 2006;14(11):1086-93

⁴ Morlion. Targeting nociceptive, neuropathic LBP. *Curr Med Res Opin*. 2011;27(1):11-33

⁵ Dale. Multimodal Rx chronic pain. *Med Clin North Am*. 2016;100(1):55-64

⁶ Provenzano. Opioids in chronic pain. *Curr Med Res Opin*. 2014;30(10):2051-62

⁷ DeBar. 1st care-interdisciplinary team, chronic pain. *Transl Behav Med*. 2012;2(4):523-30

⁸ Swift. Family involvement in chronic pain. *MS Care*. 2014;12(1):47-55

⁹ Matthias. Peer support for chronic MS pain. *Pain Med*. 2015;16(1):81-7

¹⁰ Hoppe. Pharmacy role in controlled substances. *Pain Med*. 2014;15:1996-8

¹¹ Bras. Person-centered pain management. *Croat Med J*. 2013;54(3):296-300

¹² Center for Social Innovation: Addressing Impact of Trauma Accessed 3/29/16

Treatment Principles

- Does it work ?
- Does it work without side effects ?
- Are the side effects manageable ?
- Is efficacy durable ?
- Do side effects develop over time ?

Evidence Based Medicine

Personalized Medicine

Short – Acting Opioids

- Alfentanil
- Buprenorphine
- Butorphanol
- Codeine
- Fentanyl
- Hydrocodone
- Hydromorphone
- Meperidine
- Morphine
- Nalbuphine
- Oxycodone
- Oxymorphone
- Pentazocine
- Remifentanyl
- Sufentanil
- Tapentadol
- Tramadol

Long-Acting / Extended-Release Opioids

- Buprenorphine
- Fentanyl
- Hydrocodone
- Hydromorphone
- Levorphanol
- Methadone
- Morphine
- Oxycodone
- Oxymorphone
- Tapentadol
- Tramadol

Assessing Outcomes

- Efficacy
 - Function is the endpoint
 - Analgesia is the signpost along the way
- Side effects
 - Short Term
 - Long Term

Goals: 30% improvement ^{1,2}

Side effects manageable

¹ Manchikanti. ASIPP responsible opioid prescribing guide. *Pain Phys.* 2012;15(3 Suppl):S67-116

² Ferrar. Importance of changes in chronic pain NRS scale. *Pain.* 2001;94(2):149-58

Opioid Efficacy

- Acute / Postop pain: Well established for short-term use
 - Analgesic *and* Functional improvement ¹⁻³
 - Non-opioids may be as good or better ^{4,5}
 - Amounts prescribed often > amounts needed ⁶
- Chronic pain: Long-term role uncertain, debated ⁷
 - No placebo-controlled studies $\geq$ 1 year: Unethical, won't be done
 - Open-labeled studies up to 3 years: Efficacy has been seen ⁸⁻¹¹
 - Open-labeled observational study: Opioids not superior back, hip, knee pain ¹²

¹ Deyo. Opioids for LBP. *BMJ*. 2015;350:g6380

² Acute periop pain guidelines. Am Soc Anesthesiologists. 2012

³ Prescribing opioids in the ED. Am College Emergency Phys. 2012

⁴ Moore. Ibuprofen + APAP, 3rd-molar extractions. *J Am Dent Assoc*. 2013;144(8):898-908

⁵ Derry. Ibuprofen +oxycodone, postop pain. *Cochrane Rev*. 2013;(6):CD010289

⁶ Maughan. Unused opioids, dental surgery. *Drug Alc Dep*. 2016;168:328-34

⁷ Chou. Research gaps on opioids for chronic nonCA pain. *J Pain*. 2009;10(2):147-59

⁸ Kalso. Opioids in chronic nonCA pain. *Pain*. 2004;112(3):372-80

⁹ Noble. LT opioids for chronic nonCA pain. *Cochrane Rev*. 2010;(1):CD006605

¹⁰ Trescot. Opioids in chronic nonCA pain. *Pain Phys*. 2008;11(2 Suppl):S5-S62

¹¹ da Costa. PO, TD opioids for OA knee, hip. *Cochrane Rev*. 2014;(9):CD003115

¹² Krebs. Opioids v nonopioids effect on function chronic back, hip, knee OA pain. *JAMA*. 2018;319(9):872-82

Initial Opioid Selection

- Cost
 - Coverage
 - Formulary
 - Prior authorization
-
- Relative contraindications based on type of pain
 - Headache: *AVOID* ^{1,2}
 - Fibromyalgia ? Tramadol works Others not studied ³⁻⁸

¹ Bendtsen. EFNS guide: tension-type HA Rx. *Eur J Neuro*. 2010;17:1318-25

² Johnson. Med-overuse HA, opioid hyperalgesia. *Cephalalgia*. 2013;33(1):52-64

³ MacLean. Tramadol for fibromyalgia. *Expert Rev Neurother*. 2015;15(5):469-75

⁴ Painter. Chronic opioids in FM. *J Clin Rheumatol*. 2013;19(2):72-7

⁵ Furlan. Opioids for chronic noncancer pain. *CMAJ*. 2006;174(11):1589-94

⁶ Sumpton. Fibromyalgia. *Handb Clin Neuro*. 2014;119:513-27.

⁷ Ngian. Opioids in FM. *In J Rheum Dis*. 2011;14(1):6-11

⁸ Bennett. Internet survey of 2,596 people with FM. *BMC MS Disord*. 2007;8:27

Rx

J + P

PHARMACY

HAPPY
HOUR
5-7 p.m.



SIPRESS

Definition of Trouble

- Diversion Transfer from lawful to unlawful channel ¹
- Misuse Use in a way other than intended ²
- Non-medical use Use for reason other than intended ^{2,3}
- Addiction Compulsive use + negative outcomes ⁴
- Overdose Related to
 Respiratory Depression ⁵
Overdose death Torsade de Pointes (methadone) ⁶

¹ Inciardi. Prescription opioid abuse and diversion. Pain Med. 2009;10(3):537-48

² WHO. Lexicon of alcohol, drug terms Accessed 4/2/16

³ Del Fabbro. Assessment, management of chemical coping. J Clin Onc. 2014;32(16):1734-8

⁴ ASAM. Definition of Addiction. 2011 Accessed 4/2/16

⁵ Pattison. Opioids and control of respiration. Br J Anes. 2008;100(6):747-58

⁶ Paulozzi. Risk for methadone OD. 1999-2010. MMWR Weekly. 2012;61(26):493-7

Epidemiology of Trouble

- United States 5% of world population
80% world opioid use 99% world hydrocodone use ¹
- Doctor shopping PDMP: 3% got opioids from 5-9 prescribers
0.35% from 10-19 prescribers ²
- Illegal activity Forgery 3.2% Diversion 1.6% (small study) ³
- Nonmedical use of opioids 12 million Americans ⁴ 20% of those prescribed ^{5,6}
33% ↑ nonmedical use if opioid started before 12th grade ⁷
- Addiction to opioids Prescription opioids: 1.8 million Americans ⁴
Heroin: 0.6 million Americans ⁴

¹ Manchikanti. Opioid therapeutic use, abuse, nonmedical use. *Pain Phys.* 2010;13(5):401-35
² McDonald. Estimating prevalence opioid diversion. *PLoS One.* 2013;8(7):e69241
³ Ives. Opioid misuse predictors in chronic pain. *BMC Health Services Res.* 2006;6:46
⁴ SAMHSA. 2016 National Survey on Drug Use and Health
⁵ Sullivan. Opioid possible, probable misuse in commercial, Medicaid. *Pain.* 2010;150(2):332-9
⁶ Reutsch. Empiric view of opioid dependence. *J MgeCare Pharm.* 2010;16(1 Suppl B):S9-13
⁷ Miech. Rx opioids in adolescence, future misuse. *Pediatrics.* 2015;136(5)

The Nature of Addiction

- *Not* A basic drive in all individuals
- *Not* Physiologic dependence: Tolerance Withdrawal ¹
- *Not* To be confused with pseudoaddiction, which is rare ²⁻⁴
- *Is* A chronic disease of the brain ^{5,6} characterized by ^{7,8}

Compulsion

Loss of Control

Continuation despite Adverse Consequences

Craving

¹ Savage. Definitions related to the medical use of opioids. *J Pain Symp Manage*. 2003;26(1):655-67

² Weissman. Opioid pseudoaddiction - an iatrogenic syndrome. *Pain*. 1989;36(3):363-6

³ Passik. Pseudoaddiction revisited. *Pain Manag*. 2011;1(3):239-48

⁴ Elander. Sickle cell pain, pseudoaddiction. *J Pain Sump Manage*. 2004;27(2):156-69

⁵ American Society of Addiction Medicine. Definition of addiction. 2011 Accessed 3/29/16

⁶ Hasin. DSM-5 criteria for SUDs. *Am J Psych*. 2013;170(8):834-51

⁷ Smith. Diagnostic, treatment, aftercare approaches to cocaine abuse. *J Sub Abuse Treat*. 1984;1(1):5-9

⁸ Savage. Addiction assessment in pain treatment. *Clin J Pain* 2002;18:S28-38

Watch Your Language

- Abuse → Misuse Non-medical use Hazardous use ¹⁻³ **Stigma matters** ^{4,5}
 - Dependence → Physiologic dependence: Tolerance Withdrawal ^{1,6}
 - Dependence → Substance Use Disorder (SUD) Addiction ^{1,3,5,6}
- Different Meanings**
- Person – first language ⁵
A person *with* addiction ... Not an addict ...
A person with depression... a disability ...

¹ Kelly. Do substance-related terms influence perceptions? *J Drug Issues*. 2010;40(4):805-18

² Saunders JB. Substance dependence, non-dependence in DSM, ICD. *Addiction*. 2006;101 Suppl 1:48-58

³ Ashford. Substance use, recovery, linguistics. *Drug Alc Depend*. 2018;189:131-8

⁴ Hegarty. Attributional beliefs about controllability of stigmatized traits. *J Applied Soc Psychol*. 2008;38(4):1023-44

⁵ Botticelli. Memo changing terminology regarding substance use, SUD. 9 Jan 2017. Accessed 4/27/20

⁶ Savage. Definitions related to use of opioids. *J Pain Symp Manage*. 2003;26(1):655-67

Dual Problems

39,000,000 with persistent pain ¹
47,000 opioid-related deaths ²

Persistent Pain =
Pain present most days of last 3 months

¹ Kennedy. Prevalence of persistent pain US 2010. *J Pain*. 2014;15(10):979-84

² Wilson. Opioid-involved OD deaths US 2017-2018. *MMWR*. 2020;69:290-7



There are three kinds of men:
The ones that learn by reading,
The few who learn
by observation,

The rest of them
have to pee on the electric fence

- Will Rogers

Dual Obligations

Healthy People 2020

National Pain Strategy

- Increase safe and effective treatment of pain
- Reduce non-medical use of prescription drugs

¹ National Pain Strategy 2014 Accessed 3/22/16

² Helmick. Adding Chronic Pain Objectives to Healthy People 2020. 2014 Accessed 3/22/16

Initial Visit Outcome

- Establish Goals ^{1,2}
 - Functional improvement 30% *Personalize*
 - Pain improvement 30%
- Establish Plan
 - Pain Management plan
 - Risk Management plan
- Educate the patient
 - Informed consent
 - Controlled Substance Agreement

¹ Gloth. Functional pain scale in elderly. J Am Med Dir Assoc. 2001;2(3):110-14

² Ferrar. Clinical importance of changes in chronic pain intensity by NRS. Pain. 2001;94(2):149-58

Risk Management

Stepwise Process to Help Ensure Safe Use

- 1) Risk Screening
- 2) Risk Stratification
- 3) Risk Mitigation
- 4) Risk Monitoring
- 5) Aberrancy Management

Risk Screening

- Screen history for primary risk factors (other risks: supplemental slide)
 - Personal, family Substance Use Disorder (SUD) ¹⁻⁴
 - Personal psychiatric, mood history ^{5,6} PHQ-4 → PHQ-9 (depression) GAD-7 (anxiety)
 - Personal trauma history ^{7,8} Adverse Childhood Experiences (ACEs)
- Screen for current substance use
 - Screening, Brief Intervention, Referral for Treatment (SBIRT) ^{9,10}
 - Do you use: Tobacco Alcohol Illicits Cannabis Addiction-prone prescriptions
 - How much? How often? For prescriptions: Do you use as prescribed?

¹ Edlund. Risk for OUD in vets using opioids for chronic non-cancer pain. *Pain*. 2007;129:355-62
² Hall. Patterns of abuse among unintentional pharmaceutical OD fatalities. *JAMA*. 2008;300(22):2613-20
³ Liebschutz. Factors associated with Rx drug use disorder in chronic pain. *J Pain*. 2010;11:1047-55
⁴ Michna. Predicting aberrant drug behavior in chronic pain. *J Pain Symp Manage*. 2004;28(3):250-8
⁵ Edlund. Risks for OUD. *Drug Alc Dep*. 2010;112:90-8

⁶ Wasan. Psych Hx & risk for aberrancy in chronic pain. *Clin J Pain*. 2007;23:307-15
⁷ Mullen. Childhood sexual abuse & MH in adults. *Br J Psych*. 1993;163:721-32
⁸ Sajadi. Predicting addiction on basis of early trauma. *Int J High Risk Behav Addict*. 2014;3(4):e20995
⁹ SBIRT Resources. <https://www.samhsa.gov/sbirt/resources> Accessed 4/27/20
¹⁰ Agerwala. Integrating SBIRT into clinical practice. *J Psychoact Drugs*. 2012;44(4):307-17

Risk Screening

SBIRT
Codes 99408 99409

- Screen for current substance use

- If SBIRT positive → 2^o screeners for problematic use
- Prescription Drug Monitoring Program (PDMP) ²⁻⁴
- Drug testing: Usually urine / oral fluid ^{4,5}
- Medical records / Report of others ⁶

CAGE / AUDIT
CUDIT DAST

} Verify

- Screen for future substance use risk

- Screener and Opioid Assessment for Patients with Pain (SOAPP-R) ⁷⁻⁹
- Opioid Risk Tool (ORT) ⁸⁻¹⁰ Many others ^{8,9}

¹ SAMHSA. Substance screeners. <https://www.integration.samhsa.gov/clinical-practice/sbirt/screening#brief%20initial%20screens>

² Lev. Medical examiner Rx-related deaths & PDMP data. *Am J Emerg Med*. 2016;34(3):510-4

³ Dormuth. Effect of prescription network on inappropriate Rx opioids, BZs. *CMAJ*. 2012;184(16):E852-6

⁴ Hamill-Ruth. Objective data for risk for med misuse: inconsistency score. *Pain Med*. 2013;14(12):1900-7

⁵ Manchikanti. Random UDTs reduce illicit drug use in chronic pain patients receiving opioids. *Pain Phys*. 2006; 9:123-9

⁶ Johnson. Rx opioid-related OD deaths: dependent description by best contact. *J Gen Int Med*. 2013;28(4):522-9

⁷ Butler. SOAPP-R validation. *J Pain*. 2008;9(4):360-72

⁸ Chou. Predicting drug-related aberrancies. *J Pain*. 2009;10(2):131-46

⁹ Jones. Risk screening method comparison. *Clin J Pain*. 2012;28(2):93-100

¹⁰ Webster. Predicting aberrant behaviors in opioid-Rxd patients: ORT. *Pain Med*. 2005;6(6):432-42

Risk Stratification

Risk for *Unsafe* Controlled Substance Use

- **Low Risk**
- **Intermediate Risk**
- **High Risk**

¹ Sehgal. Opioid abuse predictors, strategies. *Pain Phys.* 2012;15:ES67-92

² Brown. Assessment, stratification, monitoring risk for prescription opioid misuse and abuse in primary care. *J Opioid Manag.* 2011;7(6):467-83

Risk Mitigation

Strategies to limit future adverse outcomes

- Alternatives to opioids preferred but also have risks
- Calculate, address Morphine Milligram Equivalents (MMEs) ¹⁻³
Recommended: Practical Pain Management Calculator
- Avoid other respiratory depressants – benzodiazepines ^{2,4}
- Establish realistic goals: 30% pain and function improvement ⁵
- Provide informed consent: Risks Benefits Alternatives How to use ⁶

FDA: <https://www.fda.gov/drugs/information-drug-class/opioid-medications>

FDA ER/LA patient counseling: <https://www.fda.gov/media/86281/download>

¹ Dunn. Opioid Rx for chronic pain & OD. *Ann Int Med*. 2010;152(2):85-92

² Dasgupta. Impact of high-dose opioids on OD mortality. *Pain Med*. 2016;17:85-98

³ Shaw. Equianalgesic calculators. *Pract Pain Manage*. 2013; 13(7):61-66

⁴ Jones. ED visits, OD deaths from combined opioids + BZs. *Am J Prev Med*. 2015;49(4):493-501

⁵ Mathias. Goal attainment measure for OA, LBP. *Pain Week Abstracts*. 2012;141:211

⁶ Cheatile. Informed consent in opioid therapy. *J Pain Sump Manage*. 2012;44(10):105-16

Risk Mitigation

- Medication security: Storage Disposal ¹
- Naloxone + instructions for OD rescue ^{2,3}

- Consider opioids with lower addiction liability ⁴⁻⁸

Tramadol Tapentadol Buprenorphine Abuse-deterrent formulations

- Controlled Substance Agreement (CSA) ⁹⁻¹¹ (not a contract)

Behavior: Permitted Expected Prohibited

Consent: PDMP Drug testing Medical records

Potential aberrancy consequences

When used → 7-23% ↓ opioid misuse ¹²

¹ McCauley. Education targeting opioid safe storage, disposal. *Addict Behav.* 2013;38(6):2230-5

² Clark. Community opioid OD prevention, naloxone. *J Addict Med.* 2014;8(3):153-63

³ Wheeler. Opioid OD prevention with naloxone. *MMWR.* 2015;64(23):631-5

⁴ Surratt. Street prices of Rx opioids diverted to the illicit market. *Pain Week Abstracts.* 2012;113:172

⁵ Lehmann. Tramadol in acute pain. *Drugs.* 1997;53 Suppl 2:25-33

⁶ Cepeda. Opioid shopping risk comparison of 2 opioids. *Pain Week Abstracts.* 2012;7:10-1

⁷ Lofwall. Buprenorphine diversion, misuse. *J Addict Med.* 2014;8(5):315-26

⁸ White. Potential impact of ADF opioids on NMU rates. *J Opioid Manag.* 2015;11(3):199-210

⁹ Pergolizzi. Opioid patient-provider agreement. *Postgrad Med J.* 2017;93(1104):613-7

¹⁰ Starrels. Rx agreements, UDTs to reduce opioid misuse. *Ann Int Med.* 2010;152(11):712-20

¹¹ Downey. Implementation of patient agreement for opioids, stimulants in 1^o care. *J Fam Med Prim Care.* 2017;6(1):52-57

¹² Starrels. 1^o care attitudes about opioid agreements. *J Opioid Mge.* 2014;10(2):95-102



Image by Perry Wright

Opioid Prescribing Follow-Up

- Begin with open-ended questions
 - Continue with specifics in the Review of Systems
 - Sedation
 - Memory
 - Cognition
 - Respiratory
 - Constipation – Most frequent side effect
 - Mood – Current + Any changes related to treatment
 - Opioid use or perceived benefit for reason other than prescribed
- “Review of Nightmare”
→ Consider Addiction**

¹ Sees. Opioid use in chronic pain: assessment of addiction. *J Pain Symp Manage*. 1993;8(5):257-64

² Vuilleumier. Pharmacogenetics in opioid analgesia. *Pharmacogenomics Pers Med*. 2012;5:73-87

Opioid Prescribing Follow-Up

- Following the 5 A's^{1,2}
 - Activities (function)
 - Analgesia
 - Affect
 - Adverse events
 - Aberrancies

¹ After Passik. Tool to assess, document pain outcomes in chronic pain patients receiving opioids. *Clin Ther.* 2004;26(4):552-61

² Kirsch. 4 A's for ongoing monitoring. *Medscape Neurol.* 2005 Accessed 4/14/16

Risk Monitoring

- Behavioral aberrancy surveillance ¹⁻⁴
 - Addiction Behaviors Checklist ⁵
 - Current Opioid Misuse Measure ^{6,7}
 - Observed behavior
- Prescription Drug Monitoring Program (PDMP) ⁸⁻¹²
- Drug testing: Urine Oral fluid ¹⁰⁻¹⁵
- Product counts ^{10,15,16}

¹ Martell. Opioids for chronic back pain. *AIM*. 2007;146(2):116-27

² Fleming. Substance misuse aberrancy reports. *Pain Med*. 2008;9(8):1098-106

³ Fleming. SUDs in patients on opioids. *J Pain*. 2007;8(7):573-82

⁴ Alturi. Opioid abuse prevention in chronic pain. *Pain Phys*. 2012;15:ES177-89

⁵ Wu. Addiction Behaviors Checklist validation. *J Pain Symp Mge*. 2006;32(4):342-52

⁶ Meltzer. Identifying OUD with COMM. *Pain*. 2011;152(2):397-402

⁷ Butler. COMM cross validation. *Clin J Pain*. 2010;26(9):770-6

⁸ Dormuth. PDMP effect on inappropriate prescriptions. *CMAJ*. 2012;184(16):E852-6

⁹ Reifler. PDMP impact on opioid abuse/misuse? *Pain Med*. 2012;13(3):434-42

¹⁰ Alturi. Opioid abuse prevention in chronic pain. *Pain Phys*. 2012;15:ES177-89

¹¹ Hamill-Ruth. Med misuse risk objective data. *Pain Med*. 2013;14(12):1900-7

¹² Provenzano. Rethinking opioids in chronic pain. *Curr Med Res Opin*. 2014;30(10):2051-62

¹³ Gourlay. Urine Drug Testing in Clinical Practice monograph. 2015

¹⁴ Manchikanti. Adherence monitoring in chronic pain. *Pain Phys*. 2006;9:57-60

¹⁵ Bujold. Improving opioid use in chronic pain. *J Opioid Mge*. 2012;8(6):363-7

¹⁶ Viscomi. Pill counts & pill rental. *Clin J Pain*. 2013;29(7):623-4

TOP 10 REASONS FOR MY MEDICATION ISSUE

6) *Oxycodone* in my *Urine* ??

That CAN'T Be!

But I did have Sex with my Husband who takes it

7) I lost my pills when *THREE* Trees *Fell* on my house

8) The *Deer* ate them off the Picnic table

9) I was *Eating* my *Percocet* over the Sink when they *Fell* in !

10) Sorry I'm *Late* I got *Arrested* ... I'm in a *Rush* !
I need my refill ...

1) You won't Believe This !

I took off Fast The Pen Popped off the Dash
Hit the Prescription lying on the Car Seat

That's why there was a 1 in Front of the 20 Vicodin
Once I got to the Pharmacy !!

2) They Fell on the Floor All these Ants Carried them Off
I just watched in Amazement !

3) I Don't know *HOW* they ended in the Microwave

4) My Parakeet Carried the Bottle out the Window

5) I buy Syringes because my Trainer told me
to Inject B12 4 Times a Day

Aberrancy

- Divergence from the Controlled Substance Agreement
- Potential indicator of unsafe opioid use
- Not a diagnosis – Sets up a differential
 - Inadvertent: Loss Theft Memory problems
 - Medical: Self-directed pain management
 - Nonmedical: Diversion Personal nonmedical use
- Present in 40-50% of those prescribed opioids ^{1,2}
- Single high level aberrancy → change plan
- > 3 intermediate level aberrancies → change plan ^{3,4}

¹ Wiedemer. Opioid management for at risk pain patients. *Pain Med.* 2007;8(7):573-84

² Katz. Opioid behavioral monitoring, UDT. *Anesth Analg.* 2003;97(4):1097-102

³ Fleming. Substance misuse reported aberrancies. *Pain Med.* 2008;9(8):1098-106

⁴ Fleming. SUDs in patients on opioids. *J Pain.* 2007;8(7):573-82

Low Level Aberrancies

- Early refill once
- Self-directed dose ↑ once
- Missed / late for appointment
- Low dose alcohol for special occasion only
- Not informing prescriber of mild adverse reactions
- Non-notification of other opioid prescriber for good reason x1
- Occasional problem-solving phone calls rather than office visits
- Non-participation in non-medication pain approaches for economic reasons

Warning and
Consider ↑ Monitoring

Intermediate Level Aberrancies

- Early refill >1
- Consider self addicted
- Lost / stolen prescription
- Unauthorized overuse >1
- Focused on specific opioid
- Unauthorized cannabis use
- Limited interest in non-opioid approaches
- Multiple phone calls rather than office visits
- Not informing prescriber of significant adverse reactions
- Non-opioid substance addiction slip → return to abstinence
- Non-participation in non-medication approaches for noneconomic reasons

Warning and
↑ Monitoring

Aberrancy Management: Clinical Skills

- Plan ahead - have an exit strategy
- Drug test on a random basis
- Rely on *objective* data, not appearances and assumptions
- Team up – seek out and rely on the observations of others
- Reinforce boundaries – patients and team members
- Be vigilant for and assertively address splitting
- Use motivational interviewing

¹ Wilson. Strategies to stop Rx opioid abuse. *AIM*. 2007;146:897-900

² Parchman. 1^o care clinic design for Rx opioids. *J Am Board Fam Med*. 2017;30(1):44-51

³ Alperstein. MI efficacy in chronic pain. *J Pain*. 2016;17(4):393-403

⁴ Bohnert. RCT to reduce opioid OD risk behaviors in ED. *Drug Alc Dep*. 2016;163:40-7

⁵ Jamison. Assess, Rx abuse risk in opioid prescribing. *Pain Res Treat*. 2011;941808.

⁶ Cosio. How to set boundaries with chronic pain patients. *J Fam Prac*. 2014;63(3):S3-9

Aberrancy Management: Responding to Aberrancies

- Coach adherence + Increased monitoring ^{1,2}
- Specialist referral: Addiction Pain Psych Sleep ^{3,4}



Ultimatum

- Discontinue opioids / other addiction-prone substances ⁵⁻⁷



Ultimatum

- Discharge patient from the practice ⁴

Last resort !

Therapeutic discharge

¹ Jamison. Substance misuse Rx for high risk chronic pain patients on opioids. *Pain*. 2010;150(3):390-400

² Passik. Aberrant drug-related behavior with chronic opioids. *J Pain Sump Manage*. 2011;41(1):116-25

³ Sees. Opioid use in chronic pain: assessment of addiction. *J Pain Sump Manage*. 1993;8(5):257-64

⁴ Compton. Discharge opioid abusers from opioid-analgesic therapy? *Pain Med*. 2008;9(4):383-90

⁵ Fudin. Opioid withdrawal medication options. *Pract Pain Manage*. 2015;15(9)

⁶ Fleming. Substance misuse reported aberrancies. *Pain Med*. 2008;9(8):1098-106

⁷ Fleming. SUDs in patients on opioids. *J Pain*. 2007;8(7):573-82

High Level Aberrancies

- Forged prescription
- Cocaine / Stimulant use
- Involvement in DUI / MVA
- > 3 lower level aberrancies
- Non-pain related opioid use
- IV or IN route of administration
- Aggressive demands for opioids
- Active non-opioid substance relapse
- Refusal of non-medication approaches for pain
- Intoxication / Oversedation: Reported or observed
- Multi-sourcing: other prescribers / street / internet
- Stealing opioids / Obtaining from nonmedical sources
- Reliance on problem-solving phone calls rather than office visits

Ultimatum or
Opioid discontinuation

High Level Aberrancies

- Forged prescription
- Cocaine / Stimulant use
- Involvement in DUI / MVA

Change is
Indicated

> 3 lower level aberrancies ^{1,2}

- Non-pain related opioid use
- IV or IN route of administration
- Aggressive demands for opioids
- Active non-opioid substance relapse
- Refusal of non-medication approaches for pain
- Intoxication / Oversedation: Reported or observed
- Multi-sourcing: other prescribers / street / internet
- Stealing opioids / Obtaining from nonmedical sources
- Reliance on problem-solving phone calls rather than office visits

¹ Fleming. Substance misuse aberrancy reports. *Pain Med.* 2008;9(8):1098-106

² Fleming. SUDs in patients on opioids. *J Pain.* 2007;8(7):573-82

Pain Management Clinical Skills

Motivational Interviewing: Connecting behavior and goals¹⁻⁴

Communication and Collaboration⁵

Beware of specific medication requests⁶

“No” is a complete sentence

“I can no longer deliver these medications into an uncontrolled environment”

¹ Lundahl. Motivational interviewing effectiveness. *J Clin Psych.* 2009;65(11):1232-45

² Burke Motivational interviewing meta-analysis. *J Consult Clin Psych.* 2003;71(5):843-61

³ Dunn. Brief intervention, motivational interviewing. *Addiction.* 2001;96(12):1725-42

⁴ Jensen. Motivational interviewing, adolescent substance use. *J Consult Clin Psych.* 2011;79(4):433-40

⁵ Mędrzycka-Dąbrowska. Acute, postop pain problems. *Adv Clin Exp Med.* 2015;24(5):905-10

⁶ McKinlay. Patient med request effects. *Med Care.* 2014;52(4):294-9

Documentation

SOAP Note

- S Function-Pain *and* Risk
- O Function-Pain *and* Risk
- A Function-Pain *and* Risk
- P Function-Pain *and* Risk

Document What You

- See
- Do
- Think



Chronic

Pain

is a Disease

Whitten, Cristobel.
Chronic pain is a chronic condition.
Permanente J. 2005;9(3)

You treat a disease.

You win or lose.

You treat a person.

I guarantee you win no matter the outcome.

- Patch Adams

sleighwright@gmail.com



Supplemental Slides

Each Opioid is Different

- Receptors affected varies ¹⁻⁵
 - Opioid receptors: μ κ δ Nociceptin
 - Non-opioid receptors: NMDA Na $\alpha 2$ adrenoreceptor
- Receptor affinity varies - μ receptor affinity: ⁶⁻⁸
Buprenorphine > Naloxone > Hydromorphone > Fentanyl
- Intrinsic activity and potency varies ⁵
Does not necessarily correlate with efficacy ⁹

¹ Wikipedia. Opioid receptors Accessed 4/8/16

² Largent-Milnes Patented, promising ORL-1. *Expert Opin Ther Pat.* 2010;20(3):291-305

³ McDonald. Opioid receptors. *Contin Ed Anes Crit Care Path.* 2005;5(1):22-5

⁴ Noda. Opiate physical dependence, NMDA receptor. *Eur J Pharm.* 2004;500(1-3):121-8

⁵ Stoetzer. Methadone anesthetic-like inhibitor of neuronal Na⁺ channels. *Br J Anes.* 2014;114(1)::110-20

⁶ Bowdle. Opioid agonists, agonist-antagonists in anaesthesia. *Drug Saf.* 1998;19(3):173-89

⁷ Boas. Fentanyl, buprenorphine receptor binding. *Br J Anes.* 1985;57(2):192-6

⁸ Volpe. μ receptor binding constants for selected opioids. *Regul Tox Pharm.* 2011;59(3):385-90

⁹ Passik. Opioid analgesics: does potency matter? *J Opioid Manag.* 2014;10(4):263-75

Initial Opioid Selection

- Efficacy varies by individual patient ¹⁻⁴

Only clinical predictor for efficacy: what worked before

Potentially predictive genetic markers: OPRM1 ⁵⁻⁷

- Adverse reactions vary by individual patient

Clinical markers helpful: Non-medical use / Addiction / OD

Potentially predictive genetic markers: 3A4, 2B6, 2D6, OPRM1 ⁵⁻⁷

Key: Clinical Factors

¹ Hanks. Variability in opioid response. *Support Care Cancer*. 2005;13(3):145-52

² Lauche. Opioids in chronic noncancer pain - are opioids different? *Schmerz*. 2015;29(1):73-84

³ Chou. Efficacy, safety LA po opioids for chronic non-cancer pain. *J Pain Symp Manage*. 2003;26:1026-48

⁴ Allan. TD fentanyl, SR morphine for chronic non-cancer pain. *BMJ*. 2001;322(7295):1154-8

⁵ Quang-Cantagrel. Opioid substitution to improve efficacy. *Anes Analg*. 2000;90(4):933-7

⁶ De Capraris. OPRM1 A118G polymorphism & postop pain. *Int J Immunopath Pharm*. 2011;24(4):993-1004

⁷ Vuilleumier. Pharmacogenetics in opioid analgesia. *Pharmacogenomics Pers Med*. 2012;5:73-87

Initial Opioid Selection

Addressing Major Risks

- Respiratory Depression risk lower

Buprenorphine ¹⁻³ Tapentadol ⁴ Tramadol ⁴

- Addiction Liability risk lower

Buprenorphine ⁵⁻⁷ Tapentadol ⁸ Tramadol ⁹

Methadone ⁷

Abuse Deterrent Formulations ^{10,11}

Risk Management the Same for All Opioids

¹ Dahan. BUP induces ceiling in respiratory depression. *Br J Anes*. 2006;96(5):627-32

² Khanna. Buprenorphine in chronic pain. *J Pain Res*. 2015;8:859-70

³ Pergolizzi. Opioids in chronic severe pain in elderly. *Pain Prac*. 2008;8(4):287-313

⁴ Nossaman. Periop pain management, tramadol, tapentadol. *Anes Clin*. 2010;28(4):647-66

⁵ Cicero. Buprenorphine misuse 2008-2013. *Drug Alc Dep*. 2014;142:98-104

⁶ Coplan. Buprenorphine patch v other ER opioids. *Pain Week Abstracts*. 2014;33

⁷ Nordbø. TD buprenorphine, other addictive drugs. *Acta Anes Scand*. 2012;56(1):88-94

⁸ Surrat. Street prices of diverted prescription opioids. *Pain Week Abstracts*. 2012;113:172

⁹ Lehmann. Tramadol in acute pain. *Drugs*. 1997;53 Suppl 2:25-33

¹⁰ Cassidy. Rx opioid abuse after introduction of ADF. *Pain Med*. 2014;15(3):440-5

¹¹ Cicero. ADFs and US Rx opioid abuse epidemic. *JAMA Psych*. 2015;72:424-9

Initial Opioid Selection

Addressing Adverse Reactions

- Hypogonadism less likely
Buprenorphine ¹ Tapentadol ²
- Depressed mood associated with Rx opioids overall ³
Except buprenorphine with potential benefit ⁴
- Serotonin syndrome risk related to # serotonergic agents ⁵
High risk → avoid tramadol / tapentadol ⁶

¹ Khanna. Buprenorphine in chronic pain. *J Pain Res.* 2015;8:859-70

² Nossaman. Periop pain management, tramadol, tapentadol. *Anes Clin.* 2010;28(4):647-66

³ Scherrer. Rx opioids increase risk of depression. *J Gen Int Med.* 2014;29(3):491-9

⁴ Serafini. BUP efficacy in depression, suicidal behavior. *Int J Mol Sci.* 2018;19(8). pii: E2410

⁵ Volpi-Abadie. Serotonin syndrome. *Ochsner J.* 2013;13(4):533-40

⁶ Baldo. Opioids and serotonin syndrome. *Arch Toxicol.* 2018;92(8):2457-73

Initial Opioid Selection

Addressing Adverse Reactions

- Constipation ¹⁻⁴

Worse: Methadone Morphine

Better: Buprenorphine TD Fentanyl TD Oxycodone CR Tapentadol

- Renal Disease ⁵⁻⁹

Avoid: Morphine Codeine NSAIDs

Safer: Buprenorphine Methadone Fentanyl

- Hepatic Disease ⁹⁻¹²

Avoid: Methadone Codeine Tramadol NSAIDs APAP

Safer: Fentanyl

¹ Rosti. Opioid bowel dysfunction. *Eur Rev Med Pharmacol Sci*. 2010;14(12):1045-50

² Tzschenke. Tapentadol: μ agonist, NE reuptake inhibitor. *J Pharm Exp Ther*. 2007;323(1):265-76

³ Khanna. Buprenorphine in chronic pain. *J Pain Res*. 2015;8:859-70

⁴ Hadley. TD fentanyl for cancer pain. *Cochrane Rev*. 2013;10:CD010270

⁵ Murtagh. Opioids in ESRD without dialysis. *J Pain Palliat Care Pharmacother*. 2007;21(2):5-16

⁶ Sawe. Morphine, methadone pharmacokinetics in cancer. *Clin Pharmacokinetics*. 1986;11(2):87-106

⁷ Niscola. Analgesics in patients with renal dysfunction. *Curr Drug Targets*. 2010;11(6):752-8

⁸ Atkinson. Dialysis, opioids, pain management. *Prac Pain Mgmt*. 2014;14(8):49-57

⁹ Murphy. Acute pain care, renal or hepatic disease. *Anes Intensive Care*. 2005;33(3):311-22

¹⁰ Bosilkovska. Analgesics in hepatic impairment. *Drugs*. 2012;72(12):1645-69

¹¹ Innaurato. Analgesia in hepatic impairment. *Rev Med Suisse*. 2015;11(480):1380, 1382-4

¹² Tegeder. Pharmacokinetics of opioids in liver disease. *Clin Pharmacokinetics*. 1999;37(1):17-40

Initial Opioid Selection

Considering Adverse Reactions

- Hypogonadism less likely: Buprenorphine ¹ Tapentadol ²
- Methadone *not* 1st line - unless opioid addiction present
 - QTc > 500 → Do *not* use / refer to cardiology ³
 - QTc 450-500 → Reconsider use ³
- **Multiple** serotonergic substances ⁴ → avoid tapentadol / tramadol
 - SSRIs SNRIs Mirtazapine Bupropion MAOIs Li TCAs
 - Metoclopramide Ondansetron Linezolid Ritonavir ?Triptans
 - Methamphetamine Cocaine Dextromethorphan
 - St John's wort Nutmeg Ginseng
 - Carbamazepine Valproic acid

¹ Khanna. Buprenorphine in chronic pain. *J Pain Res.* 2015;8:859-70

² Nossaman. Periop pain management, tramadol, tapentadol. *Anes Clin.* 2010;28(4):647-66

³ Methadone safety guide: American Pain Society. 2014. Accessed 2/20/16

⁴ Volpi-Abadie. Serotonin syndrome. *Ochsner J.* 2013;13(4):533-40

Opioids in Renal Disease

- Pain common, under-treated in patients with renal disease ^{1,2}
- Accumulation of agent / metabolites → potential problems
- If GFR ↓ ²⁻¹⁰
 - Avoid: Morphine Codeine NSAIDs
 - Consider dose reduction:

Oxycodone	Hydrocodone	Tramadol
Oxymorphone	Hydromorphone	Tapentadol
 - Safer in renal dysfunction: Methadone Buprenorphine Fentanyl

¹ Davison. Pain in hemodialysis. *Am J Kidney Dis.* 2003;42(6):1239-47

² Murtagh. Opioids in ESRD without dialysis. *J Pain Palliat Care Pharmacother.* 2007;21(2):5-16

³ King. Opioids in cancer pain +renal impairment. *Palliat Med.* 2011;25(5):525-52

⁴ Sawe. Morphine, methadone pharmacokinetics in cancer. *Clin Pharmacokinetics.* 1986;11(2):87-106

⁵ Lugo. Methadone pharmacokinetics. *J Pain Palliat Care.* 2005;19(4):13-24

⁶ Murphy. Acute pain care, renal or hepatic disease. *Anes Intensive Care.* 2005;33(3):311-22

⁷ Niscola. Analgesics in patients with renal dysfunction. *Curr Drug Targets.* 2010;11(6):752-8

⁸ Atkinson. Dialysis, opioids, pain management. *Prac Pain Mgmt.* 2014;14(8):49-57

⁹ Dean. Opioids in renal failure and dialysis patients. *J Pain Symp Manage.* 2004;28(5):497-504

¹⁰ Pergolizzi. Opioids, chronic severe pain in elderly. *Pain Pract.* 2008;8(4):287-313

Opioids in Hepatic Disease

- Pain common, under-treated in patients with hepatic disease ¹
- Hepatitis is risk factor for opioid non-medical use (IVDU) ²
- Accumulation of agent / metabolites → potential problems
- If hepatic function ↓ ²⁻⁹ Marker: ↑ INR when not anti-coagulated
 - Avoid: Methadone Tramadol Codeine NSAIDs
 - Consider dose reduction:
Oxycodone Hydromorphone Morphine
Tapentadol APAP
 - Safer in hepatic dysfunction: Fentanyl

¹ An. Chronic liver disease Sxs. *J Nurs Scholarsh*. 2015;47(4):310-7

² McAdam-Marx. Opioid misuse costs. *J Pain Palliat Care Pharmther*. 2010;24(1):5-18

³ Bosilkovska. Analgesics in hepatic impairment. *Drugs*. 2012;72(12):1645-69

⁴ Innaurato. Analgesia in hepatic impairment. *Rev Med Suisse*. 2015;11(480):1380, 1382-4

⁵ Tegeder. Pharmacokinetics of opioids in liver disease. *Clin Pharmacokinet*. 1999;37(1):17-40

⁶ Murphy. Acute pain care in renal /hepatic disease. *Anes Intensive Care*. 2005;33(3):311-22

⁷ Niscola. Analgesics in patients with renal dysfunction. *Curr Drug Targets*. 2010;11(6):752-8

⁸ Atkinson. Dialysis, opioids, pain management. *Prac Pain Mgmt*. 2014;14(8):49-57

⁹ Dean. Opioids in renal failure, dialysis. *J Pain Symp Manage*. 2004;28(5):497-504

Short – Acting Opioids

- Advantages

Inexpensive

Can use prn, for breakthrough pain

Some patients do better with short-actings

Relationship with efficacy / adverse reactions easier to judge

Adverse reaction duration shorter

- Disadvantages

Inconsistent analgesia / function benefit: Chase pain Clock-watch Cyclic WD

↑ prescribed pill number

3rd party unit # limitations → possible ↓ analgesic continuity

↑ addiction liability *in theory*

Extended-Release / Long-Acting Opioids

- Advantages

More *consistent* analgesia through the day

- Disadvantages

Cannot use prn

Expensive (except methadone)

3rd party limitations → prior authorization

Unsuccessful s/p bariatric surgery

Adverse reaction duration longer

↑ OD risk ^{2,3}

- May have abuse deterrent features

- Begin with short-acting ¹ → tolerance, clearer efficacy / AE signal

LA = SA opioids ³
Analgesia
Function
Sleep

¹ Dhalla. Mortality before, after introduction LA oxycodone. *CMAJ*. 2009;181:891-6

² Zedler. Risk factors for serious Rx opioid OD among vets. *Pain Med*. 2014;15(11):1911-29

³ Pederson. Long- or short-acting opioids for chronic non-malignant pain. *Acta Anaesthesiol Scand*. 2014;58(4):390-401

Opioid Prescribing Follow-Up: Insufficient Efficacy

- Opioid discontinuation by tapering ^{1,2}
- Opioid rotation / switching ³⁻⁵ **Conversion tables problematic ⁶**
- Opioid dosing change – Think twice !
 - Dosage amount ↑ No technical limit *but* there are practical limits
 - Dosage interval ↓ To address end-of-dose failure ⁷

Methadone

Every 6-8 hours ⁸

Oxycodone CR

Every 6-12 hours ^{9,10}

Fentanyl TD

Every 48-72 hours ¹⁰

Buprenorphine TD

Every 6-7 days

**Typical Effective
Dosing Intervals**

¹ Darnall. Patient-centered Rx opioid tapering in chronic pain. *JAMA Int Med.* 2018; e178709

² Baron. Pain ↓ after detox from high-dose opioids. *J Opioid Manag.* 2006;2(5):277-82

³ Nalamachu. Opioid rotation. *Adv Ther.* 2012;29(10):849-63

⁴ Smith. Systematic approach to opioid rotation. *J Pain Res.* 2014;7:589-608

⁵ Quang-Cantagrel. Opioid substitution to improve efficacy. *Anes Analg.* 2000;90(4):933-7

⁶ Shaheen. Opioid equianalgesic tables equally dangerous? *J Pain Symp Manage.* 2009;38(3):409-17

⁷ Zimmerman. End-of-dose pain, LA opioids. *Pain Pract.* 2014;14(8):757-69

⁸ Eap. Interindividual methadone pharmacokinetic variability. *Clin Pharmacokinet.* 2002; 41(14):1153-93

⁹ Pickard. Consumption of TAP ER, OXY CR, OXM ER. *Pain Week Abstracts.* 2013;67:117-8

¹⁰ Ackerman. Patient utilization of fentanyl TD, oxycodone CR. *J Manag Care Pharm.* 2003;9(3):223-31

Risk Screening: Patient Specific OD Risk Factors

- Caucasian ¹
- Opioid addiction ²
- Opioid-related aberrancies ³
- Psychiatric problems ^{1,4,5}
- HIV, hepatitis ⁷
- Family history of addiction ¹
- Male ¹
- Other substance addiction ¹
- Pain-related limitations ¹
- Trauma ⁶
- Legal involvement ¹
- Genetics ⁸

Especially: Multiple Co-Morbidities

¹ Liebschutz. Factors associated with Rx drug use disorder in chronic pain. *J Pain*. 2010;11(11):1047-55

² Boscarino. Risk factors for drug dependence in patients on opioids. *Addiction*. 2010;105:1776-82

³ Fleming. Lifetime drug-taking aberrancies predict current SA, MH problems. *Pain Med*. 2008;9(8):1098-106

⁴ Wasan. Psych risk factors for aberrancies. *Clin J Pain*. 2007;23:307-15

⁵ Riley. Individual differences in opioid efficacy chronic noncancer pain. *Clin J Pain*. 2008;24(6):509-20

⁶ Swan. Child abuse role in later drug abuse. *NIDA Notes*. 1998;13(2) Accessed 3/26/16

⁷ McAdam-Marx. Opioid abuse, misuse cost. *J Pain Palliat Care Pharmacother*. 2010;24(1):5-18

⁸ Manchikanti. ASIPP opioid guide in chronic noncancer pain: evidence. *Pain Phys*. 2012;15(3 Suppl):S1-65

⁹ Blum. Molecular genetic testing in pain, addiction: facts, fiction, clinical utility. *Addict Genet*. 2015;2(1):1-5.

Opioid Adverse Events

**Diversion
Misuse
Non-medical use
Addiction
Overdose**

- Psychomotor (small effects) ^{1,2}
- Hypogonadism in men ^{3,4}
- Drowsiness 3-88% ^{2,5-8}
- Falls / Fractures ^{9,10}
- Depression ¹¹ except buprenorphine ¹²
- Opioid Bowel Dysfunction ^{5,13,14}
3-85% nausea, vomiting ⁸
5-97% constipation ^{5,8,14,15}

¹ Larsen. LT opioid psychomotor effects. *Anesthesist*. 1999;48(9):613-24

² Dassanayake. Benzodiazepine, antidepressant, opioid & driving. *Drug Saf*. 2011;34(2):125-56

³ Bawor. Testosterone suppression in opioid users. *Drug Alc Dep*. 2015;149:1-9

⁴ Birthi. Hypogonadism associated with LT opioids. *J Opioid Manag*. 2015;11(3):255-78

⁵ Zlott. Mechanisms pharmacologic agents contribute to fatigue. *PMR*. 2010;2(5):451-5

⁶ Wiffen. Opioids & consciousness, appetite, thirst. *Cochrane Rev*. 2014;5:CD011056

⁷ Kalso. Opioids in chronic non-cancer pain review. *Pain*. 2004;112(3):372-80

⁸ Oosten. Opioid AEs in cancer-related pain. *J Pain*. 2015;16(10):935-46

⁹ Bushel. Medication fall injury risk in elderly. *Eur J Pub Health*. 2014;25(3):527-3

¹⁰ Solomon. Comparative analgesic safety in elderly arthritics. *Arch Int Med*. 2010;170(22):1968-76

¹¹ Scherer. Prescription opioid duration increases depression risk. *Ann Fam Med*. 2016;14:54-62

¹² Bodkin. Buprenorphine for refractory depression. *J Clin Psychopharmacol*. 1995;15(1):49-57

¹³ Panchal. Opioid-induced bowel dysfunction. *Int J Clin Pract*. 2007;61(7):1181-7

¹⁴ Szigethy. Narcotic bowel syndrome, OIC. *Curr Gastroenterol Rep*. 2014;16(10):410

¹⁵ Rosti. Opioid-related bowel dysfunction. *Eur Rev Med Pharm Sci*. 2010;14(12):1045-50

Opioid Adverse Events: Hyperalgesia

**Does morphia encourage
the very pain
it pretends to relieve ?**

- Albutt, 1870

Opioid Rotation = Opioid Switching

Change opioid or route of administration to improve outcomes ¹

- Reasons for rotation ^{1,2}

- | | | | |
|--------------------|-----------------|-----------|------------------------|
| • Adverse effects: | Intolerable AEs | Allergy | Drug-drug interactions |
| • Poor efficacy: | Primary failure | Tolerance | Hyperalgesia |
| • Other factors: | Adherence | Insurance | Organ dysfunction |

- Reasons for the need to rotate ³

- Individual variation of opioid receptor effects: Pharmacodynamics
- Individual variation of opioid metabolism: Pharmacokinetics

¹ Fine. Evidence review, guidelines for opioid rotation. *J Pain Symp Manage*. 2009;38(3):418-25

² Dale. Opioid switching to improve analgesia, reduce AEs. *Palliat Med*. 2011;25(5):494-503

³ Vuilleumier. Pharmacogenetics in opioid analgesia. *Pharmacogenomics Pers Med*. 2012;5:73-87

Opioid Rotation = Opioid Switching

- Goals
 - Efficacy ^{1,2}
 - Side effects ↓ ^{1,2}
 - Safety ³
 - Absence of withdrawal ²
- Outcomes
 - Systematic reviews: favorable in 50-80% ⁴
 - Single switch opioid studies favorable ^{1,4-9}
 - Sequential switch opioid study ¹⁰
 - 36% good efficacy with 1st opioid
 - 56% cumulative success after 2nd opioid *
 - 73% cumulative success after 3rd opioid *
 - 88% cumulative success after 4th opioid *
 - 90% cumulative success after 5th opioid *

* My calculations

¹ Dale. Opioid switching to improve analgesia, reduce AEs. *Palliat Med.* 2011;25(5):494-503

² Knotkova. Equianalgesic table science, limits. *J Pain Symp Manag.* 2009;38(3):426-39

³ Webster. Opioid rotation practices, associated toxicity. *Pain Med.* 2012;13(4):562-70

⁴ Nalamachu. Opioid rotation in clinical practice. *Adv Ther.* 2012;29(10):849-63

⁵ Mercadante. Morphine to methadone switching in cancer pain. *J Clin Onc.* 2011;19(11):2898-904

⁶ Mercadante. Opioid levels during switch: TD fentanyl to methadone. *Palliat Med.* 2007;10(2):338-44

⁷ Riley. Morphine sensitivity variation, switching in cancer. *Support Care Cancer.* 2006;14(1):56-64

⁸ Weschules. Methadone conversion in pain. *Pain Med.* 2008;9(5):595-612

⁹ Quigley. Opioid switching to improve pain, tolerability. *Cochrane Rev.* 2004;(3)

¹⁰ Quang-Cantagrel. Opioid substitution to improve efficacy. *Anes Analg.* 2000;90(4):933-7

Opioid Rotation: Methadone Calculation

$$\text{Methadone (mg)} = \frac{x}{21} \times \left\{ 5.7 - 3 \times \sin \left(\frac{90}{\left(\frac{110^5}{x} \right) + 1} \right) - \sin \left(\frac{90}{\left(\frac{320^7}{x} \right) + 1} \right) \right\}$$

x = morphine in mg

Opioid Rotation Calculation

- Calculate opioid equivalent dose using Prescribing Information
 - Studies often single-agent, low-dose, inconsistent ¹⁻⁷
 - Ratios vary depending on direction of the switch ²
- MED calculators vary widely ^{1,2,4,6-8} - methadone by 300% ⁷
 - Recommended: Practical Pain Management Calculator ⁷
- Due to incomplete cross tolerance ⁹ reduce calculated amount 25-50% ¹⁰
- Make additional reductions ³ based on
 - Other sedating meds
 - Individual patient considerations

¹ Shaw. Comparison of online equianalgesic opioid calculators. *Prac Pain Mgmt.* 2013;13(7):61-6

² Pereira. Equianalgesic dose ratios for opioids. *J Pain Symp Manage.* 2001;22(2):672-87

³ Fine. Evidence review, guidelines for opioid rotation. *J Pain Symp Manage.* 2009;38(3):418-25

⁴ Shaheen. Opioid equianalgesic tables: equally dangerous? *J Pain Symp Manage.* 2009;38(3):409-17

⁵ Mercadante. Conversion ratios for opioid switching in cancer pain. *Palliat Med.* 2011;25(5):504-15

⁶ Pantanwala. Opioid conversion in acute care. *Ann Pharmacother.* 2007;41(2):255-66

⁷ Fudin. Mathematical model for methadone conversion. *Prac Pain Mgmt.* 2012;12(8):46-51

⁸ O'Bryant. Opioid equianalgesic ratio inconsistencies. *J Pain Palliat Care Pharmacother.* 2008;22(4):282-90

⁹ Bruera. Dose ratio comparison: methadone, hydromorphone, morphine. *Cancer.* 1996;78(4):852-7

¹⁰ Nalamachu. Opioid rotation. *Adv Ther.* 2012;29(10):849-63

Opioid Rotation Methods

- Stop - and - Go Method
Stop the old opioid
Go (start) new opioid at calculated dose
- Cross Taper Method
Reduce old opioid
Start proportionate amount of new opioid
Sequentially out with the old ... in with the new ...
- Methadone ¹⁻⁴
Cross taper
Stop-and-Go not recommended unless low dose
Initial maximum daily dose ≤ 30 mg

¹ Methadone safety guide: American Pain Society. 2014 Accessed 2/20/16

² Modesto-Lowe. Methadone death risk factors. *J Gen Int Med.* 2010;25(4):306-9

³ Fredheim. Methadone pharmacology in pain. *Acta Anes Scand.* 2008;52(7):879-89

⁴ Corkery. Methadone effects, fatalities. *Hum Psychopharm.* 2004;19(8):565-76

Opioid Rotation Process

- Short-acting opioids for breakthrough pain ¹
Patience !
Under-dosing initially is safer
- Manage patient expectations and transition anxiety
- Individualize dose titration according to steady state ²
↑ most ER/LA opioids q3-4d ²
↑ methadone weekly ³
- *Risk Manage every step of the way*
- *Have an Exit Strategy* ⁴

¹ Zucco. Breakthrough cancer pain. *Adv Ther.* 2014;31(7):657-82

² Zimmerman. End-of-dose pain & long-acting opioids. *Pain Prac.* 2014;14(8):757-69

³ Methadone safety guide: American Pain Society. 2014. Accessed 2/20/16

⁴ Smith. Toward systematic approach to opioid rotation. *J Pain Res.* 2014;7:589-608