A FREE CONTINUING EDUCATION SEMINAR

PAIN MANAGEMENT AND BEYOND

OCTOBER 14, 2017

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Continuing Medical Education (CME) &
Pharmacy Continuing Education (CE) Seminar

Pain Management and Beyond

on
October 14, 2017
at
Alagia Auditorium, St. Agnes Hospital

7:30 am –	Breakfast and Registration	
8:30 am –	Introductions	Maryland Medicaid Pharmacy Program
8:45 am –	Updates in Opioid Management for Chronic Pain: A critical review with practice recommendations: The Good, the Bad & the Ugly	Howard J. Hoffberg, MD Associate Medical Director Rehabilitation and Pain Management Associates
10:45 am –	Break	
11:00 am –	Maintenance Treatments for Opioid Use Disorder	Christopher Welsh, MD Addiction Medicine University of Maryland School of Medicine
12:00 pm –	Maryland Medicaid Opioid DUR and SUD initiatives	Lisa Burgess, MD Chief Medical Officer Maryland Department of Health
1:00 pm –	Closing Remarks	

The views and opinions expressed by the speakers are not necessarily the views and opinions of the Maryland Department of Health.

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Disclosures:

Presenter Disclosure:
Dr. Hoffberg states that he does have relevant financial relationship with commercial interests within the past 12 months and will be discussing "Off-Label" uses of products or devices. Dr. Hoffberg is a promotional speaker for Depomed, Purdue and Collegium. He is an advisory board consultant for Primus. This information is on file with Health Information Designs, LLC.

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Activity Type: Knowledge-Based

Updates in Opioid Management for Chronic Pain

A critical review with practice recommendations: The Good, the Bad & the Ugly

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Maryland Department of Health
Maryland Medicaid Pharmacy Program CME
St. Agnes Hosp Alagia Auditorium Oct 14, 2017

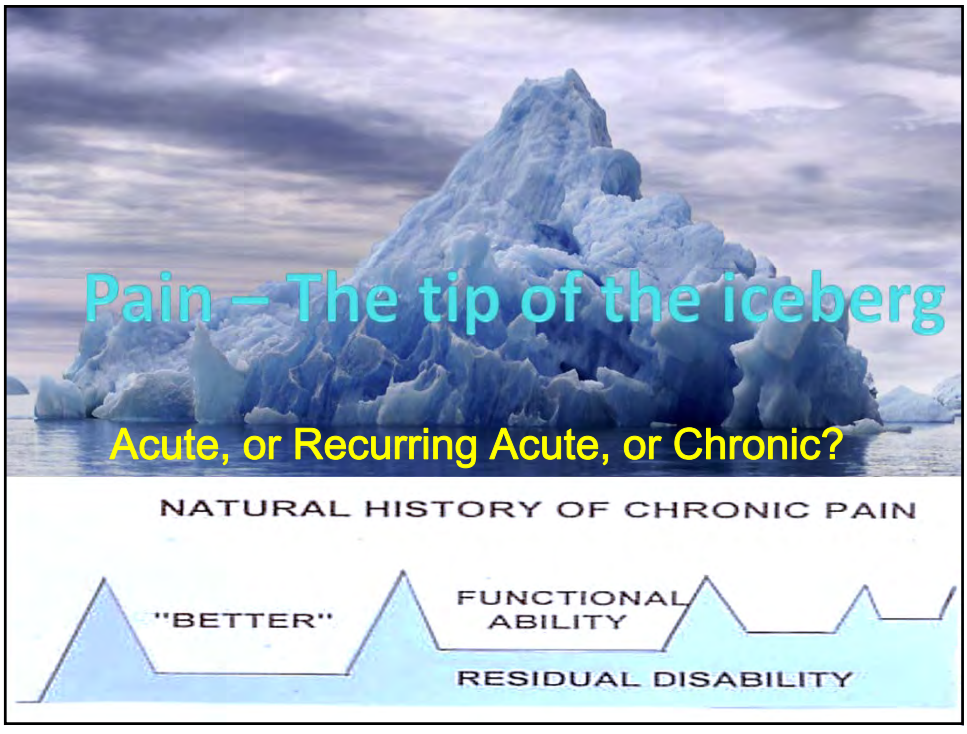
Disclosures – 2017:

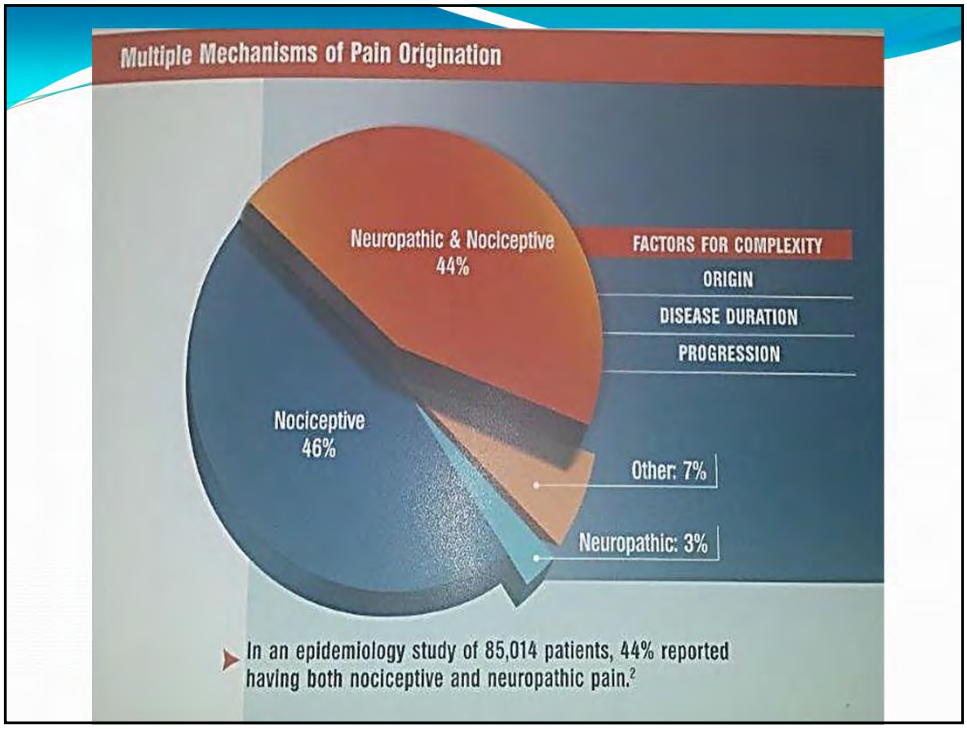
- Speaker's bureau: Depomed, Collegium Pharma
- Consultant: Primus Pharma, Realtox labs

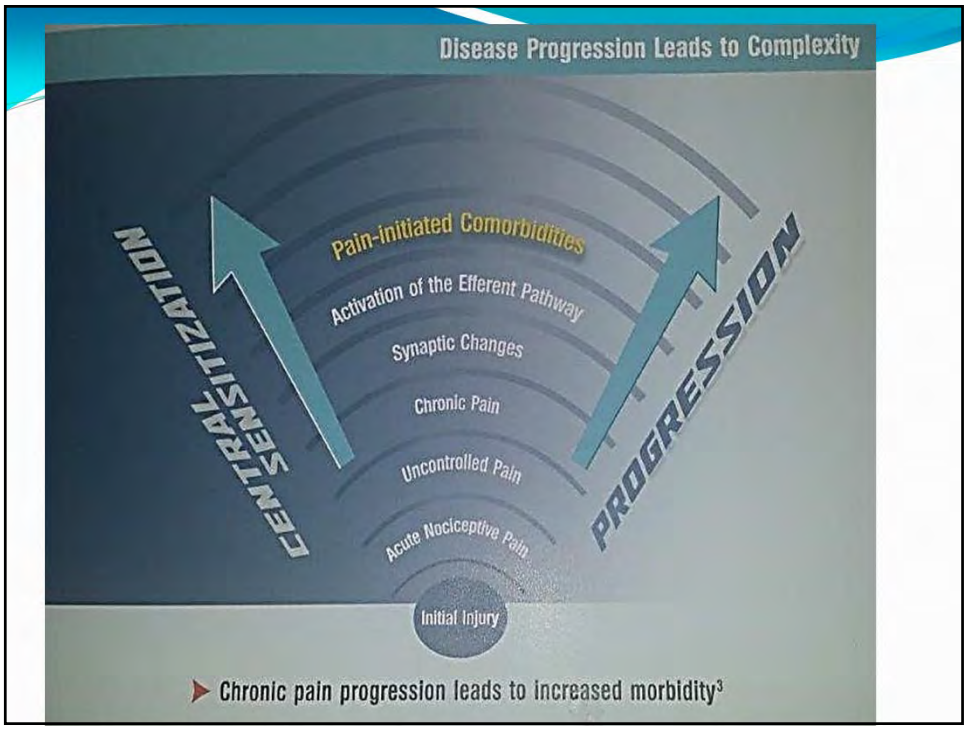
- I will be discussing off-label use of certain opioid therapies

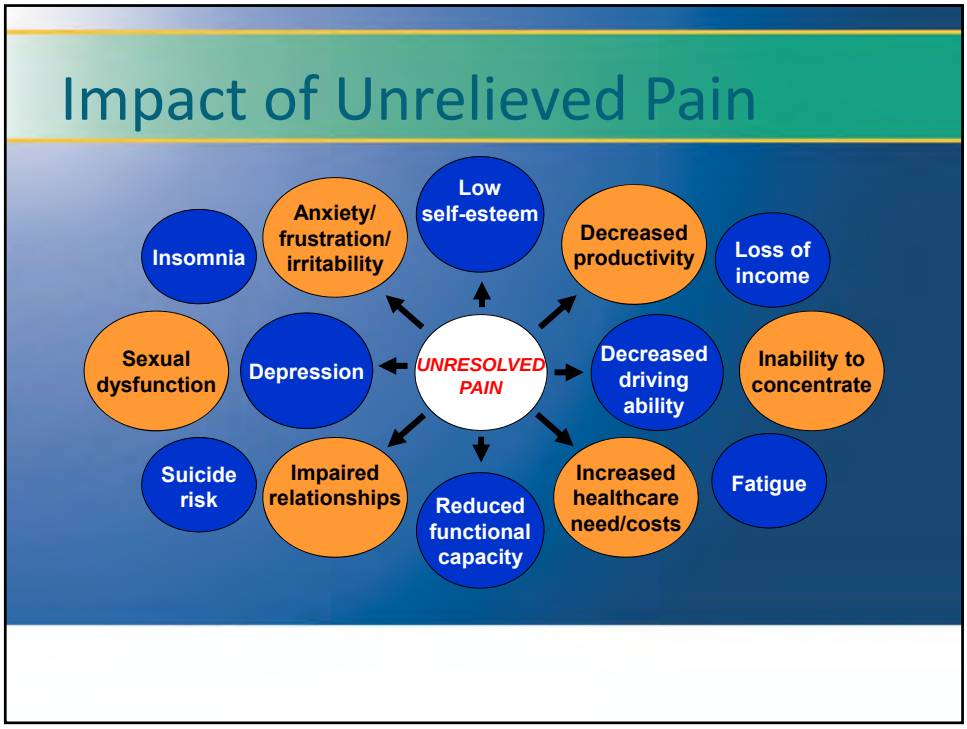
Opioids for chronic pain – Lecture outline

- Pain definition, pathophysiology, classification
- Pain generators spectrum of responsiveness to opioids
- Opioid therapy – specific medication characteristics and formulations
- Opioid therapy controversies, opioid use disorders
- Prescription opioid and opioid overdose epidemic statistics
- Opioid overdose scenarios and risk stratification scales
- Origins / description of CDC's pain management guidelines with critique
- Other recently published guidelines (ACP, FSMB, DoD, ASAM, NAS)
- Proper Patient selection & Risk stratification
- 10 Universal precautions of pain management (Goulay and Heit)
- Informed consent treatment **agreement** with education, and office policies
- 4 A's of Pain Medicine (+ 2 A's) (Passik)
- Aberrant behaviors and Red flags
- Goals of treatment
- Documentation
- Exit strategies, when to taper
- Defensive medicine and advice to providers
- Conclusion

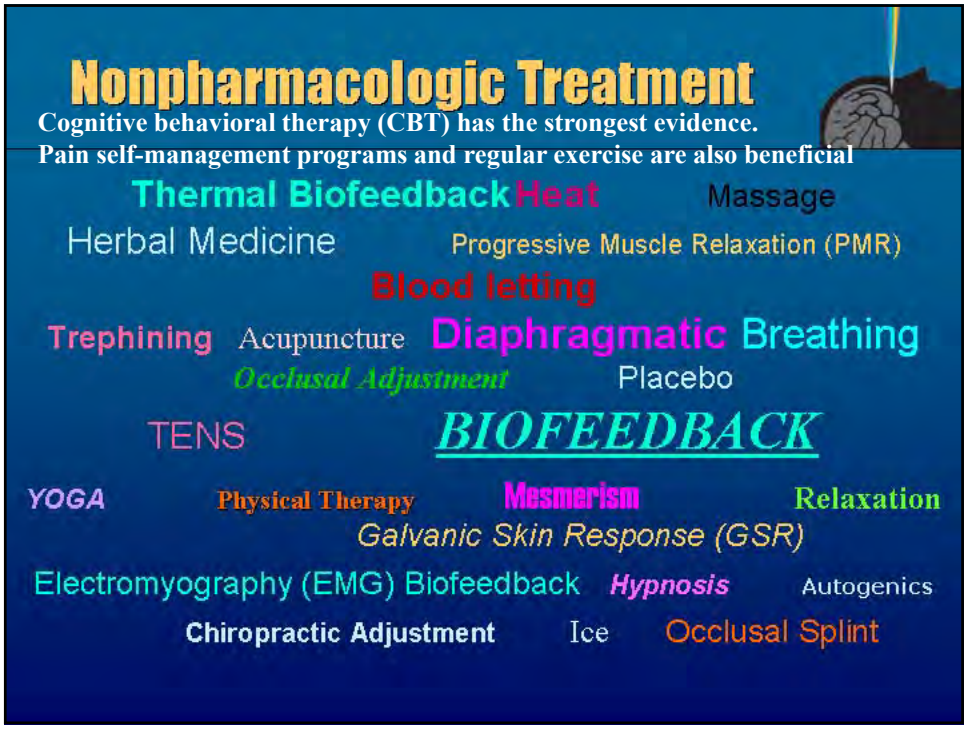



Multiple Mechanisms of Pain Origination
Neuropathic & Nociceptive
44%
Nociceptive
46%
Other: 7%
Neuropathic: 3%
FACTORS FOR COMPLEXITY
ORIGIN
DISEASE DURATION
PROGRESSION
In an epidemiology study of 85,014 patients, 44% reported having both nociceptive and neuropathic pain.[2]


Disease Progression Leads to Complexity
CENTRAL SENSITIZATION
PROGRESSION
Pain-initiated Comorbidities
Activation of the Efferent Pathway
Synaptic Changes
Chronic Pain
Uncontrolled Pain
Acute Nociceptive Pain
Initial Injury
Chronic pain progression leads to increased morbidity[3]


Impact of Unrelieved Pain
Low self-esteem
Anxiety/ frustration/ irritability
Insomnia
Decreased productivity
Loss of income
Sexual dysfunction
Depression
UNRESOLVED PAIN
Decreased driving ability
Inability to concentrate
Suicide risk
Impaired relationships
Reduced functional capacity
Increased healthcare need/costs
Fatigue


The Joint Commission:
PAIN –FIFTH VITAL SIGN
(now a controversial topic)
Represents 2/3 of Hospital satisfaction scores for reimbursement
50-75% of patients present to ED with pain;
Communications, Education & Patient-Provider expectations need improvement
Still need to treat pain to improve outcomes;
May contribute to opioid "overmedication" tendencies
Suffering - an emotional response to a noxious stimulus
Pain is universal;
Suffering is optional (Dahli Lama)
Suffering is not always obvious and does not equal pain
Pain Patients need compassionate & empathetic care
Pain is not good without an audience (Chinese proverb)
Pain changes with an audience (Dan Doleys, M.D.)



Nonpharmacologic, Therapeutic, conservative Strategies: start first

Multimodal conservative therapies

Multidisciplinary pain programs including psychotherapy have been shown to be beneficial for pain control, reduced dependency and improved quality of life, but have been limited due to reimbursements

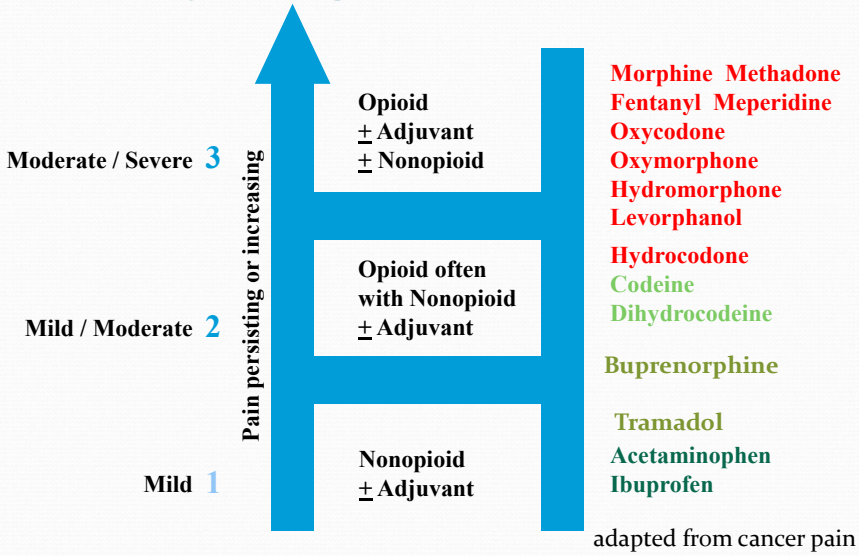
If acute: RICE (rest, ice, compression, elevation)

Reimbursement often favor non–evidence-based procedural or surgical pain treatments

Rehabilitative approaches
(exercise, adaptive equip, physical medicine modalities including PT, E-stim, chiro, aquatics)

- **Psychologic approaches (individual and family counseling, biofeedback & hypnosis)**
- **Anesthesiologic or interventional approaches (trigger point, prolotherapy, nerve, RFA, joint injections, PRP, intrathecal)**
- **Complementary and alternative medicine (CAM) approaches including mindfulness therapies, acupuncture, yoga, Tai Chi, Pilates, massage, craniosacral)**
- **Lifestyle changes (dietary, smoking cessation, family dynamics, voc rehab)**
- **Neurostimulatory approaches (peripheral, spinal or brain stim)**
- **Surgical approaches**

WHO Choice of Agent pharmaco: Three-Step Analgesic Ladder



adapted from cancer pain

Analgesic Pain responses to placebos range from 30% to 70%

Clinical practice: maximize placebo responses vs. identify nocebo responders (18%)
Small analgesic effect on average of most pain drugs, the few classes of analgesic options, and the frequent need for combination therapy with limited evidence by meta-analysis,
Long-term effectiveness is weak for nonpharmacological and analgesic treatments alike
Acetaminophen has been found to have minimal efficacy for low back pain and only small benefit for osteoarthritis
Nonsteroidal anti-inflammatory drugs (NSAIDs) for low back pain effects are very small
Some antiepileptic drugs and serotonin-norepinephrine reuptake inhibitors (duloxetine, milnacipran) are FDA-approved for neuropathic pain and fibromyalgia, but it is unclear if they are effective for the broader group of patients with low back pain, osteoarthritis, and other musculoskeletal pain disorders.
Tricyclic antidepressants and muscle relaxants are often used as adjunctive pain treatments but have a relatively weak evidence base for chronic pain
Cannabinoids showed modest analgesic benefits, especially for neuropathic pain
Opioids in placebo-controlled trials have shown a modest analgesic effect for long term use
With > 10M current opioid recipients, the probability of transitioning to long-term opioids was only 1.3% by 1.5 years after the first prescription, 2.1% by 3 years, 3.7% by 6 years, and 5.3% by 9 year. This would not be considered an “opioid epidemic”, but OD deaths are
Specific placebo effects of evidence-based pain treatments is compassionate rather than disingenuous care. Imperfect treatments do not justify therapeutic nihilism. A broad menu of partially effective treatment options maximizes the chances of achieving at least partial amelioration of chronic pain. Reimbursement strategies often favor non–evidence-based procedural or surgical pain treatments. Kroenke, JAMA, 5-17

Opioids are an effective, time honored treatment for pain

- **Medically necessary, legitimate pain in the usual course of clinical practice**
- **Pain of at least moderate to severe intensity (>3/10)**
- Other **prior treatments have not been effective enough**.
- In acute pain, analgesic effects are generally proportional to the dose, but physical ("therapeutic") tolerance to the respiratory depression effects is delayed, and may take 1-2 weeks to occur following a stable dosing
- No "ceiling effect" for most opioids, although in chronic pain, there may be habituation or tolerance, in which higher dosing over time is required for the same analgesic effect
- **No Rx are entirely safe, and risks may occur with any drug or treatment**

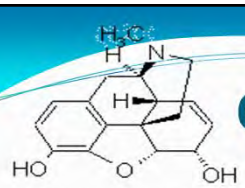
Opioid therapy:
Pain management is part of the "standard of care" in appropriate patients

- Healthcare costs due to pain management have skyrocketed
- Epidemic of inadvertent overdoses resulting in deaths, particularly in females, due to prescription medications, which often involves combining opioids with other sedating medications
- Nomenclature: Opioids (any, including synthetics)/ opiates (natural occurring) vs. Narcotics (pejorative)
  Opioid (physical) dependency vs. Addiction
  Tapering vs. Detoxification (for addiction)

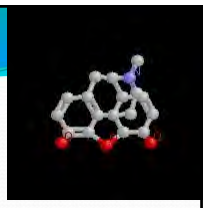
Opioid crisis: Prescribed opioid use is endemic for chronic pain, but chronic pain is pandemic (common prevalence) vs. Opioid overdose death epidemic (undesirable widespread outbreaks)

Patient reports of opioid therapy: survey 2017

- Opioids for chronic pain (44%), after surgery (25%), accident or injury (25%), or for recreational use (3%): the vast majority felt that opioids reduce their pain at least somewhat
- 57% improved quality of life, but 16% worsened
- 67% concerned about future access/ regulations
- Majority are "complex" patients, & described their health as fair to poor (42%), with polypharmacy (57%)
- 20% admitted taking for "fun or euphoria", 10 / 14% respectively for relaxation / stress
- 34% patients vs. 54% of household members believe that they are "addicted" (not medically defined) or physically dependent
- Household members reported higher rates of worsening personal (34%), physical or mental (39%), financial (37%) or job (27%) effects vs. patient (16%, 19%, 17%, 14% respectively)
- Patient defense mechanisms, self-serving, limited options



Opioid Receptors



Mu receptor agonists (MOR = u) has polymorphisms
MOR-1 is for therapeutic analgesia (increased spinal binding to dorsal root ganglion with up-regulation in peripheral inflammation), brain binding; MOR-2 for side effects (SEs)
Affects numerous body systems, influences mood and reward behavior and has immunologic suppression effects (especially codeine, morphine or fentanyl)
Affects numerous body systems, influences mood and reward behavior and has immunologic suppression effects (especially codeine, morphine or fentanyl)
Fentanyl has been associated with reduced angiogenesis, reducing cancer spread
At least 23 identified MOR sub-receptors morphology: variability of response
Kappa-receptor agonists (KOR) SAM: Sedation, Analgesia (spinal), Miosis, activated by stress
Delta-receptor agonists (DOR) direct (peripheral) analgesic effects, analgesia (spinal & supraspinal), smooth muscle relaxation, release of GH
PEAR: Physical dependence, Euphoria, Analgesic (supraspinal) and Respiratory depression
Sigma receptors agonists CNS Activation: dysphoria, hallucination, convulsions, respiratory and vasomotor stimulation, mydriasis (no longer classified as an "opioid" receptor)
Tolerance: DOR regulation of MOR, resulting in activation of NMDA receptors, which in turn activates calcium/calmodulin dependent kinase II, which inhibits G-protein coupled MOR; nitric oxide synthetase protein kinase A,C also involved
Dynamic interactions: KOR activation may reduce the MOR tolerance effect
Receptor CNS plasticity changes with stimulus intensity or chronicity of binding

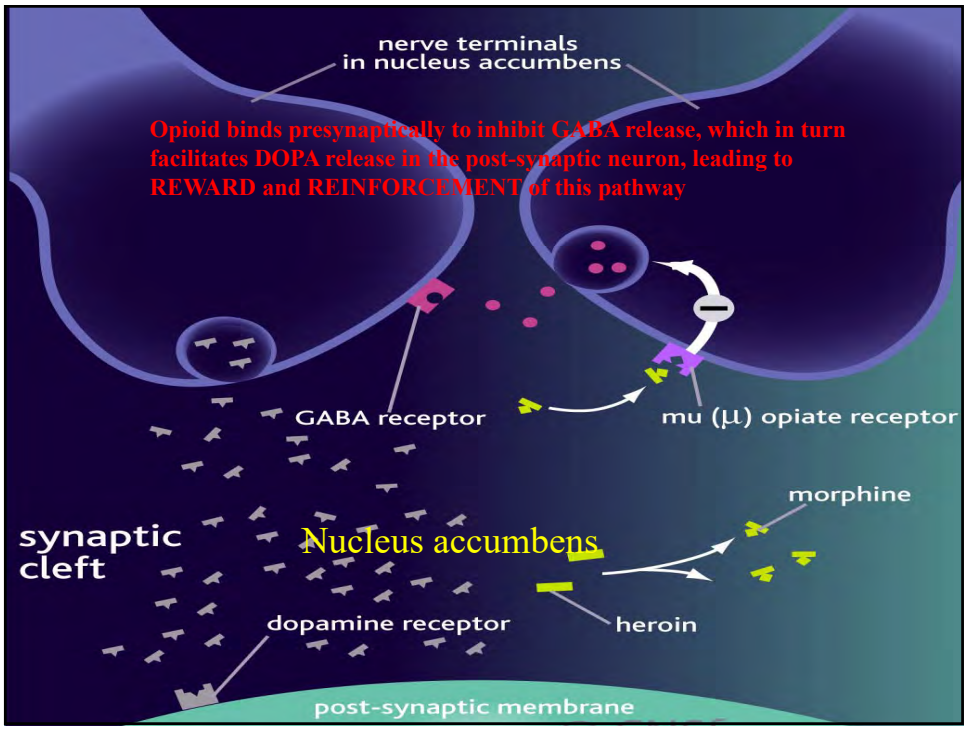
Opioid receptor locations

MOR-2 receptor: Inhibits Smooth muscle contraction of the Intestinal tract, especially the small intestine (constipation), CNS

MOR-1 receptor: Granulocytes, macrophages/ monocytes, lymphocytes and plasma cells which are up-regulated in patients with inflammatory conditions
PNS: nociceptive sensory dendrites (A delta and c fibers), DRG
CNS: Dorsal horn cells, spinal sensory neurons (especially lamina I and II), Brainstem (peri-aqueductal grey, reticular formation, locus ceruleus, and the rostral ventromedial medulla), Hypothalamus, olfactory bulb, Medial thalamic, amygdala , striatum, nucleus accumbens, solitary tract, Cerebral cortex, and in glial cells.

DOR receptors: Dilation: Vascular, Cardiac (negative inotropic), GI, Respiratory (inhibits bronchoconstriction via vagal sensory nerve endings, Vas deferens, Skeletal muscle metabolism and vasodilation (animals)

Peripheral binding of opioids do not result in a tolerance effect



Opioids better for acute, postoperative, traumatic, cancer related, burns, renal colic, sickle cell, arthritic, spinal, "real" pain

Less effective (higher dosing) for chronic, neuropathic, central sensitization (IBS, IC, headaches, fibromyalgia), visceral, hypermobility (EDS), central, "subjective" pain

Avoid with paralytic ileus, obstruction, head injury, acute asthma, or hypersensitivity

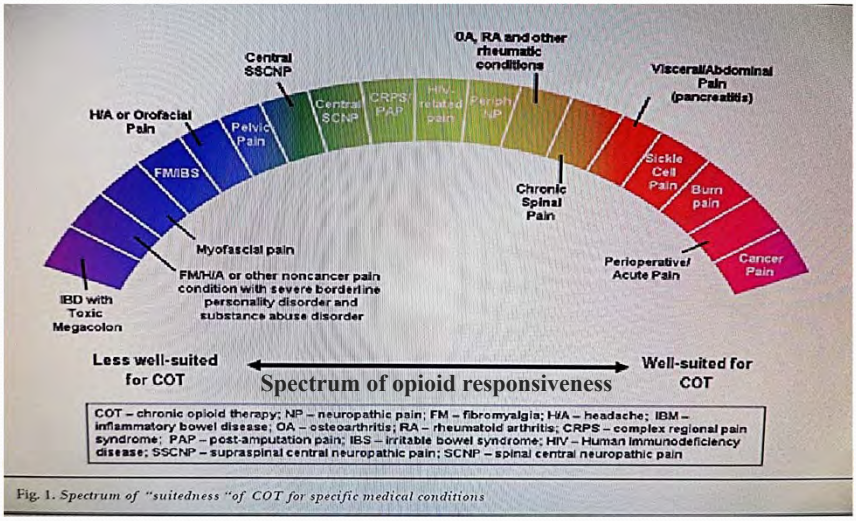


Fig. 1. *Spectrum of "suitedness "of COT for specific medical conditions*

Opioid Pharmacology

Pharmacokinetics (absorption, excretion, T1/2 concentration, drug interactions) Metabolism: glucuronidation +/- cytochrome (CY)P450: mainly 3A4 (60%), 2D6

CYP450, upregulated with age, acute illness; has sex differences vary with ethnicity; Polymorphism alleles: ultrafast, rapid (normal), intermediate ('"lazy")

Mainly studied in liver, but also present at BBB, lungs, GI & renal, which can also influence opioid metabolism. CYP450 system more sensitive to hepatic disease.

20-30% of patients may have metabolic defect affecting response & dosing

Pharmacogenetics (opioid receptor polymorphism, affinities for binding and variation in efficacy), "designer " drug choices based histocompatibility testing

Ultra-fast metabolism may present as a "drug seeker", requiring higher dosing

Potential drug interactions with many commonly prescribed adjunctive pain meds

Estimated risk of adverse drug interaction is 2-30% with polypharmacy,

Pharmacodynamics Axonal transport of opioid molecule (usually passive) by P-glycoprotein through BBB

mechanism of action: cross BBB, inhibiting pre-synaptic neuronal activity by hyperpolarization of membrane potential by K+ currents and inhibition of the Ca2+ influx which prevents neurotransmitter release and effects

Pain transmission in ascending (sensory) and descending (modulation) pathway

Receptor binding opioid is bound by a G protein complex

with a proportional dose response curve: NO CEILING EFFECT

Tolerance to sedating, respiratory (central) side effects but not constipation (peripheral, about 10% of the effect with hydrophilic opioids, <5% with lipophilic)

Dysphoric effects are minimized if there is a pain generator

Opioids MOA, Tolerance, Precautions

- Act by binding to CNS (central nervous system including many regions of brain, dorsal horn of spinal cord) primarily by mu opioid receptors.
- Peripheral opioid receptors in nerves (dorsal horn cells) are also up-regulated in the region of noxious tissue damage (sensory nerve terminals) and found in lungs, leukocytes (immune system, including intraluminal gut), smooth muscles (opioid induced constipation - OIC)
- Opioids are an effective analgesics, particularly for acute and cancer pain as well as anti-tussive agents
- FDA definition of "opioid tolerance" in adults are those who are taking around-the-clock medicine consisting of ≥ 60 mg of oral morphine daily, or equivalency (MME) ≥ 25 mcg/hr of transdermal fentanyl, ≥ 30 mg of oral oxycodone daily, ≥ 8 mg of oral hydromorphone daily, ≥ 25 mg oral oxymorphone daily, or an equianalgesic dose of another opioid daily for at least one week. Controversial conversion data
- Caution should be made with dose conversions because there is controversy, especially with methadone and tapentadol
- All can cause respiratory depression especially in elderly or naïve patients or with higher doses

Classification of opioids

- u-opioid agonists potency: po (1x), IV (3x), intrathecal (10x), avoid IM (also submucosal incl rectal, intranasal) transdermal most utilized opioids

Oxycodone has some k-agonist binding affinity, with higher oral bioavailability, and an active transport through blood brain barrier. This results in faster binding, higher CNS permeability & concentrations. Oxycodone is minimally transported through P-glycoprotein (P-gp), which effectively reduces its efflux out of Blood Brain Barrier (BBB)

Other u opioids have passive transport (slower), and morphine has lower oral bioavailability

- Atypical opioids

Levorphanol & Methadone has u-agonist, 5HT, NE reuptake inhibitor,
NMDA receptor antagonist binding (may reduce opioid analgesic tolerance)

Methadone has an unpredictable long half life, but its analgesic effects last 6-8 hrs (classified as SAO by FDA); LARGE LIST OF POTENTIAL DRUG INTERACTIONS

Due to Mult Cytochrome P450 metabolism esp. Cyp-3B6, 3A4 & 2D6

↑ QTc due to inactive isomer metabolized by 3B6 (monitor if ECG > QTc 450)

Used for chronic pain & opioid dependency

Tapentadol selective NE reuptake inhibitor (avoid with pregnancy), u-agonist
Extended release (ER) has an indication for diabetic neuropathic pain

Tramadol (pro-drug) selective 5HT reuptake inhibitor (avoid with pregnancy), weak u- agonist

Buprenorphine partial u-agonist (ceiling effect), with k-antagonist activity
Avoid naloxone containing products with pregnancy

Used for pain (lower dosing) and opioid dependency, has 27% renal metabolites, which is safer with CKD

At lower dose formulations, may be used in combination with u-opioids

- Long acting opioid (LAO): Methadone, levorphanol and buprenorphine (lipophilic), as well as extended release (ER) products: morphine, hydromorphone, hydrocodone (now considered Schedule II), oxycodone, oxymorphone, fentanyl (lipophilic), tapentadol & tramadol (now considered Schedule IV); Methadone & levorphanol considered short acting opioid (SAO) by FDA
- Short acting (SAO): Codeine (pro-drug), oxycodone, hydrocodone, hydromorphone, tapentadol, tramadol (pro-drug), meperidine, and transmucosal rapid onset fentanyl (TIRF)
- Morphine, oxymorphone, hydromorphone, levorphanol and tapentadol have potentially less drug interactions to consider because negligible metabolism by the cytochrome P450 pathways (for other opioids: mainly 3A4 & to a lesser extent, 2D6)
- Morphine has a toxic renal metabolite (? Hydromorphone also)
- Morphine, fentanyl & tramadol: P–gp, (found in brain, intestines and liver; facilitate efflux of drug through BBB & upregulation contributes to opioid tolerance); interactions with absorption, drug metabolism and CNS concentrations: (e.g. quinidine, digoxin, loperamide, TCN, macrolides, protease inhibitors, licorice, lidocaine, some statins, H2/ Ca channel blockers, anticonvulsants, steroids, chemotherapy, anti- fungal – most are also metabolized by Cyp 3A 4/5) may increase the absorption / clinical effects by two-fold of either substrate
- Loperamide (peripheral u opioid agonist): P-gp prevents transport across BBB, limited CNS binding. When combined with P-gp inhibitors (i.e. verapamil), its effects in CNS are augmented, which may result in respiratory depression (case reports of fatal loperamide overdose)
- Increased risk of sedation for morphine with amitriptyline, haloperidol;
- Increased risk resp depression for: morphine & oxymorphone with cimetidine
- Tramadol & meperidine can cause seizures
- Tramadol, tapentadol (labeling of all opioids) may cause serotonin syn particularly if combined with SNRIs, SSRIs, or neuroleptic malignant syn (NMS) with NRIs, MAOIs, dopa/adrenergics
- Cyp 2D6 in liver converts codeine to morphine; oxycodone to oxymorphone; hydrocodone to hydromorphone (< 10%).
- Small amounts of morphine to hydromorphone, codeine to hydrocodone by hepatic metabolism

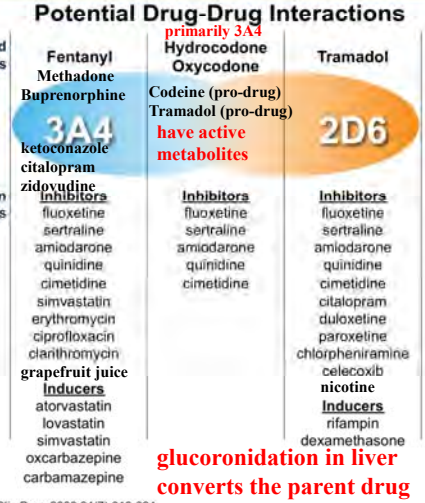
Morphine, Oxymorphone, Tapentadol, Levorphanol and Hydromorphone Has a Reduced Potential for Certain Drug-Drug Interactions

Concomitant Medications

- Consider the use of opioid analgesics that do not rely on metabolism by the CYP pathway, such as hydromorphone[1,23,24]
- 32% of patients reported taking ≥5 concomitant medications*[25]
- 21% of patients reported taking ≥10 concomitant medications*[25]
- Those metabolized by the CYP pathway may reduce analgesia or increase adverse effects[23,24,26]

*Population-based survey data.

Potential Drug-Drug Interactions



For an active drug (substrate):
Inhibitors would increase the substrate drug conc
Inducers would lower substrate drug conc
Pro-drug would have opposite effect

glucoronidation in liver converts the parent drug to the inactive "nor-" drug

1. EXALGO [package insert]. Hazelwood, MO: Mallinckrodt Brand Pharmaceuticals, Inc.; 2012.
23. Pergolizzi JV et al. *Pain Pract.* 2011;11(4):325-336.
24. Smith HS. *Mayo Clin Proc.* 2009;84(7):613-624.
25. Parsells Kelly J et al. *Pain.* 2008;138(3):507-513.
26. Overholser BR et al. *Am J Manag Care.* 2011;17(Suppl 11):S276-S287.

14

Tenets of Opioid Prescribing

Order opioids (SAO) on a scheduled "around-the-clock" basis to optimize relief and to achieve steady state levels in within 3 days at stable dosing

Order an as-needed opioid to treat breakthrough or incident pain. An effective Breakthrough dose is typically 5-20% of the total 24 hour dose of the opioid.

Up to 80% of patients given opioids have a side effect (SE); 25% report dry mouth

Initiate a prophylactic bowel regimen at the same time opioids are prescribed. Patients usually require a combination of detergent and stimulant cathartics to treat opioid-induced constipation (OIC) (15-30%); 4 FDA approved drugs: peripheral mu opioid receptor antagonists(PAMORAs) (oral & subcut) and lubiprostone (oral).

Treat opioid-induced nausea & vomiting (OINV) (15-32%) with aggressive antiemetic management. This includes giving patients antiemetics on an around-the-clock basis. Patients often become tolerant to this side effect several days after beginning opioids. Nausea may also be a symptom of OIC. FDA approval for OINV drug pending for promethazine, ADF (abuse deterrent formulation) hydrocodone & APAP.

Morphine has higher prevalence of OIC or OINV

Once baseline opioid requirements are determined with opioid tolerance,

extended-release (ER) or long acting opioid (LAO) preparations can be used, especially if >4 doses of short acting opioids (SAO) are required

Frequent (re)assessment of pain relief during the opioid titration period. Titrate doses based on the patient's report of pain relief and/or the amount of as-needed opioid that has been required for patient comfort.

Possible Reasons for Transitioning to an Extended-Release Opioid

- Chronic persistent pain requiring around-the-clock analgesia[12,13]
- Avoid large peak-to-trough fluctuations[12,13]
  - More stable plasma concentrations[12-14]
- Improve adherence and compliance[12-17]
  - May lead to more consistent control of pain[12,13,15]
- Avoid potential acetaminophen toxicity[12,14]
- Improve convenience[13,14]
- Reduce pill load[18]

12. Argoff CE et al. *Mayo Clin Proc*. 2009;84(7):602-612.
13. Fine PG et al. *Pain Med*. 2009;10(Suppl 2):S79-S88.
14. McCarberg BH et al. *Am J Ther*. 2001;8(3):181-186.
15. Chou R et al. *J Pain*. 2009;10(2):113-130.
16. Claxton AJ et al. *Clin Ther*. 2001;23(8):1296-1310.
17. Saini SD et al. *Am J Manag Care*. 2009;15(6):e22-e33.
18. Gourlay DL et al. *Pain Med*. 2009;10(Suppl 2):S115-S123.

9

Caution: must have TOLERANCE TO SEDATING AND RESPIRATORY-DEPRESSANT EFFECTS before starting ER opioid (LAOs) products:

- Approved for patients who require around the clock opioids for mod to severe pain, when other alternatives are ineffective
- FDA label: Patients MUST be opioid tolerant before using any strength Transdermal fentanyl (? Exception 12 mcg/hr)
- Avoid fentanyl for postoperative pain
- ER hydromorphone
- Other ER/LA opioids may be utilized in the lower dosing strengths or lower total daily doses in opioid naïve patients
- CDC guidelines: AVOID starting ER/ LAO in all opioid naïve patients

- Deviations in FDA labeling: In 2011, of the elderly NHP who required a long-acting opioid (representing 5% total patients), 9% were opioid naive within 60 days, and fentanyl was prescribed 52% of the time (of which 50% received the 25-50 mcg/h patch).
- This decision may be related to cost effectiveness to administer pills (prn vs around the clock), communication by patients for pain complaints, or problems with swallowing/ absorption.

Extended release (ER) opioids benefit/ liabilities Higher cost

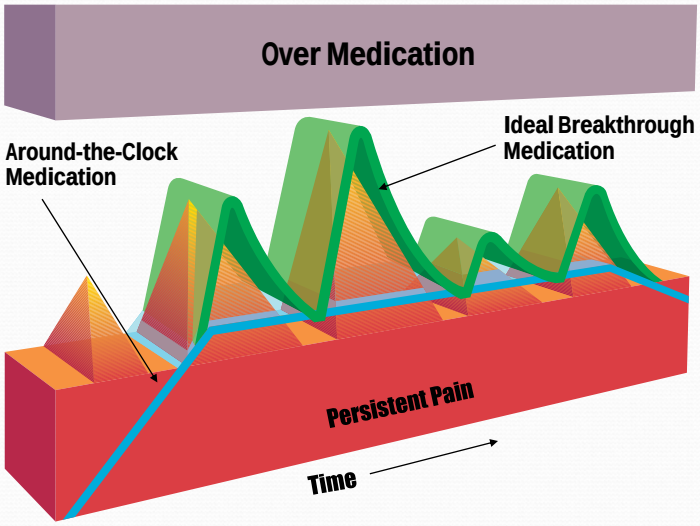
- Improved sleep or less re-awakenings
- Less euphoric effect if no bolus
- Greater risk of respiratory depression, esp with apnea, disordered resp problems
- Longer duration of side effects (i.e. cognitive changes, safety awareness)
- Greater dose unit for potential adulteration, misuse, abuse, or dose "dump"
- Increased constipation due to prolonged binding effects on peristalsis
- "Dose creep" tendency of total daily opioid consumption when titrating
- Not validated to be better than short acting opioids (SAO)
- Opioids for breakthrough pain are often also required / prescribed to supplement pain control in addition to LAO, some with “20-30% bolus effect”
- Oral malabsorption may occur with impaired GI, gastric bypass, short loop
- Larger pill size may contribute dysphagia, limited options with enteral feedings
- Some have dose limits due to prolonged QTc intervals (bupren, hydrocodone)
- With ADF formulations: Some excipients used may have a toxic or dose limiting effect, or serious morbidity if injected (abused)
- Crush resistant (? Greater risk for abuse) vs. crush / grinding deterrent granules
- May contribute to withdrawal syndrome (if combined with opioid antagonists)
- May require food for proper absorption (inconsistent intervals between meals)
- Obstruction with GI stenotic regions including GI cancer, diverticulitis may occur due to gelatinous pill mass size and stickiness

Abuse deterrent formulations (ADF) attributes

- Usually branded long acting formulations (2 short acting opioids are now available commercially), with higher costs
- Difficulty obtaining authorizations, with copays, MD-SB 606 legislates parity
- Expected to reduce the risk of misuse (adulteration) to avoid dose dumping
- Deter diversion for both the patient and others living in the household (less demand for stealing, trade or street value)
- Best used in those at risk (including the support system) for opioid use disorder (OUD), aberrant behavior, psych problems
- In vitro extraction testing: fortress, neutralizing, aversive, pro-drug designs with technologies to resist dissolving to prevent IV, intranasal abuse, or crushing
- Tested in recreational opioid drug misusers ("enriched trials")
- Post-marketing meaningful reductions in misuse (none have this designation)
- ADF cannot prevent patients from overtaking orally (most commonly ingesting, without actually altering the formulation, although less risky for drug OD)
- Patient acceptance with ADF concept implies they are at less risk for misuse
- Provider's reassurance that they are appropriately prescribing opioids with proper patient selection
- Pharmaco-economic data projects cost effectiveness; (Kirson, Rossiter)
- Estimated $430 Min medical savings and an additional $605 M in indirect costs

Treating Chronic Pain – Ideal

Try to approximate the opioid effects to the pain patterns



Opioid controversies

- Medically necessary vs. Appropriate vs. Nicety; ICD-10, payer coverage of service
- Conundrum: What is "better"? High dose opioids to improve function Vs. Minimizing opioids resulting in impaired function; quantification of "function"
- Does treating acute pain aggressively with opioids reduce the risk of chronic pain
- Opioid induced hyperalgesia (may be central or peripheral) - paradoxical opioid response, may actually be related to neuroendocrine hormonal imbalances with "spread" of pain (centralization), may require taper
- Ceiling doses (maximum limits) of opioids vs. ultra-high dose opioids for effective pain relief in selected patients, "forced" opioid taper
- "Therapeutic tolerance" = acclimation, "good pain control while maintaining normal physiologic functions" may protect against overdose
- Limited studies of highest level of medical evidence to show efficacy >3 months for continued functional improvements, especially with headaches, fibromyalgia, peripheral neuropathy, chronic back pain & work related injuries for chronic pain
- Behavioral changes directly related to opioids resulting in misuse or aberrancy (drug vs. person taking the drug)
- Opioid therapy for anhedonia or psychiatric care (? Endogenous Opioid deficiency); Hippocampal atrophy with untreated chronic pain
- Iatrogenic unanticipated complications from financially incentivized elective interventions/ surgery resulting in chronic pain with opioid dependency

Opioid controversies (2)

- PROP (Physicians for Responsible Opioid Prescribing): restricted access vs. PROMPT (Professionals for Rational Opioid Monitoring & Pharmaco Therapy): balanced view with education; Addiction vs. Pain medicine
- Best clinical practice: Standard of care vs. guidelines vs. expert opinion for opioid therapy; Levels of medical evidence to support clinical decisions
- Delivery of care: Interventionalists, pain physicians, extenders; credentialing, $
- Academic vs. clinical practice of medicine
- State boards vs. medicolegal (malpractice) vs. product liability civil/criminal
- Patient-provider care vs. IME (workman's comp) vs. health insurance coverage
- CDC: opioid prescribing guidelines extrapolations/ generalizations
- DEA: supply vs. demand of opioid availability; production & pharmacy quotas
- Effectiveness of FDA sponsored educational programs (REMS), urine drug testing (UDT), opioid agreements, and prescription monitoring programs (PDMP) to prevent opioid use disorder (OUD) or diversion (not proven), product labeling changes, future (dis)approvals with bureaucratic issues
- Cost effectiveness of pain management with opioid therapy
- Effectiveness of abuse deterrent properties (not yet substantiated) including short acting opioids (SAO): Does not prevent oral misuse
- Beneficial effects of long acting opioids (LAO) for all patients including substance use disorders (SUD); PRN use vs. around the clock efficacy
- Medical cannabis (legal in some states) have reduced # opioid overdose deaths
- Societal priorities: Darwinian approach vs. Behavioral strategies for treating SUD; Pre-existing; Goal definition: remissions vs. palliation (damage control)

Philosophical issues "Just say NO"

- Golden rule: He who has the gold rules ($ talks, …) vs. do unto others…
- What the big print giveth, the small print taketh away
- Robert Durnst (Jinx): The American system "the truth, …., and nothing but the truth, … but the whole truth will never be told"
- When you point, three fingers go back to you; Do as I say, not as I do; Blame game
- Mike Tyson "Everyone has a plan until they are punched in the face"; Murphy's Law
- Medical teaching/ mastery: See one, do one, teach one
- Do people or pencils make mistakes? Or Monday morning quarterback
- Internal locus of control (Buffett's Margaritaville) self realization vs. external locus of control (Dylan's Who killed Davie Moore?) blamers
- You can't fly like an eagle when you play with turkeys, but don't allow them to turn into carcasses
- It's easier to let the flood gates out, then to reign them back in
- You get what you get, & don't be upset; Too bad, so sad!
- Law of unintended consequences; balloon pushes in another direction, what goes around
- Promotional speaking fees / meals for education by pharma vs. kickbacks/ bribes
- Self interest/ agendas vs transparency: e.g.. NC senator who receives campaign funds from special interest groups or lobbyists removed a prominent academic pharmacist in MD from FDA opioid advisory committee because her fellowship program was partially funded by an unrestricted grant from an opioid pharmaceutical company

FDA Opioid policy steering committee (Dr. Gottlieb) 5/17

- Explore and develop additional tools or strategies that FDA can use to confront the crisis of opioid addiction, by using full authorities to reduce the scope of this epidemic
- Solicit input, and engage the public
- Mandatory education for health care professionals
- Identify the risk of abuse in individual patients
- How to get addicted patients into treatment
- REMS for SAOs (50 companies), similar to that implemented for LAOs (34 companies / 65 drugs, some pending)
- Prescribed opioid dose and duration is more closely tailored to the medical indication so that dispensing of opioids more consistently reflects the clinical circumstances (3 day vs. 30 day scripts) may result in duration of therapy labeling
- Re-evaluation of approval protocols for newer opioid drugs
- Employing computer/electronic technologies for REMS

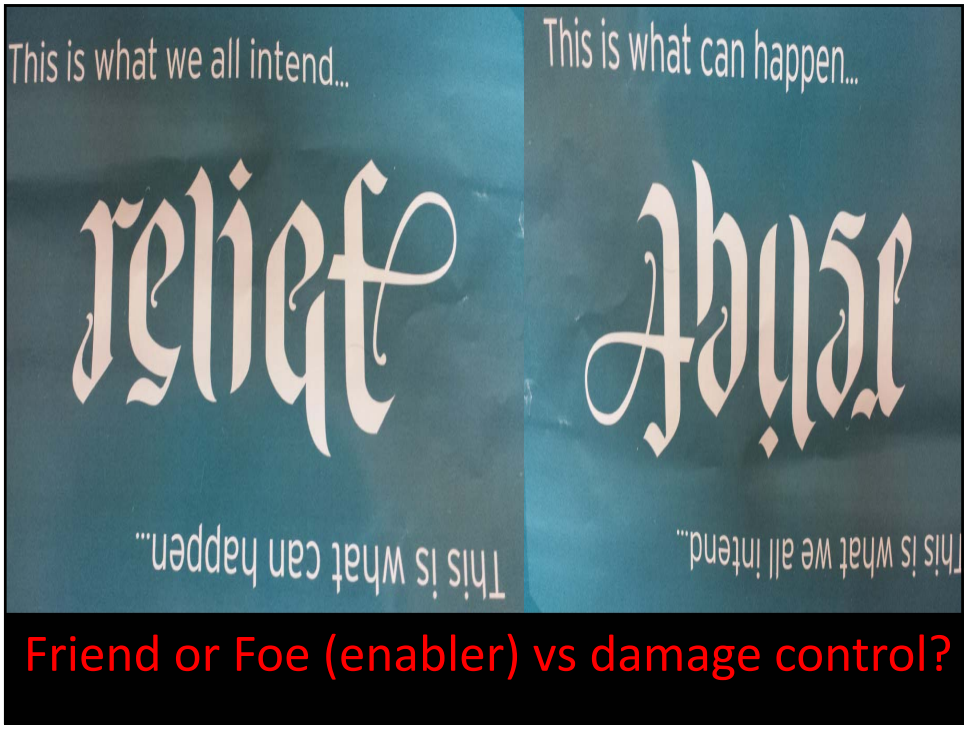
"Pseudo-Addiction" controversy

- Pattern of drug seeking behavior of pain patients receiving inadequate pain management that can be mistaken for addiction
  - Cravings and aberrant behavior
  - Concerns about availability
  - "Clock-watching"
  - Unsanctioned dose escalation
- Resolves with reestablishing analgesia Weissman DE, Haddox JD.
- "Therapeutic dependence" whereby patients exhibit what is considered drug-seeking because they fear the re-emergence of pain and/or withdrawal symptoms from lack of adequate medication; their ongoing quest for more analgesics is in hopes of insuring an acceptable level of comfort. Alford DP
- Can Pseudoaddiction coexist with addiction?

Pseudoaddiction: an iatrogenic syndrome. *Pain* 1989;36:363.

Opioid therapy (cont)

- Trial of opioids is warranted to determine whether the chronic painful condition is opioid "responsive", by mutually determining that the prescribed opioid regimen has a greater therapeutic benefit for pain control with improved function, than its harmful liabilities, with tolerable side effects, and without significant "aberrant" behavioral changes which can result in noncompliance, misuse, abuse or diversion of the prescribed opioids. The prescribed treatment should be individualized, and patient centered with realistic goals/ outcomes
- **Discontinuation or tapering of opioids may be considered** if there are significant side effects, including altered mentation, sedation, and respiratory depression. Dose reductions may occur if there are any concerns for impaired judgment and safety awareness for work, recreation, driving or self-care activities, or aberrant drug taking behaviors
- "**Less is better**" for adequate pain control in chronic pain, from all available treatment options with a goal of 30 (?20)% - 50% reduction in pain intensity (How can this be "measured?") , while improving function and activity tolerances, at the **least effective therapeutic dosing**, which will minimize undesired side effects, and reduces the possibility of excess or unaccounted for medications (that could be stolen, lost, borrowed, or bartered), which could in turn, can potentially contribute to unauthorized non-medical use.



Friend or Foe (enabler) vs damage control?

Opioid "Epidemic" vs. "Endemic" vs. "Pandemic": Perfect Storm

Jick & Porter letter NEJM 1980 4/12K had "addiction", Portenoy Pain 1986: 2/38 cases aberrant with noncancer pain

"Decade of Pain" 2001-2010; federal regulatory agencies asked physicians and medical providers to pay more attention to pain & undertreatment; the fifth vital sign.

Simultaneously, providers with limited training in employing alternative pain coping strategies, were encouraged to treat pain, resulting in unrealistic treatment goals, even with high dose opioids (no "ceiling" dose).

Affordable copays for many opioids (generics), limited coverage of other options favored or incentivized over opioid sparing options based on health insurance coverage policies

Generous approach to prescribing opioids, and development of higher dosing and long-acting pain opioids (LAO), without abuse deterrence, with pharmaceutical promotion, Contributed to misuse & addiction (OUD) to genetically & socioeconomic susceptible patients with pain

Opioid "Crisis": Perfect Storm 2

- Societal values incl "freedom of choice", "spare time", pop culture, permissiveness, dysfn families lacking supervision/ parenting, core values, entitlements, disincentives to wellness, disadvantaged socioeconomics, violence (firearms), tolerance: risky behaviors
- Addictions: food, sex, gambling, tobacco, alcohol, & marijuana
- Societal acceptance of "chemical coping", Rx medicines, with an expectation of immediate gratification, lending / borrowing pills, non-medical (recreational) use with high "street value"
- Influx of cheap & plentiful heroin & fentanyl from illicit sources; drug diversion, with ineffective/ inadeq law enforcement; leniency
- Increasing pressures on providers to see more patients in less time spent on cognitive / educational services for less reimbursements
- Limited access or ineffective chemical dependency programs (MAT)
- Greater legislative and regulatory actions affecting access for chronic pain care, with low medical research priorities for funding
- Lobbyist, special interest groups influences
- With these combined effects, along with communication & educational failures, it exploded into the public health crisis.

Solutions: Prevent, Rescue, Treat, Educate (mentorships with "academic detailing or immersive training"), Hope & Technology

National Academies of Sciences, Engineering, and Medicine, 7-17

- National Strategy to Reduce Opioid Epidemic
- **INVEST IN RESEARCH TO BETTER UNDERSTAND PAIN AND OPIOID USE DISORDER**
- **CONSIDER POTENTIAL EFFECTS ON ILLICIT MARKETS OF POLICIES AND PROGRAMS FOR PRESCRIPTION OPIOIDS**
- **IMPROVE REPORTING OF DATA ON PAIN AND OPIOID USE DISORDER**
- **INVEST IN DATA AND RESEARCH TO BETTER CHARACTERIZE THE OPIOID EPIDEMIC**
- **IMPROVE ACCESS TO DRUG TAKE-BACK PROGRAMS**
- **ESTABLISH COMPREHENSIVE PAIN EDUCATION MATERIALS AND CURRICULA FOR HEALTH CARE PROVIDERS**
- **FACILITATE REIMBURSEMENT FOR COMPREHENSIVE PAIN MANAGEMENT**
- **IMPROVE THE USE OF PRESCRIPTION DRUG MONITORING PROGRAM DATA FOR SURVEILLANCE AND INTERVENTION**
- **EVALUATE THE IMPACT OF PATIENT AND PUBLIC EDUCATION ABOUT OPIOIDS ON PROMOTING SAFE AND EFFECTIVE PAIN MANAGEMENT**
- **EXPAND TREATMENT FOR OPIOID USE DISORDER**

National Academies of Sciences, Engineering, and Medicine, part 2

- IMPROVE EDUCATION IN TREATMENT OF OPIOID USE DISORDER FOR HEALTH CARE PROVIDERS
- REMOVE BARRIERS TO COVERAGE OF APPROVED MEDICATIONS FOR TREATMENT OF OPIOID USE DISORDER
- LEVERAGE PRESCRIBERS AND PHARMACISTS TO HELP ADDRESS OPIOID USE DISORDER
- IMPROVE ACCESS TO NALOXONE AND SAFE INJECTION EQUIPMENT
- INCORPORATE PUBLIC HEALTH CONSIDERATIONS INTO OPIOID-RELATED REGULATORY DECISIONS
- REQUIRE ADDITIONAL STUDIES AND THE COLLECTION AND ANALYSIS OF DATA NEEDED FOR A THOROUGH ASSESSMENT OF BROAD PUBLIC HEALTH CONSIDERATIONS
- ENSURE THAT PUBLIC HEALTH CONSIDERATIONS ARE ADEQUATELY INCORPORATED INTO CLINICAL DEVELOPMENT
- INCREASE THE TRANSPARENCY OF REGULATORY DECISIONS FOR OPIOIDS IN LIGHT OF THE COMMITTEE'S PROPOSED SYSTEMS APPROACH
- STRENGTHEN THE POST-APPROVAL OVERSIGHT OF OPIOIDS
- CONDUCT A FULL REVIEW OF CURRENTLY MARKETED/APPROVED OPIOIDS
- APPLY PUBLIC HEALTH CONSIDERATIONS TO OPIOID SCHEDULING DECISIONS

Pain Epidemiology

- 116M American living with chronic pain, represents 20% visits, costing $635B annually, with $335B in lost productivity (2010); **40% of 14M cancer survivors experience chronic pain, similar risks**
- With the aging population, higher rates (30% >65 years) of OA pain and other chronic painful conditions, with a higher demand for pain management; however, the actual intensity & prevalence of chronic pain (30%) has been relatively stable, but with a greater prevalence of SUD
- Prevalence of chronic pain is 15-64%; 79% rate as at least moderate intensity; 47% intense pain >2 yrs
- US is 4-5% of the world population, yet uses 80-90% of the world's opioid production , **with 11% (33 million) were taking opioids regularly in 2014; over time this prevalence predictably incr**
- **240 million opioid prescriptions were written (13% decrease over past 4 yrs, down 2.7% in 2015, and another 1.7% reduction in 2016, but 3x rate of 1999); 13% were LAO, 5% high dose; 1/3 of US prescribed opioids in 2015**
- **DEA mandated reduction in opioid manufacture by 25% (33% for hydrocodone) for 2017, further reductions planned for 2018 by >20%**
- 42 million have taken opioids for an acute painful condition, with a higher proportion prescribed opioids in US than other countries. Some may have contraindications to non-habituating pain relievers due to other co-morbidities. $11B sales revenue of opioid by drug companies in 2014

Pain and opioid statistics

- The longer a person's first exposure to opioids, the greater the risk that they will continue using opioids after one year; increases from 6% (1 day given) to about 35% (if 30 day supply given), esp following surgery; 10-90% have chronic pain of which 2-10% progress to severe
- Duration of opioid therapy (90 d) & dose dep, greater risk of OUD (15x risk), OD, death, trends: misuse incr in >50 y.o. (2%)
- one in four patients had at least 200 unused MME leftover at 1 month (post ortho surgery). 85% said they had unused pills remaining, with an average of 30 remaining pills, with only 11% stored the drugs securely
- For minor injuries, in ED in 2012, 1.6% of patients in Delaware were treated with opioids, 16% of Mississippi patients received opioid prescriptions. Although the median prescription quantity was 20 pills, 5% of prescriptions were for ≥60 doses. Having a second opioid RX after acute pain, doubles the risk of using opioids after 1 year.

Surplus opioids: Over vs. Under shoot

- 2/3 have leftover opioids after surgery/ procedures
- Potential for stolen pills or diversion
- May represent a prudent patient taking opioids
- Need proper education & guidance for storage & disposal
- What about the 1/3 who complete the course of opioids Are they at risk for substance use disorder?
- Can a provider exactly calculate an analgesic dosing regimen for a given procedure?
- What about the extra handling for those requiring refills?
- Can this phenomenon be reduced with incentivization
- MN Guidelines: up to 7 days, or < 200mg MME total pills
- Women and elderly generally were prescribed greater pills

Comorbidities are common among those who have an opioid use disorder (OUD) for prescription opioids

- **16% of Americans who have mental health disorders (**anxiety, depression, and other mood disorders) **receive 51% opioids prescribed in the United States**
- People with mood disorders are at increased risk of abusing opioids, and yet they received many more prescriptions than the general population
- With OUD: > 85% suffer chronic pain, > 55% have mental disorders, 40% to 56% have concurrent alcohol dependence, and > 60% are nicotine dependent
- Chemically coping with misuse (common): use illegally obtained or prescribed opioids in an effort to reconcile underlying mental health disorders
- Opioid misuse risk and pain catastrophizing, associated with women, with lower pain intensity; given an opioid script

Prescription Opioid Use among Adults with Mental Health Disorders in the United States *Matthew A. Davis* **J Am Board Fam Med 2017;30**

RADARS System is a national surveillance system that monitors the abuse, misuse, and diversion of prescription opioids

- 2014: past year use of nonmedical opioids are 3.4-5.6%, approx 11.3M US/ yr,
- Cost: $75B/ yr: Prescription opioids (2002-2007): 4.1% to 4.6% in young adults aged 18-25, and 1.3% to 1.6% for adults aged 26 years and older, with more men than women had lifetime (15.9% vs. 11.2%) and past-year (5.9% vs. 4.2%) usage
- Men are more likely than women to obtain prescription opioids, much of which for illegitimate purposes, for free from family or friends, and are more likely to purchase them from a dealer
- Women are at greater risk of misusing opioids because of emotional issues and affective distress, whereas men tend to misuse opioids because of legal and problematic behavioral issues. Fewer women than men receive SUD treatment
- Hydrocodone and oxycodone are the drugs of choice in 75% Oral route preferred
- 20% of Americans report using prescription opioids for nonmedical use, and those with health insurance have an increased risk
- First exposure to an opioid in 79% of males and 85% of females was a legitimate prescription for pain, which subsequently led 60-70% to misuse to get high
- Cannabis use in patients prescribed opioids ranged from 6.2% to 39%, compared with 5.8% in the general population

Safety profile of buprenorphine seems superior to that of methadone for OUD

Chronic opioid therapy liability

- Opioid therapy may actually increase disability and cost of care.
- More importantly, opioid use has been associated with subsequent surgery and continued or late opioid use
- Association between opioid prescribing and an increase in overall health care costs & higher levels of utilization (3x utilization for ED)
- For low back pain on opioids, more disability & reduced function
- For >20mg/d MME more likely to be receiving disability benefits, and this condition was associated with greater pain intensity, more impairments in functioning and quality of life, poorer self-efficacy for managing pain, greater fear avoidance, anxiety, depression, more health care utilization, and problematic substance uses disorders (other than alcohol) If <20 mg/d MME to be working or retired, but had higher rates of problematic alcohol use
- Workman's compensation claims in 2014: prescription opioid users, on average, missed 13.3 more days of work because of disability or medical absenteeism annually versus non-users, or higher doses correlated with increased time loss, with 3x risk for surgery
- If >7 days of lost work time, with 65% to 75% of injured workers with analgesics receiving at least one opioid medication
- Opioids may account for 20% reduction in US manual labor workforce

Medicolegal issues

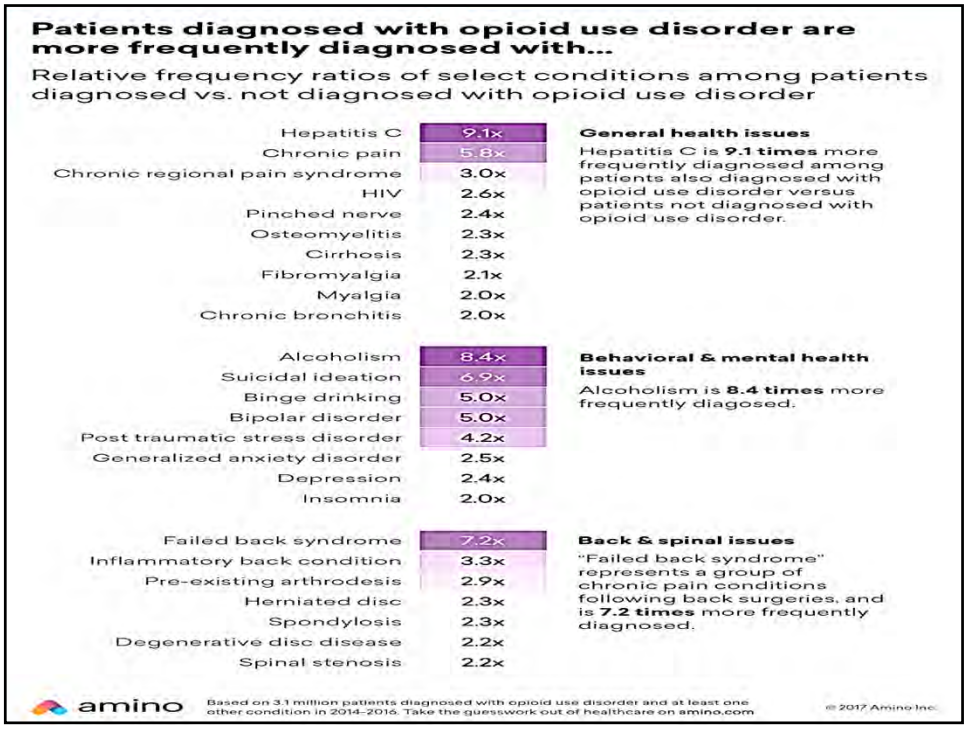
- Civil lawsuit, Professional Board inquiry, criminal prosecution
- Malpractice claims that arise from chronic pain management have increased in number (3% in 1980 to 18% in 2012 for anesthesia specialty) *as well as* severity
- Most anesthesiologist claims (82%) involved patients who did not cooperate in their care (69%) or who had inappropriate medication management by physicians (59%)
- Death was the most common outcome in medication management claims; factors associated with death included long-acting opioids, additional psychoactive medications
- Need to meticulously document with kind, caring, competent and credible, based on clinical judgment, experience & training). Informed consent may not be a sufficient defense.
- Pharmacists may be liable for opioid OD deaths; have discretion based on the prescribing provider & red flags
- Small disciplinary risk for under-treatment of pain (avoid opioids)

OUD epidemiology and Associations

- 12 month prevalence 0.37% among adults (2007), with male to female ratio typically being 1.5:1, highest among adults <29 years, lower among African Americans, higher among Native Americans, cost at least $78.5B/yr. Dx OUD is 2M in 2015, compared to 241K in 2012 (criteria have changed)
- Prevalence of 30 day use of illicit drugs in 10.2% Whites, 9.2% Hispanics and 14.2% Native Americans, 12.5% Blacks, 4% Asians, 9.8% Native Hawaiians
- 1.0% of those ages 12–17 years, most commonly first observed in the late teens
- Relapse following abstinence is common, with mortality rates may be as high as 2% per year, about 20%–30% of individuals with OUD achieve long-term abstinence
- Behavioral health problems associated with SUD include impaired driving, violence, risky sexual activity and mental health problems, and are the leading cause of death in those aged 15-24

OUD

- Associated with chronic pain, cardio-vasc/pulm diseases; OUD starts after exposure to opioids
- In 2015, 20.8M had SUD, 27.1M were current users of illicit drugs or misused prescription drugs, 7.7M required treatment for illicit drug use disorder (3.8% men, 2% women)
- In 2014, 47K died from drug overdose (17.5K illicit drugs, 25.7K prescription drugs, of which some due to non-medical use or combinations, i.e. alcohol 20%), prediction for a 35% increased deaths by 2027
- SUD treatments cost $36B, with additional $402B due to crime, health care and lost productivity, twice that for care of DM. In 2007, the cost was $193B for illegal or non-prescribed drugs.
- 2012, the national rate of opioid-related mortality was 5.1 per 100,000, >3.5 times the rate in 1999
- prescriptions for opioids in Medicaid nearly doubled between 1998 and 2003 to >27.5 million, an estimated 4% of the program's prescription drug expenditures,
- 6 fold risk of OD, compared to non-Medicaid (WA) esp ages 45-54 years, males, >50mg/d MME if combined with sedative-hypnotic > muscle relaxants, or >90mg/d MME without benzos
- Having health insurance has a 20% relative reduction in OD compared to being uninsured, but 40% of Medicaid enrollees had $\geq$1 indicator of OUD/ aberrancy


Patients diagnosed with opioid use disorder are more frequently diagnosed with...
Relative frequency ratios of select conditions among patients diagnosed vs. not diagnosed with opioid use disorder
Hepatitis C 9.1x
Chronic pain 5.8x
Chronic regional pain syndrome 3.0x
HIV 2.6x
Pinched nerve 2.4x
Osteomyelitis 2.3x
Cirrhosis 2.3x
Fibromyalgia 2.1x
Myalgia 2.0x
Chronic bronchitis 2.0x
General health issues
Hepatitis C is 9.1 times more frequently diagnosed among patients also diagnosed with opioid use disorder versus patients not diagnosed with opioid use disorder.
Alcoholism 8.4x
Suicidal ideation 6.9x
Binge drinking 5.0x
Bipolar disorder 5.0x
Post traumatic stress disorder 4.2x
Generalized anxiety disorder 2.5x
Depression 2.4x
Insomnia 2.0x
Behavioral & mental health issues
Alcoholism is 8.4 times more frequently diagosed.
Failed back syndrome 7.2x
Inflammatory back condition 3.3x
Pre-existing arthrodesis 2.9x
Herniated disc 2.3x
Spondylosis 2.3x
Degenerative disc disease 2.2x
Spinal stenosis 2.2x
Back & spinal issues
"Failed back syndrome" represents a group of chronic pain conditions following back surgeries, and is 7.2 times more frequently diagnosed.
amino
Based on 3.1 million patients diagnosed with opioid use disorder and at least one other condition in 2014-2016. Take the guesswork out of healthcare on amino.com
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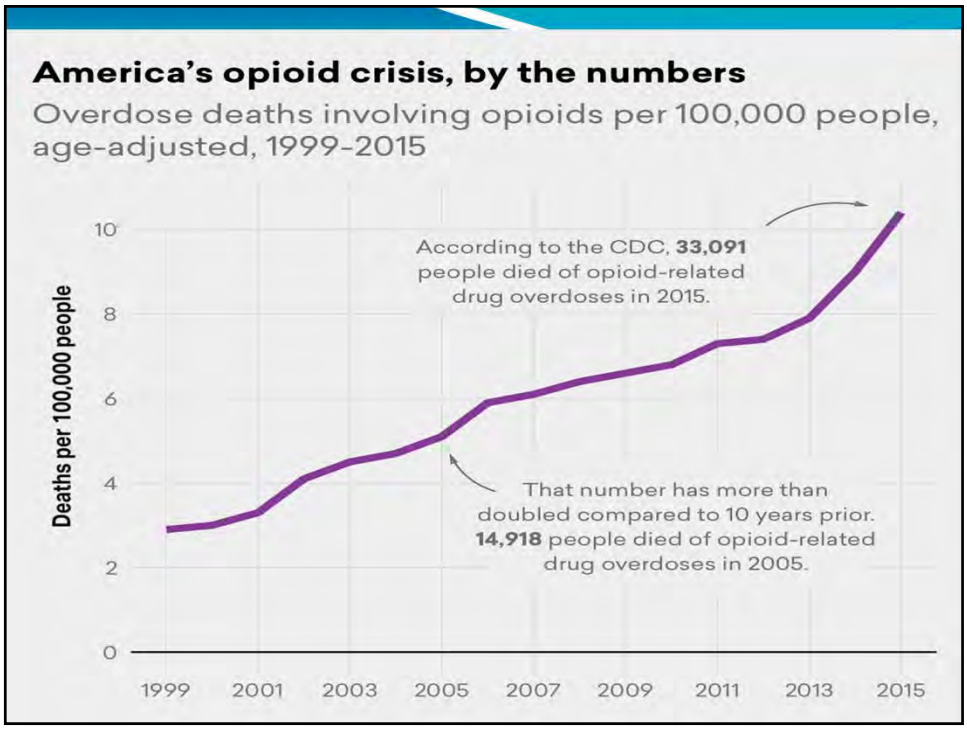
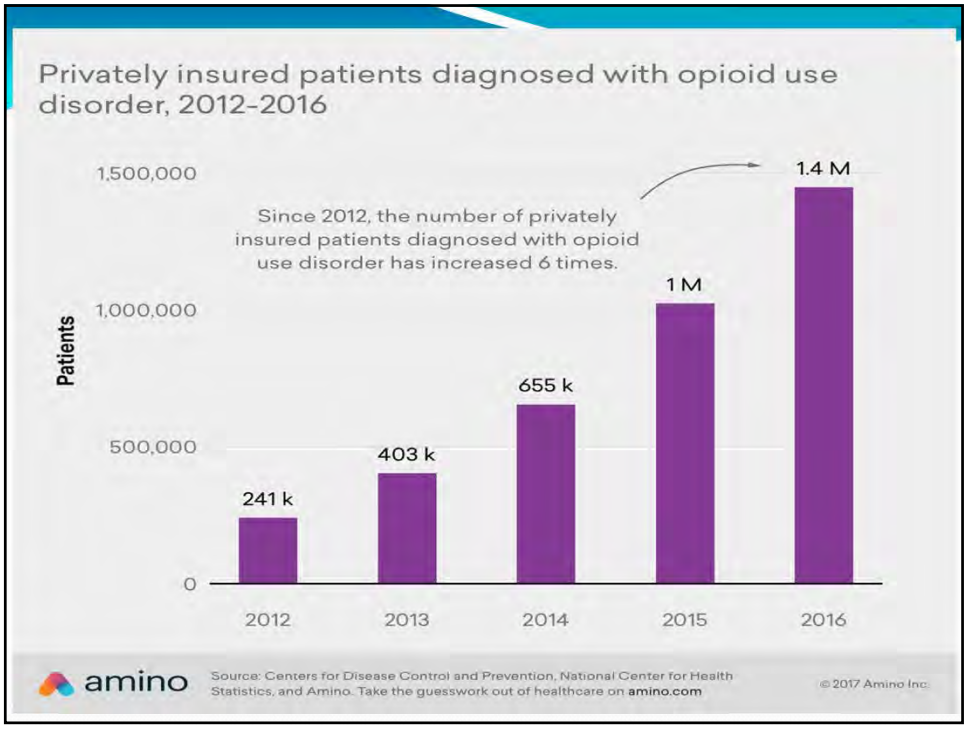

America's opioid crisis, by the numbers
Overdose deaths involving opioids per 100,000 people, age-adjusted, 1999-2015
Deaths per 100,000 people
10
8
6
4
2
0
1999
2001
2003
2005
2007
2009
2011
2013
2015
According to the CDC, 33,091 people died of opioid-related drug overdoses in 2015.
That number has more than doubled compared to 10 years prior. 14,918 people died of opioid-related drug overdoses in 2005.



OUD comorbidities

- Genetic factors play a particularly important role (60%) both directly (OPM(K,D)R1, PENK, COMT, FKBP5, MC2R genes) and indirectly, greater risk with lower socioeconomic status, but over time, OUD is seen more often among white middle-class individuals, especially females
- Often associated with other SUD, especially those involving tobacco, alcohol, cannabis, stimulants, and benzodiazepines, which are often taken to reduce symptoms of opioid withdrawal or craving for opioids, or to enhance the effects of administered opioids
- High risk of medical comorbidities from SUD including infections esp from injections, physical trauma including nasal or from intoxication, or adverse effects from opioids (dry mouth, GI, pupillary, sexual dysfunction, i.e. ED or infertility)
- Psychiatric disorders: Depressive disorders, Posttraumatic stress disorder, Antisocial personality disorder, Conduct disorder in childhood
- Heightened risk for self-harms including suicides or attempts

Opioid statistics in US

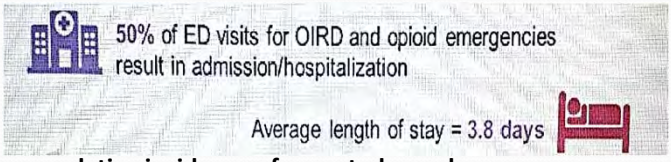
- **OD deaths involving prescription opioids have quadrupled since 1999. In 2015, opioids were involved in the deaths of 33.1K people (of 52K total drug overdoses); over 22,000 deaths involved "prescription" opioids (may have been obtained for non-medical reasons), 2016 death rate increased by 19% (may be underestimated)**
- **Methadone: used 1% for pain but found in 23% prescription OD deaths in 2014**
- **75% of those who began abusing heroin in the 2000's started with prescription opioid product**
- **29K deaths related to opioids in 2014, of which 17K overdoses involved "prescription" opioids, often associated with other factors, including combining with alcohol (20%) and/or CNS depressants particularly benzodiazepines, 30%; some of which was due to non-medical use**
- For every death, there are 32 emergency department visits for opioid related adverse events, as well as requiring detoxification and addiction care, which has resulted in a strain on healthcare delivery systems , costing $16K more, with a greater rate of increase
- Non-medical use of opioids has dropped from 2009 to 2014 (SAMHSA data)
- Deaths from pharmaceutical opioids has been leveling off from 2010 to 2014, although there is rising death rates due to heroin/ fentanyl illicit drug use (NIH data)
- 2015 survey: 4.4% >age 12 respondents misused prescriptions opioids within past year, with 54% of misusers of prescriptions opioids first obtained them from family or friends, with estimated 12.5M U.S. misused over past year
- Mandatory provider reviews and pain clinic laws have reduced opioid OD deaths rates by 12%, and reduced opioid prescriptions by 8%.

1.3M ED/admitted for opioid related issues in 2014

Maryland was #1 state (may be related to coding)

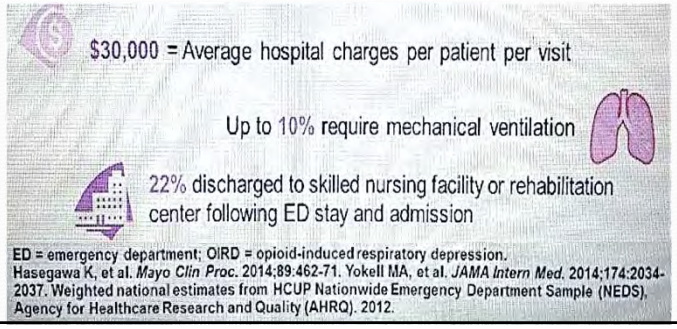
135,971 ED Visits in 2010

Increased by 64% for ED, and 99% for hosp, esp poorer & 25-44 yo since 2005



At 2 years, the cumulative incidence of repeated overdose was 17% vs 8% if no opioids prescribed

Larochelle, Opioid Prescribing After Nonfatal Overdose and Association With Repeated Overdose: A Cohort Study, Annals of Internal Medicine; 2015



Maryland Opioid statistics in 2016, a death epidemic

- Overdose deaths = 2089, 3x since 2010, highest ever, alcohol = 582, cocaine = 464, benzodiazepines = 126, greatest surge ≥ 55 years
- Heroin overdose deaths = 1212, increased by 72% from 2015, much of which contained fentanyl = 1119 deaths (overlapping)
- Fatal prescription opioids = 418, jumped 17% from 2015 (some of which was taken for non-medical use)
- Naloxone saved 800 lives since 2015; More judicious opioid prescribing
- 37% reduction in opioid prescriptions for injured workers from 2010-2015
- CDC review of retail pharmacy prescriptions in US by zip code Published 6-8-17 MME US: 640 in 2015 vs 782 in 2010: (does not include MAT with methadone, buprenorphine products, cough medicines); Higher: Whites, urban, unemployment, Medicaid, DM, OA
- MD state scripts below national average, dropped 13% from 2010 (4.2M scripts) -2015 (3.6M scripts); 8th lowest state per capita, & below national average
- MME: Baltimore City 519 in 2015 vs 554 in 2010 (census incl incarceration anywhere in state= 25K); Balt Co 883 in 2015 vs 1072 in 2010; 21/24 MD counties opioids amounts declined from 2010-2015 , highest: Kent Co.; 18/24 MD counties above national average
- Baltimore City data may be due to higher rates of MAT, diversion & incarceration
- Attributable to educational efforts both patients and providers (CME)
- FDA: Safe Opioid Prescribing & Risk Evaluation Mitigation Strategies (REMS) for LAO
- PDMP through Chesapeake Regional Information System (CRISP)

Comparators of deaths ANNUALLY

250K deaths due to any medical errors, with 45-100K due to medication errors
At home: 15% due to OTC analgesics; Need better packaging/ labeling readability

- Estimated **16K deaths from nonsteroidal anti-inflammatory drugs** (NSAIDs) (usually due to gastrointestinal bleeding), not included in above
- **3K deaths due to acetaminophen** (over the counter) overdoses caused by acute liver failure.
- This may have occurred due to the unintended consequences of limited access to pain management including opioids, with less publicized media coverage due to bias, or ineffective educational awareness regarding these analgesics
- **41K suicides** and 16K homicides in 2013, mainly from gun violence of 36K deaths in 2015. Since 1999 there have been over 600K suicides, with a disturbing increase in rates for males and adolescents, which can be attributable to hopelessness (suicides due to intentional drug overdose were 13%, or at least 5K deaths) some of which had intractable pain. May have violent deaths due to "suicide by proxy"
- **38K deaths** (out of a total of 310K accidental injuries) due to **motor vehicle collisions** in 2015, with declining rates, but higher proportion due to non-alcohol
- **480K deaths due to tobacco** related illnesses
- **3K deaths due to acute alcohol intoxication**, with 88K due to alcohol related illness & additional deaths due to drugged driving, which has included in other statistics.
- 16M alcoholics costing $250B/ yr, 60% recidivism
- Nicotine and alcohol are not considered scheduled substances by the DEA

Black Box warnings DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

Addiction, Abuse, and Misuse

- **Opioid exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk prior to prescribing Opioids and monitor all patients regularly for the development of these behaviors and conditions.**
- **Serious, life-threatening, or fatal respiratory depression may occur with use of opioids. Monitor for respiratory depression, especially during initiation of opioids or following a dose increase**
- **Accidental ingestion of even one dose of opioids, especially by children, can result in a fatal overdose of opioids.**
- **Prolonged use of opioids during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available Risks increase if combined with antidepressants, benzos or gabapentin**
- **Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing of opioids and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.**
  - **Limit dosages and durations to the minimum required.**
  - **Follow patients for signs and symptoms of respiratory depression and sedation.**

Opioid warnings FDA labeling in adults, monitor in geriatrics

- Life-Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients: Monitor closely, particularly during initiation and titration.
- Serotonin Syndrome: Potentially life-threatening condition could result from concomitant serotonergic drug administration. Discontinue opioids if serotonin syndrome is suspected.
- Adrenal Insufficiency: If diagnosed, treat with physiologic replacement of corticosteroids, and wean patient off of the opioid.
- Severe Hypotension: Monitor during dosage initiation and titration. Avoid use of opioids in patients with circulatory shock.
- Risks of Use in Patients with Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness: Monitor for sedation and respiratory depression. Avoid use of opioids in patients with impaired consciousness/ coma
- May cause spasm of the sphincter of Oddi, especially with biliary tract or pancreatitis
- Lowers seizure threshold, monitor closely with seizure disorders or head injury
- Severe Renal or Hepatic Impairment: Not recommended, monitor closely
- Pregnancy: Based on animal data, may cause fetal harm.
- Lactation: Closely monitor infants of nursing women receiving opioids

Opioid precautions - class effects

Concurrent use with other central nervous system depressants (sedatives, hypnotics, general anesthetics, antiemetics, phenothiazines, other tranquilizers, tricyclic antidepressants and alcohol) can increase the risk of respiratory depression, hypotension, profound sedation, or coma. Reduce the initial dose of one or both agents.

Avoid concurrent use of mixed opioid agonist/antagonists (i.e., pentazocine, nalbuphine, and butorphanol) or partial opioid agonists (buprenorphine) in patients who have received or are receiving a course of therapy with a full opioid agonist. In these patients, mixed opioid agonist/antagonists and partial opioid agonists may reduce the analgesic effect and/or may precipitate withdrawal symptoms.

DRUG INTERACTIONS :
Opioids may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression.
Concurrent use with anticholinergic medication increases the risk of urinary retention and severe constipation, which may lead to paralytic ileus.

Opioid precautions (2)

- "Dose Dumping". Exposure to alcohol may cause rapid release of some ER opioid formulations.
- Alcohol exposure may cause some opioid drug levels to increase, even without dose dumping.
- Use of opioids with MAOIs may result in possible increase in respiratory depression. Wait for 14 day "washout".
- Use of opioids with MAOIs may cause serotonin syndrome (interference with serotonin metabolism, resulting in neuromuscular, autonomic, and behavioral changes due to increased CNS serotonin activity)
- Diuretics. Opioids can reduce the efficacy of diuretics by inducing the release of antidiuretic hormone.
- For selected opioids: Concomitant use with CYP3A4 inhibitors (or discontinuation of CYP3A4 inducers) can result in a fatal overdose of opioids from toxic levels

Opioid side effects are dose related, and can be life threatening

- **Opioid overdose, which is usually related to respiratory depression**, due to the effects of opioids on the midbrain's CO2 detection, especially in those individuals with significant respiratory problems including disordered sleep breathing or sleep apnea (this potential condition may require further evaluation), which is associated with snoring, obesity and aging. "Slippery slope"
- **Opioid overdose risk is associated with a combination of certain medications (usually CNS depressants such as benzodiazepines) or substances (alcohol or illicit drugs) concurrently taken with any opioids**.
- **Naloxone** availability in the household (including "overdose drills" education) as an **overdose treatment** until first responders arrive is recommended in those patients who are receiving at least **morphine (≥50 mg/ day) or another opioid at morphine mg equivalent doses (MME)**, history of substance use disorder, using sedatives (especially benzodiazepines), or co-morbidities that increase the risk of respiratory depression

Opioids (for medical use) taken for pain management can result in an unintentional (accidental) overdose from some of the following scenarios (described below is an incomplete list of possibilities):

- 1. accidental exposure or poisoning possibly due to labeling mistakes or confusion about dosing regimen; poor literacy, language barrier, cognitive impairments
- 2. inadvertently, by starting at an opioid at higher doses, too rapidly escalating the dose or interval between doses, initially using opioids of a long duration of action (especially with methadone, or with higher dose extended release formulations, particularly fentanyl patch), or taking more than what has been recommended which may be due to miscommunication with the provider; May occur after hospital D/C, but the provider was not informed of reduction.
- 3. inadvertently, by taking an additional dose because the patient forgot when they took their last dose, resuming the medication at the previous higher dosing even after having a brief lapse in use (plausible explanations which may contribute to these occurrences include problems with transportation or pharmacy access, or pre-authorization delays), altering the intended route of medication (unknowingly chewing or crushing an extended release formulation due to mechanic or neurologic dysphagia, including fear of swallowing pills);
- 4. following an acute and dramatic change in a patient's medical condition or abrupt changes in their metabolism, resulting in less physical tolerance or resiliency, particularly with respiratory problems or dehydration;

Explanations for unintentional overdose

- 5. age related (higher opioid levels in children or elderly);
- 6. habitus related (higher absorption of fentanyl patch in fatty tissue or with increased body temperature);
- 7. gender related effects on the metabolism (higher opioid levels in women);
- 8. unexpected drug interactions, some of which may be predicable with genetic testing, or due to rapid absorption ("dose dumping") from gastrointestinal disorders or when mixed with alcohol;
- 9. pregnancy (resulting in high risks or fetal exposure) or breast feeding (especially related to infants or neonates) FDA warning for tramadol and codeine in young children due to metabolic diff.
- 10. In those accustomed to higher opioid usage (may be legitimate or recreational use), who are currently opioid naïve, re-initiate opioid usage, but over-estimate their body's resiliency when they resume a higher, but previously tolerated dose.

Life-Threatening OIRD Risks May Be Out of Our Control

- ~60% of patients taking opioids were prescribed potentially dangerous medication combinations (eg, opioid + benzodiazepine)
  - Two-thirds were prescribed by ≥2 providers
- 20%-30% of opioid-related deaths involve alcohol
  - Consuming alcohol may result in some extended-release formulations to rapidly release opioid
- In 2011, >5000 children aged ≤5 years were admitted to the ED for accidental opioid ingestion

An Express Scripts Report. A Nation in Pain. Focusing on U.S. Opioid Trends for Treatment of Short-Term and Longer-Term Pain. 2014. Gudin JA, et al. *Postgrad Med*. 2013;125:115-130. Wunsch MJ, et al. *Am J Addict*. 2009;18:5-14. Green TC, et al. Drug Alcohol Depend. 2011;115:221-228. Jones CM, et al. *MMWR*. 2014;63:881-885. Substance Abuse and Mental Health Services Administration. *Drug Abuse Warning Network, 2011: National Estimates of Drug-Related Emergency Department Visits*. HHS Publication No. (SMA) 13-4760, DAWN Series D-39. Rockville, MD: SAMHSA, 2013.

Opioid Induced Respiratory Depression (OIRD)

Probability based on Calculated Risk Index Risk

Index score	OIRD probability (%)	Index score	OIRD probability (%)
0-24	3	47-49	55
25-32	14	50-54	60
33-37	23	55-59	79
38-42	37	60-66	75
43-46	51	≥67	86

- Substance use disorder, bipolar disorder, schizophrenia, stroke, chronic headache, chronic kidney, lung (COPD, sleep apnea) or heart disease and pancreatic disease. (also: liver disease, anxiety)
- Opioid characteristics (methadone, oxycodone, fentanyl, extended-release or long-acting opioids, and a total maximum MME of 100 mg or more) and benzodiazepines or any type of antidepressant

Opioid use disorder (OUD) clarified

- The categories of opioid use disorders (OUD) should be considered separately and not combined (i.e. nonmedical use, including recreational misusers)
- OUD (from any cause) has 5 times increase risk of overdose and increased mortality rates (life tables slightly reduced expectancy)
- Many of the **prescription opioid "unintentional" overdose deaths may, in fact, be related to non-medical use, combined with other drugs (i.e. benzodiazepines), or even may be intentional** (i.e. passive suicide or suicide by proxy)
- 8-15% of the total drug overdose deaths were attributable to accidental prescription opioids alone, used for their pain, in the states that keep more accurate databases
- Due to the current scrutiny of pain practices, with education, the incidence of opioids overdose deaths due to legitimate medical use has been declining
- BC private insurance retrospective review 16M in US 2017 (from 2010-2015): OUD increased 5x, but MAT increased by 65%, buprenorphine used in states with less prevalence of OUD, although the definition for Dx has become more common 2016: 1% prev OUD; 2015: 20% were prescribed opioids, of which 45% > MME≥50, resulting in 6% rate if given < 90 day supply, 4% if given >90 day supply
- Considered the 5th most impactful conditions affecting commercially insured pts

Diversion (nonmedical use) in 2010

- 12.5M US >12 years old misused opioid prescription
- 76% of the opioids obtained was originally prescribed for another patient
- Of those who misused opioid prescriptions, 54% borrowed or given from patient's supply (friend or relative), with 80% from a single prescriber
- 14% bought (4% from a drug dealer)
- 5% stolen
- 5% forged, unauthorized or altered prescription
- 18% obtained from medical provider (i.e. pill mill) (no legitimate purpose)
- 63% of overdose deaths were from pharmaceutical diversion and 21% were from doctor shopping

Providers liability

- Adherence to DEA protocols for both written & electronic scripts; JHH 92% deficient (≥2 patient identifiers, ICD-10, proper mg, sig, quantity, refills, DEA, NPI, legible, abbrev.)
- Legitimate prescriptions written for a patient with high quantities so that patient had "extra" to give to others
- Opioid medication that was not used due to side effects
- Improper storage of prescription pads, including security from employees
- Education to patient and support system for proper usage, security, and disposal
- Enforcement of opioid policies and laws
- 60% of providers (mostly primary care & physician extenders) lack confidence in managing chronic pain – need education to improve knowledge and attitudes toward opioid prescribing
- Risk of patient reprisals, including murder (PM&R in IN 7-26-17)

Other reasons for potential opioid overdose

- **If opioids are improperly stored or secured at home, inadvertently taken by children** (especially < 2 years old from mother – codeine), or pets
- taken unexpectedly (**stolen**) **by family members** or guests, without consent.
- purposeful as the result of taking extra doses (patches or pills) for uncontrolled pain or recreational use – Most common source
- self-harm behaviors with psychological distress including depression, anxiety (especially post-traumatic stress disorder) or "chemical coping"
- Intentional prescription overdose incidence is 17% , as a suicide attempt
- tampering with abuse deterrent features with higher unit dose formulations of other opioids, or adulterating any opioid to administer it through crushing, dissolving, injecting, snorting or other inserting it in other non-oral orifices.
- recreational/ non-medical use (for its mind altering effects)
- **increasing rates of overdose deaths due non-medical substance abuse** (i.e. heroin, which is often laced with an even more powerful opioid, fentanyl; or this may be combined with other illicit or mind altering drugs or sedatives).
- "unintentional or intentional" or abuse (usually "intentional") are considered as part of the diagnosis of "opioid use disorder" (OUD), & have collectively been analyzed by regulatory agencies as the major problem, instead of considering true "accidental" episodes in those patients with pain, as a separate issue.

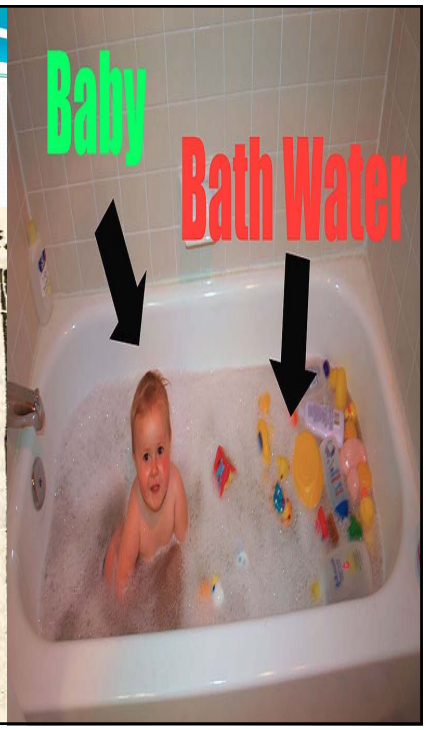
Nonmedical opioid scenarios

- Small overlapping subset of chronic pain patients prescribed opioids who also misuse them intentionally, with abuse and diversion.
- Criminal activity: divert, sell, trade, borrow or barter prescription opioids, and/ or use another person's prescribed opioids, alter or forge a prescription in any way, or make an unauthorized fax or phone call (by a non-health care provider) to prescribe medications
- Pharmaceutical grade opioids for non-medical use can be related to smuggled or counterfeited products
- Internet access for prescribing or dark web transactions
- "Pill mills" prescribed by illegitimate providers
- Stolen products obtained through drug heists from the manufacturer, or pharmacy burglary or thefts (often, with higher quantities of drugs involved) and diversion by workers or patients from institutions
- Difficult to fully distinguish these other sources of pharmaceutical opioids for non-medical use from the legitimately dispensed opioids by a pharmacy, and often, this combined data has also been included in "prescription" opioid overdose statistics.

NIH consensus meeting 2014:

- The "current reimbursement for evaluation and management may be inadequate to reflect the time and team-based approaches needed for integrative treatment. In some instances, payment structures place barriers on non-opioid therapy. Other payment structures, such as tiered coverage systems, keep non-opioid alternatives as second- or third-line options rather than placing them more appropriately as first-line therapy. Other incentives encourage prescribing opioids for several months at a time rather than for a shorter term…Given the current vagaries of payment structures, perhaps it is not surprising that providers and patients chose opioids more often than is clinically appropriate and more often than guidelines suggest".
- "There is little evidence to guide clinicians once they have made the decision to initiate opioids for chronic pain therapy. Data on selection of specific agents based on opioid characteristics, dosing strategies, and titration or tapering of opioids are insufficient to guide current clinical practice."
- Consensus is for non-specific "exit" strategies with very few data on how one should implement" this option

Don't throw the baby out with the bath water



Professionals for Rational Opioid Monitoring & PharmacoTherapy (PROMPT) Balanced approach:

- To take a rational, evidence-based approach to those problems and their solutions
- To promote provider education, preferably mandatory, as a primary approach to safe and effective pain care
- Make Risk stratification a standard of care for chronic pain
- No one accepted definition of equi-analgesic doses to use as a standard, and patient variability for "high" dose opioids
- Flexible duration of opioid therapy, not a mandated 90th day duration – what about withdrawal considerations
- Chronic use (>3 months) very often carries a stigma associated with it, with potential disciplinary action
- Integrate prescription drug monitoring programs (PDMPs), communicate between states (evolving)
- More research into the safety and effectiveness of opioid drugs
- Law enforcement approaches to eliminate pill mills Jeff Fudin, Pharmacologist
- Alliance for Balanced Pain Management - innovative delivery solutions
- encourage awareness, education, insurance coverage and access to the broad range of balanced pain management options, which are grossly underutilized due to increased barriers in medicine including limited time commitments

CDC guidelines pain mgmt - Released Mar, 2016

- Intended for primary care providers who prescribe opioids for chronic pain in adults, in outpatient setting .
- It does not apply to management of pain associated with active cancer treatment, palliative care, or end-of-life care.
- Intended to enhance communications with treating clinicians and patient, for pain management to inform of the benefits, harms of chronic opioid therapy to in order to improve the effectiveness and safety (harms) of long term opioid therapy and reduce the risk for opioid use disorder, overdose, and death.
- 12 recommendations in 3 areas of consideration:

1 initiation of opioid therapy
2 opioid selection, dosage, duration, follow-up, D/C
3 assessing risk and harm of chronic opioid therapy

Level of evidence behind all the recommendations is low and never higher than level 3 on a scale of 1 to 4

CDC guidelines (12 recommendations)

- Determining when to initiate/continue opioids:
- 1. Do not use opioids as first-line therapy. If used, combine with other therapies.
- 2. Before starting opioids, establish realistic pain and functional goals. Continue opioids only if meaningful improvements outweigh risks.
- 3. Before starting and then periodically during therapy, discuss risks and benefits of opioids.
- Selection, dosage, duration, follow-up, and discontinuation of opioids:
- 4. When starting opioids, use immediate-release formulations.
- 5. Prescribe the lowest effective opioid dose. Use caution with any dose, if possible avoid doses ≥90 mg MME

CDC guidelines (12 recommendations)

- 6. Prescribe short durations for acute pain. Three days or less often sufficient; more than 7 days rarely needed.
- 7. Evaluate benefits and harms within 4 weeks of starting an opioid and at least every 3 months thereafter.
- Assessing risks and addressing harms of opioids:
- 8. Use strategies to mitigate risk (e.g., naloxone co-prescribing).
- 9. Review prescription drug monitoring program data. 10. Use urine drug testing at least annually.
- 11. Avoid concurrent benzodiazepines.
- 12. Offer or arrange treatment for patients with an opioid use disorder.

CDC - Opioid initiation

- Non-pharmacologic or non-opioid pharmacologic agents preferred for chronic pain. Opioids to be used only if the anticipated benefits outweigh the risks for both analgesia and function. Multidisciplinary care should be provided if opioids are prescribed.
- Establish realistic treatment goals, exit strategies, if opioid therapy is ineffective or has adverse effects. Continue opioids if there are meaningful improvements.
- Periodic re-assessments of the therapeutic response, with mutual responsibility for continued effectiveness of pain management by the patient and provider. Informed consent to address the benefit / harms of opioid therapy.

CDC - Opioid selection by primary care

- Initiation of opioids should begin with short acting, immediate release formulations.
- Start conservatively, with the lowest effective dosage, with close monitoring and careful dose titration. Extra caution if exceeding $\geq$ 50 mg/day morphine equivalency (MME).
- Avoid dosing above $\geq$ 90 mg/day MME (for primary care) or if required, carefully justify this decision
- If acute pain, prescribe the lowest effective dose for the anticipated shortest duration of the pain, if severe enough to warrant opioids, often estimated at 3-7 days.
- Reassessments every 1-4 weeks for dose titration, and at every 3 months duration thereafter, the provider should critically assess for benefit to potential harms risk, with considerations of lowering or tapering dosages for D/C.

CDC - Subsequent care

- Attempts to reduce their opioid dosing with non-pharmacologic options or opioid sparing medications, and/ or minimize adverse events due to other sedating medications.
- Suggested intermittent use of opioids for chronic pain

90 mg/d morphine equivalency (MME) tables per CDC (8/16):

- MORPHINE 90 mg/ day IV equivalency is 1/3 of oral formulations = 30 mg/ d
- For opioid rotation, use 50-75% calculated dose to start (lower with methadone)
- oxycodone 60 mg/ day hydrocodone 90 mg/ day codeine 600 mg/day
- oxymorphone 30 mg/ day (IV= 3 mg/ d) dihydrocodeine 360 mg/ day
- fentanyl 37 mcg/hr patch q3d; 90% bioavailable (IV = 0.3 mg or 300 mcg/ d)
- TIRF fentanyl 500- 700 ug/d (50-80% bioavail) approved for cancer related pain
- hydromorphone 22 – 18 (Canadian guidelines) mg/day, (IV = 4.5 mg/d)
- methadone 22-30 mg/day (with nonlinear equivalencies, resulting in disproportionally higher MME, with higher methadone dosing)
- tapentadol 225 – 300 mg/day (max dose = 600mg/ d)
- Based on other references (wider dose ranges for equivalency):
- tramadol 540-900 mg/ day (max dose = 400 mg/d)
- meperidine 900 mg/ day (IV= 300 mg/ d)
- levorphanol 8-12 mg/day levomethadyl 11 mg/day butorphanol 13 mg/day
- buprenorphine 3 (newer CDC) - 8 mg/ day SL (<40 % bioavail), (IV = 1.2 mg/ d)
- bupren buccal film 750-3000 ug/day (max dose = 900 ug bid) (55% bioavail)
- bupren transdermal 110 ug/hr (max dose weekly patch = 20 ug/h) (15% bioavail)
- pentozacine 243-450 mg/ day, nalbuphine 30 mg/d (IV only) Pract Pain Mgmt opioid calculator

MME controversies

- There are many pain experts who opine that these dose equivalencies have wide variability, and cannot be reliably or accurately used for determination for a specific patient's morphine equivalency requirements. Furthermore, the usual starting doses of alternatives for an opioid rotation (switching) are generally lower that the morphine equivalency predictions (25-50% lower than calculated), due to the diversity and variability of opioid receptor binding and for safety, due to potential risks of serious side effects, particularly with fentanyl, methadone (may affect heart rhythms), levorphanol, tramadol or tapentadol (related to drug interactions). Variable buprenorphine dosing (submucosal or transdermal differences due to bioavailability by routes of administration) and partial agonist mechanism of action, with ceiling effect.

Opioid Rotation

- Indications for opioid rotation
  - Poor tolerability
  - Poor analgesic efficacy despite aggressive dose titration
  - Drug-drug interactions
  - Preference or need for a different route of administration
  - Change in clinical status (e.g., concern about abuse)
  - Change in clinical setting that suggests patient may benefit from a different pharmacokinetic profile
  - Financial or drug availability (e.g., insurance coverage)
- Types of opioid rotation
  - Change in route of administration
  - Change of opioid drug (i.e., molecule or formulation)

10. Fine PG et al. *J Pain Symptom Manage.* 2009;38(3):418-425.

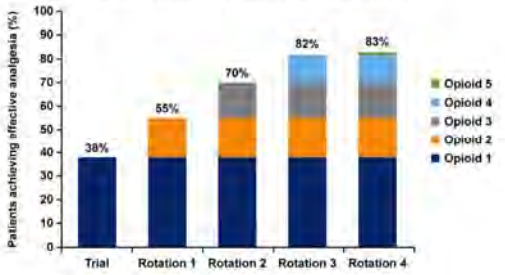
Officially, discontinue previous opioid, and using equianalgesic dosing calculations, decrease the predicted new opioid dose by 25-50% (except methadone), while considering more liberal use of SAO during the transition, to allow for possible enhanced analgesia and avoidance of adverse events due to incomplete cross tolerance

Variability in Response to Treatment

- Large individual differences in response[8-11]
- Drug-related and biological factors[8,9,11]
- Effective management requires opioid rotation for most patients[10]
  - Change in treatment (switch) to improve outcomes

Opioid rotation strategies due to
Opioid receptor polymorphisms
Incomplete cross-tolerance

Opioid rotation in pain management[8*]



* Retrospective chart review of 86 outpatients with chronic non-cancer pain who were treated with long-acting or extended-release opioids.[8]

8. Quang-Cantagrel ND et al. *Anesth Analg.* 2000;90(4):933-937.
9. Pasternak GW. *Life Sci.* 2001;68(19-20):2213-2219.
10. Fine PG et al. *J Pain Symptom Manage.* 2009;38(3):418-425.
11. Knotkova H et al. *J Pain Symptom Manage.* 2009;38(3):426-439.

7

CDC- Potential Harms of opioid usage

- Incorporate risk management strategies to minimize harms such as personal or family history of substance use disorder, psychiatric history, risk of overdoses due to comorbid medical conditions, aberrant use, or use concurrent sedating medications (i.e. benzodiazepines) or alcohol.
- Recommend naloxone with proper administration education, in those taking ≥ 50 mg/d MME
- Periodically review state prescription drug monitoring programs (PDMP), if available, or alternative pharmacy benefit profiles to determine concurrent overlapping usage, or other controlled medications in combination.
- Drug toxicology testing initially and periodically (randomly), at least annually, to determine adherence.
- Avoid opioids with sedating medications especially benzos
- Offer medication assisted treatment (MAT) (better than abstinence) along with behavioral therapies in those with an opioid use disorder. (based on level III, IV weak medical evidence)

CDC guideline critique by Canadian opioid guidelines 5/8/17

- Heavy involvement of experts critical of opioid use for chronic non-cancer pain (limited pain experts involved)
- Limited involvement of patient input as stakeholders
- Excessive restrictions on the selection of evidence
- Suboptimal application of GRADE rating system
- Excessive use of strong recommendations in the face of low quality medical evidence of supporting data
- Vagueness of some recommendations
- No comprehensive assessments of outcomes after 1 year
- None of the screening tools for OUD have been shown to accurately predict patients unsuitable for opioids
- No risk mitigation strategy has been shown to reduce harm in chronic opioid therapy
- Need more research to address these issues

CDC guidelines Critique by Dr. Argoff

12 principles have common sense approaches

CDC guidelines used same data as Chou guidelines in 2009 (AAPM approved), to draw different conclusions

Medical evidence cannot determine whether increased unintentional opioid overdose deaths is related to opioid therapy for chronic pain

Developed with a political imperative, bias based on the author's background. Authors has no clinical experience in actively treating chronic pain with opioids, based on PROP

Used low evidence data to conclude no significant benefit from chronic opioids, yet there is other data (not necessarily randomized controlled) to support beneficial effects. For opioid ER to gain FDA approval, randomized control for 12 weeks, with extension "open label" of the study to 52 weeks in which patients continued their therapy to evaluate safety, with presumed benefit (CDC never stated this fact in context)

CDC guidelines critique by Dr. Webster

- "I can't understand why payer representatives are part of any guideline where their vested interest is to limit access to treatments. They obviously profit from limiting dosing."
- Perpetuation of opioid crisis through cost containment & profitability
- "The guidelines proposed by the CDC fail to address any of the root causes to either the addiction or pain epidemics in America. This is a travesty." "We need the CDC to recognize that addiction is a disease that needs access to care not available today. We need to destigmatize the disease so people can get treatment without fearing prosecution and persecution. The CDC could lobby Congress to enact laws to increase access to treatment. We need the CDC to recognize that **pain is a disease** as well and is associated with an alarming rate of suicides due to lack of effective therapies. Making it harder for many patients to access opioids will increase the suicide rates among people with severe pain."
- He produced documentary film, "The Painful Truth", explaining, "People in pain are being sacrificed….because of lack of access to pain medicine"; film focuses on inadequate pain care for veterans
- Risks of *not* treating pain, that include suffering, loss of function, and even loss of life.

Dr. Lynn Webster, former president AAPM, developer of ORT

CDC critique

- Dr. Kertesz: Nowhere in the CDC Guideline did CDC experts suggest that patients be "forced to taper", even though the Guideline recommended caution in regard to key dosage thresholds. While some small studies do report favorable outcomes from voluntary opioid tapers carried out by experts, there exist no data to justify involuntary dose tapering carried out by clinicians lacking expertise. And worse, there are a rising number of reports of patient harms, including suicide and death
- Implementation of the CDC Guideline be monitored for "unintended consequences."
- Dr. Ziegler: Limited stakeholder participation and short deadline for feedback, Opioid sparing alternatives not necessarily achieve better outcomes, may not covered by insurance, dose thresholds not limits, Balance opioid availability vs. misuse, need more research for cost effective opioid alternatives
- Dr. Fudin: Bias of participants by CDC panel, conflicts of interest, done in secretive manner, MME not validated due to metabolic, genetic variants & drug interactions, quantification of function improvement vs. maintenance as goal, interdisciplinary panel including non-physicians for pain recommendations
- Denying pain treatment due to nonadherence is unethical, SUD is stigmatizing, and deincentivizes a patient's participation in an active, patient centered treatment program

Dr. Hoffberg's critique of CDC guidelines and barriers to care

- These are guidelines, not handcuffs.
- Intended for primary care providers, not pain specialists, which have additional expertise to manage chronic pain with chronic opioids.
- Many providers will limit opioid use, which will severely limit patient access for any pain management, particularly minorities, elderly and those in rural communities. Discriminatory policies based on gender, mental health, OUD
- Buprenorphine transdermal / buccal patch, a long acting opioid, is actually a safer option compared to short acting opioids, but is not even considered in this policy. Many insurance plans have already restricted this as a treatment option
- Urine drug testing for THC is not recommended. Fentanyl not part of POC cups
- Methadone and Levorphanol be reclassified as LAOs by DEA classification
- Opioid sparing techniques are strongly recommended but disincentivized by most health insurance carriers (limited benefits, high deductibles & copays), delays in approvals, some options considered "investigational / experimental" and not a covered benefit
- Little advice of practical implementation of the guidelines i.e. taper, alternative Rx
- Medical directors of insur plans who impose restrictive policies or deny pre-authorization appeals as the result of "guidelines" need to be legally liable for clinical decisions (have MD/pt relationship) made for any adverse consequences as the result of overriding the provider's recommendations and treatment plans

These guidelines/recommendations are being applied universally by health insurance carriers, irrespective of the justification of higher opioid dosing requirements

- now being considered as policies, and are being **globally applied to all providers, including pain specialists, by regulatory agencies and health insurance carriers/ pharmacy benefit plans**.
- do not account for the diversity of painful conditions, individual dosing variability and limited access to other treatment options that were actually encouraged in this document. Cancer pain has similar pathophysiologic mechanisms as non-cancer pain, and many of these patients same similar risk factors; their cancer may have been the result of poor lifestyle choices
- expert panel recommended that patients who are complex, at high risk for an opioid use disorder (which includes those with current or past psychological problems or substance use disorders, as well as socioeconomic and demographic factors), or on higher dose opioids, be referred to pain specialists, but there are not enough to fill the demand
- guidelines do not fully endorse that pain providers have the expertise and competency to safely and effectively titrate and maintain high dose opioid therapy for chronic pain.
- patients with OUD and chronic pain often require opioid therapy for pain

Consider the Risk of Not Treating Pain in Addicts – act of omission

- Study comparing addicts with AIDS to cancer patients and their response to under-treatment
  - Aberrant behavior is set in motion by under-treatment

    Passik, et al. 2001.
- Other consequences
  - Suicidal or self destructive risks/ harm
  - Using OTC medications with adverse effects:

  NSAIDs: GI bleed, cardiovasc or renal disease, deep venous thrombosis, A fibrillation, renal carcinoma

  APAP: hepatotoxicity, renal disease, renal carcinoma, ? Cardiac risks

Unintended consequences

- Increased risk of self-harm behaviors due to uncontrolled pain (i.e. suicidal or homicidal thoughts/ actions, anger, hopelessness, depression, anxiety, substance misuse/ abuse, including overdose deaths, with societal consequences)
- Functional, psych and socioeconomic impact of those who cannot tolerate work or function as the result of opioid dose reductions (i.e. applying for disability)
- Affects of uncontrolled pain on the neuroendocrine system (i.e. adrenal hyperactivity, labile hypertension, pain sensitization)
- Increased utilization of other medical resources with risks of greater harms (i.e. ED visits or desperation surgery).
- Need for written & signed scripts (limited tel refills or prescribing
- Economic credentialing and fee reductions for providers with patients prescribing above 120mg/d MME (i.e. insurance panels or Medicare MACRA)
- Disciplinary actions (i.e. "overprescribing" by Board of Physicians)

By using opioids for chronic pain, are providers enabling OUD, or is this mitigating other risks by reducing self-harm behaviors including SUD, or improving quality of life?

Opioid addiction discussion

- Prescription Opioids are a key contributor to the opioid use crisis. Recent study shows no correlation with the increased rates of illicit opioid OD deaths with declining prescriptions
- There is **no current medical evidence to conclude that legitimate medical use of an opioid is the "gateway" drug, as the major contributory factor for opioid "addiction", which is defined simply as compulsive use, despite harm,** in which the binding of opioids to the "pleasure/ reward" regions of the brain releases excess dopamine, which reinforces its continued use.
- Some individuals may have been exposed to opioids (neonatal, cough syrup, following injuries, possibly from high risk activities, painful surgery, procedures, medical problems, or recreational use) many years prior to developing chronic pain, which resulted in a high tolerance, requiring higher dosing. These repeated exposures, in conjunction with **hereditary predisposition, with socioeconomic and environmental factors can lead to addiction**. You need to have a substance exposure in order to Dx SUD
- Aberrant opioid use behaviors may frequently occur in chronic pain patients, and should be individually addressed, and closely monitored to minimize progression to addiction, through comprehensive care including education and counseling. There are estimates that opioid **"addiction"** can occur in 8% (**< 15%) of patients** (this statistic includes opioid use disorders with physical dependency, with lower values in the medical literature based on a stricter definition of addiction; however, these rates of addiction are similar with other habituating substances). In 2014, it was estimated that 12.5 million Americans obtained "prescription" opioids for non-medical use. There are **18000 deaths per year due to non-medical opioids overdoses** (with an increasing rate) including illicit drugs.

Opioid addiction discussion (cont)

- **Physical dependence does not mean addiction**, but affected patients can have of fear of experiencing **withdrawal symptoms**, or have reinforced use due to its mind altering or **euphoric effects** (which may also be considered for recreational usage for "escapism"). Some misusers cannot control their desire, in which they subsequently develop long standing psychological or irreversible **cravings** for opioids which can result in **harmful behaviors** with negative consequences.
- However, there are a large proportion of **addicts who also have chronic pain** (which may be related to their lifestyle or painful consequences of their misuse). To deal with this problem, regulatory agencies have decided to **reduce the available supply, thereby preventing "exposure" to the "at risk" population**, and this plan is now being used by insurance carriers (with possible financial incentives) to implement dose reductions for chronic pain patients. Other experts believe this strategy will not prevent the problem because an opioid addict may likely obtain these drugs anyway, but unfortunately, this will occur through illicit sources, which actually increases the risk of other more serious complications.
- Main perpetuators: avoidance of withdrawal symptoms ("chasing your tail or catch your shadow") vs. euphonic / hedonic reinforcing ("feels like the first time") effect of opioids. Chronic pain is usually avoidance of withdrawal

Opioid addiction discussion (cont)

- Education, law enforcement strategies and the legal systems to prevent, curtail or prosecute illicit drug usage or diversion has generally been inadequate. Unfortunately, the **treatments for opioid chemical dependency or addiction** (including those individuals from prescription sources) generally have a **low success rate**.
- They often require a long term medication assisted treatment (usually methadone, buprenorphine or naltrexone) approach using multidisciplinary care, including education, counseling with empowerment, and self-realization strategies, teaching an "internal locus of control", in conjunction with involving significant others for support.
- Additional resources need to be made for financially accessible programs of longer duration for more successful outcomes. Following "successful" completion of such programs, there may be recidivism.
- EVEN Opioid dependent **chronic pain** patients may benefit from participating in comprehensive multidisciplinary pain programs (medical literature supports this care with positive outcomes) if there are sufficient treatment goals, using acceptance, operant, or cognitive behavioral strategies to reduce their reliance on habituating medications, but they are expensive, limited availability, and not well covered by health insurance plans.
- "Lemonade glass is half full" incorporates acceptance & cognitive reframing
- Acceptance and commitment therapy delivered via video was as effective and acceptable as in-person delivery for chronic pain. Telemedicine approaches are being explored

Other recent guidelines in addition to CDC recommendations:

- Dept of Defense VA pain guidelines, Dec, 2016
- Avoid long term opioids < 90mg/d MME, esp if <30 yo, OUD
- Assess suicide risk
- "absolutely no safe dose of opioids"
- ASIPP guidelines for opioid therapy, Feb, 2017
- Methadone only for experienced providers, get initial and interval ECGs
- LAOs or high dose only in specific cases with severe intractable pain
- Canadian guideline for opioid therapy, May, 2017
- Consider opioid rotation with problematic pain or adverse effects of meds
- Avoid opioids in any patient with active SUD
- Patients >90mg/d MME should be encouraged to grad taper dose over no change
- If this is ineffective after 1 month, tapering may be paused or abandoned
- Multidisciplinary care is recommended in those with difficulty in tapering doses
- American College of Physicians on Substance Use Disorders, May 2017
- SUD is a treatable medical condition including education, prevention, diagnostic and research with decriminalization
- Evidence based pain management guidelines, naloxone, law enforcement, first responders, improved access to medication assisted treatment, mental health coverage, better training for treatments, national PDMP and other monitoring programs
- American Society of Addiction Medicine guidelines for drug testing (May, 2017)
- Frequency and interpretation of urine drug testing

Strategy for Prescribing Opioids

- Careful assessment and formation of an appropriate differential diagnosis
- Psychological assessment including risk of addictive disorders
- Informed consent
- Treatment agreement
- Appropriate trial of opioid therapy +/- adjunctive medications
- Assessment and reassessment of pain and level of function
- Regularly assess the 4 A's of pain medicine (Analgesia, Activities, Adverse Effects and Aberrant Behavior) Steps to reduce risk
- Thorough documentation in the medical records
- Adapted from Gourlay DL, Heit HA et al Pain Med. 2005; 6 107-12

Federation of State Medical Boards, April, 2017

- Balanced, not intended as "standard of care", variable decisions depending on pain characteristics, patient provider preferences, available treatment resources and other concurrent issues
- Controlled substance act does not limit amount of drug prescribed (no "ceiling effect")
- Physical dependence alone is neither necessary nor sufficient to diagnose addiction
- Thorough patient evaluation and risk stratification
- Treatment plan and goals, diagnostics, consultations including considerations for multidisciplinary pan management programs
- Informed consent and treatment agreement
- joint responsibility of provider and patient
- Opioid trial, ongoing monitoring, and adapting treatment plan
- Drug testing, adapting treatment to results, exit plan
- DOCUMENTATION former MD state chairman, Dr Gupta was a member of this panel

10 Steps of Universal Precautions in Pain Medicine Basis of 2017 FSMB policy

- Addresses ANY potential patient who is prescribed opioids, including HIV, SS, cancer, palliative care and hospice programs
- Many patients have co-morbid risks for OUD
- Improve communications and adherence
- Address the presence of significant psychiatric dual Dx, or co-morbidities, including substance use disorders
- Represent treatable conditions that must be concurrently addressed in order to optimize outcomes.
- Universal Precautions as a concept should be based upon mutual trust and respect between patient and practitioner, both of whom should be committed to setting and achieving realistic goals in both cancer and non-cancer pain patients in a non-judgmental and non-punitive way to improve outcomes

Heit (member of FSMB advisory committee) & Gourlay, 2005, 2009

Ten-step process: An algorithmic approach for long-term opioid therapy in chronic pain.

- STEP I Comprehensive initial evaluation
- STEP II Establish diagnosis: X-rays, MRI, CT, neuro-physiologic studies, Precision diagnostic interventions, Psychological evaluation
- STEP III Establish medical necessity: (lack of progress or as supplemental therapy), Physical diagnosis, Therapeutic interventional pain management, Physical modalities, Behavior therapy
- STEP IV Assess risk-benefit ratio: Treatment is beneficial
- Assess/ stratify risk for Opioid Use Disorder
- STEP V Establish treatment goals
- STEP VI Obtain informed consent and agreement

Alan D. Kaye et al **Prescription Opioid Abuse in Chronic Pain: An Updated Review of Opioid Abuse Predictors and Strategies to Curb Opioid Abuse, Pain Physician,** 2017;20:S3-92,S111-S133

An algorithmic approach for long-term opioid therapy in chronic pain

- STEP VII Initial dose adjustment phase (up to 8-12 weeks): Start low dose, Utilize opioids, NSAID's and adjuvants; Discontinue: Lack of analgesia, Side effects, Lack of functional improvement; Avoid long-acting opioids for the initiation of opioid therapy
  Low dose: < 50mg MME. Mod dose: 51 to 89 MME. High dose: >90 mg MME
- STEP VIII Stable phase (stable – moderate doses): Monthly refills; Assess for four A's: Analgesia, Activity, Aberrant behavior, Adverse effects; Manage side effects
  Prescribe methadone only after failure of other opioid therapy and only by clinicians with specific training in its risks and uses, within FDA recommended doses, get ECG
  Prescribe long-acting or high dose opioids only in specific circumstances with severe intractable pain
- STEP IX Adherence monitoring: Prescription monitoring programs, Random drug screens, Pill counts
- STEP X Outcomes: if Successful – continue: Stable doses, Analgesia, activity, No abuse, or side effects;
- if Failed – discontinue: Dose escalation, No analgesia, No activity, Abuse, Side effects, Non-compliance

Chronic opioid therapy should be provided by experienced providers only to patients with proven medical necessity and stability with improvement in pain and function, independently or in conjunction with other modalities of treatments in the lowest effective doses, with appropriate adherence monitoring and understanding of adverse events.
Due to the evolving body of evidence, this approach is not intended to be a "standard of care."

Patient education/ empowerment and mutual treatment agreement

- Proper education for the patient with considerations to involve the patient's support system for additional feedback of care and implementation of the treatment plan. This can improve patient compliance and allow the providers to properly titrate the analgesic regimen. It is necessary to instruct the patient for safe usage, storage, security, and disposal
- Treatment recommendations should be patient centered and individualized for the patient's pain problem including rational polypharmacy, opioid sparing treatments (nonopioid analgesics, nonpharmacologic care including psychological counseling, particularly cognitive behavioral therapies

The Risk-Benefit Framework: Judge the treatment, not the patient

INAPPROPRIATE

- Is the patient good or bad?
- Does the patient deserve pain meds?
- Should this patient be punished or rewarded?
- Should I trust him/her?

APPROPRIATE

Do the benefits of this treatment outweigh the untoward effects and risks in this patient*?
***(or to society)**

1. Make a Diagnosis With Appropriate Differential.

- Treatable causes for pain should be identified when they exist, and therapy should be directed to the cause of pain.
- Any comorbid conditions or dual diagnoses, including substance use disorders and other psychiatric illnesses, must also be addressed
- Complete evaluation (including details of their general medical conditions), and the following:
- History: previous treatment and with emphasis on how the pain affects function, and goals.
- Examination: Physical stigmata of a substance use disorder (i.e. skin tracks, spider nevi, etc).
- Detailed primarily musculoskeletal and neurological exam of the painful body locations. May include other body regions
- Establish working diagnosis and differential diagnoses (including a pain generator), in conjunction with objective diagnostic testing, as well as acknowledging psychosocial co-morbidities

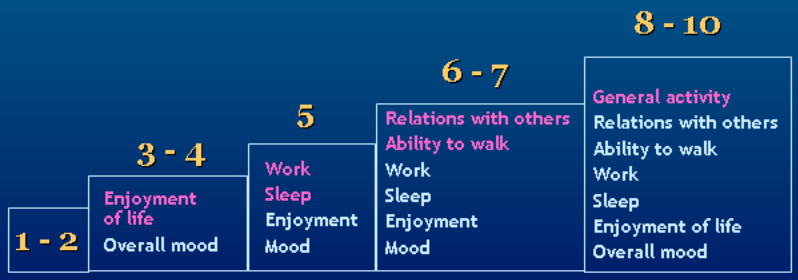
Comprehensive Pain Assessment

- I. Detailed history of current pain problem
  - A. Catalog of pain (number and locations)
  - B. Information for each pain
- 1. Intensity (0–10 VAS)
- 2. Locations and radiation
- 3. Onset and changes over time
- 4. Temporal pattern (constant, intermittent, etc.) and quality (sharp, dull, burning, etc.), breakthrough pain
- 5. Exacerbating and relieving factors
- 6. Associated neurologic or vasomotor abnormalities
- 7. Other associated factors
- 8. How the pain interferes with the patient's life
- 9. Current therapeutic modalities
- (schedule, efficacy, side effects)
- 10. Prior therapeutic modalities (schedule, efficacy, side effects)
- 11. Pain coping strategies, chemical coping, locus of control
- 12. Pain behaviors, perception expectations and consequences

Pain Intensity and Functional Interference

PEG: Pain, Enjoyment, General Activity

Functional impact is significantly correlated with pain severity ($P<0.0001$)



Breitbart W et al. *Pain* 1996;68:315-321.

2. Psychological Assessment, Including Risk of Addictive Disorders.

- A complete inquiry into past personal and family history of substance misuse is essential to adequately assess any patient.
- A sensitive and respectful assessment of risk should not be seen in any way as diminishing a patient's complaint of pain.
- Patient-centered urine drug testing (UDT) should be discussed with all patients regardless of the meds that they are currently taking. Repeated UDT can improve compliance of patients on opioid medications and can improve overall pain management.
- Patients found to be using illicit or unprescribed licit drugs should be offered further assessment for possible substance use disorders.
- Those refusing such assessment should be considered unsuitable for pain management with a controlled substance.
- Pain disorder associated with Psychosocial factors including anxiety, PTSD, depression (suicidal risk), bipolar, personality traits/ disorders (especially somatization, histrionic, borderline or conversion), ADHD, insomnia, schizophrenia (may have altered pain thresholds, associated with headaches), abuse (physical, emotional or sexual), stressors or interpersonal relationships
- Judicial or criminal background

Screening Instruments for Misuse, Abuse or Addiction Risk

Risk assessment and stratification is critical, and requires a comprehensive benefit-to-harm evaluation that weighs the potential positive effects of opioids on pain and function against potential risks. Consider collaborative care model

Specific for opioid prescription abuse with validity studies:

- **ORT (Opioid Risk Tool) predicts aberrancy prior to prescribing**
- **SOAPP-R (Screener and Opioid Assessment for Patients with Pain, rev)**
- **DIRE (Diagnosis, Intractability, Risk, Efficacy risk assessment tool)**
- **PMQ (Pain Medicine Questionnaire) identify misuse once started**
- **PDUQ (Prescription Drug Use Questionnaire)**
- **COMM (Current Opioid Misuse Measure)**
- **CAGE-AID (Cut, Annoyed, Guilty, Eye opener- And Illegal Drugs)**
- **STAR (Screening Tool for Addiction Risk)**
- **SISAP(Screening Instrument for Substance Abuse Potential)**
- **POTQ (Prescription Opioid Therapy Questionnaire)**
- **ABC (Addiction Behaviors Checklist)**
- **SAFE (Social fn, Analgesia, Physical Fn, and Emotional fn)**
- **PADT (Pain Assessment and Documentation Tool = 4 "A's") for therapeutic efficacy and functional improvements**

Opioid Risk Tool (ORT) by Dr. Lynn Webster

screening questions (3 min) given prior to prescribing opioids:

	(scoring)	Female	Male
1. FH of alcohol / illicit subs,		(1/2)	(3/3)
prescribed opioids		(4)	(4)
2. Past Hx alcohol, illicit subs,		(3/4)	(3/4)
prescribed opioids		(5)	(5)
3. Age less than 45		(1)	(1)
4. Hx of preadolescent sex abuse (female)		(3)	(0)
5. Hx of ADHD, OCD, schizo, bipolar; depression		(2) (1)	(2) (1)
SCORING TOTALS		____	_____

If ≥ 8 high risk, 4-7 moderate risk, 0-3 low risk

Risk Assessment Tools

- ORT, SOAPP-2 & DIRE – Best assess abuse potential prior to starting long-term opioid therapy
- COMM (17 ques), PMQ (26 ques), PDUQ (40 ques) – Characterize degree of medication misuse or aberrant behavior once opioids are started
- DAST-10 & PMQ – More suitable for assessing current alcohol and/or drug abuse than potential for such abuse Passik SD, et al. Pain Med. 2008;10 Suppl 2:S145-166
- SOAPP version 1 (5 ques, 0/1/2/3/4 = never/seldom/sometimes/often/ very often)
- How often do you have mood swings?
- How often to you smoke nicotine in mornings?
- How often do you take meds other than its prescribed sig?
- How often have you used illicit drugs (incl THC) over past 5 years?
- How often in your lifetime have you had legal problems or arrests?

Other risks: tobacco, tattoos, head injury, eating disorders, multiple surgeries with poor outcomes, occupational including landscaping, construction, bartenders, musicians, high risk sports, violent or multiple trauma injuries (even if victim) limited educational/ socioeconomic backgrounds, males

Functional scales may be used to assess opioid use justification, with interval changes and goal definition

SAMSHA approved, SBIRT reduces:

Brief Screen: NIDA or DAST-1, drug abuse quick screen:
Over past year, NON-medical use of illegal or prescription drugs?
NIAAA (alcohol): Past year, drinks $\geq$ 4 (men), $\geq$ 3 (women) per day?
Screen, if yes, to the above questions: ASSIST, DAST-10, AUDIT-C (alcohol)
ASSIST: 8 screening ques for substance ever used (includes tobacco), freq over past 3 months, freq of urges to use, negative consequences of use, impaired function, friend or family concerns, failed to control usage
Brief Intervention: takes 5-20 min to perform; patient centered, respectful, motivationally based, increased insight and awareness of SUD, education, how behavior may affect health and personal problems, suggest behavioral changes, consultative referral
Referral to Treatment: more advanced, selecting program
Quick screen for Anxiety, PTSD, Depression, Substance use disorder

Atluri and Sudarshan

- Risk of inappropriate use of prescription opioids in patients with chronic pain.
- The tool was developed for use in interventional pain management settings
- Six items (each individually scored)
- 1. Focus on opioids
- 2. Opioid overuse
- 3. Other substance abuse
- 4. Low functional status
- 5. Unclear etiology of pain
- 6. Exaggeration of pain
- ≥ 3 items positive is predictive of abuse

Urine Drug Testing

- Advantages – Can confirm that prescribed drug is taken and that other drugs are not – Makes a strong statement potentially useful in monitoring
- Disadvantages – Cannot confirm that the proper dose is taken – Can be misinterpreted – Can be stigmatizing
- When to Test?
- Initial testing (lab or POC) done with class specific immunoassay drug panels – Typically do not identify individual drugs within a class (rapid results, not quantitative, low specificity)
- Followed by a technique such as LC or GC/MS – To identify or confirm the presence or absence of a specific drug and/or its metabolites
- Heit HA, Gourlay D. J Pain Sympt Manage. 2004:27:260-267.

Urine Drug Testing (UDT): Why, What, Decision made
Use motivational interviewing to best communicate

- Urine: best biologic detection with window of 1-3 days with validation and confirmation (GC or LC/MS) for metabolites & parent drug, noninvasive, less costly than serum. Point of service cup dipstick (IA): 25% false negative or positive
- (55–63%) of de-identified patient GC/MS test results between 2011 and 2013 were inconsistent, suggesting that many patients are misusing prescription drugs
- Heit: UDT be utilized as **one** component of a "risk management (tool) to be first and foremost about protecting patients"
- Unexpected confirmed results can only result in a differential diagnosis: inconsistent due to no parent drug, no metabolites or a pharmaceutical contaminant . Draw no conclusions
- Use UDT, history and screening questionnaires helpful to Stratify patients into 3 groups
- False conclusions due to impurities in the pharmaceutical preparation, detection of substances below the cutoff thresholds, timing of when UDT obtained vs. when drug taken, alcohol found due to fermentation (i.e. DM), cough syrup or freq hand washing with sanitizer, "passive exposure" (seen with THC or nicotine), poppy seeds may result in morphine, variability in metabolism by Cytochrome P450 phenogenetics

Patient self-reporting combined with drug testing is "best bang for the buck"

- Limited medical evidence to support its effectiveness, variable opinions
- Evolving field including urine, saliva, serum, hair
- Qualitative (presumptive screen by IA by POS cup) vs. Semi-quantitative (analyzer IA) vs. Quantitative (confirmation by LC or GC/MS)
- Freq of testing, substrates tested, cutoffs, detection windows
- Difficult to correlate quantitative result with drug doses, new exposure vs. fade out effect
- Quantification does not correlate with CNS levels, therapeutic effect
- May use serum level at steady state to establish baseline vs. toxic forensic levels
- Evaluation of parent drug vs. expected metabolites and its relative titers
- Interpretation of Inconsistent tox results can be problematic
- PAMORAs metabolize into Naloxone which in turn metabolizes into noroxymorphone, (usually with buprenorphine)
- Fade out vs. repeat exposure with quantitative testing
- Negative findings may include increased use, prn use, discontinuation (may be related to reduced access or missed appt), diversion,
- Positive findings of unexpected drugs may include non-medical or medical use, inadvertent exposure
- Discussion of inconsistencies in a supportive, non-threatening , non-confrontational, open ended ques, motivational interviewing, patient centered, may be non-punitive, may be done prior to obtaining test
- Facilitate mutual trust, communications and adherence

Reasonable assessment of risk of a concurrent substance use disorder or other comorbid psychopathology

- **Group I — Low Risk, Primary Care Patients:**
  No past or current history or FH of substance use disorders, stable Psych
- **Group II — Medium Risk, Primary Care Patient With Specialist Support:**
  Past history of a treated substance use disorder or a significant family history of problematic drug use; past or concurrent psychiatric disorder
- **Group III — High Risk, Specialty Pain Management:**
  Complex cases to manage due to an active substance use disorder or major untreated psychopathology, positive FH, risk to provider or patient
  or with higher opioid dosing (≥ 90 mg MME)

Groups II and III can be dynamic, & may need be reclassified,
Need frequent reassessments of all groups to stratify patient risks

- "Opioid Renewal Clinic," a multidisciplinary model for highest-risk patients with chronic pain on long-term opioids

Outpatient Management of the Chemically Dependent Pain Patient/or Patient with Aberrant Drug-taking (Group III)

Universal Precautions: applies to All patients at the beginning of therapy
Use with a Maximally structured approach including:

- Frequent visits with multidisciplinary care, one pharmacy
- Limited supply of meds (freq scripts with "to be filled dates")
- Can be managed with abuse deterrent formulations long-acting opioids with low street value, with limited dose escalation and close monitoring
- Judicious use of rescue opioids or breakthrough pain meds
- Avoid prescribing morphine (or fentanyl) as it may be indistinguishable from active heroin, often combined with fentanyl (not detected by UDT)
- PDMP for adherence initially, and every 3-6 months thereafter
- Urine Toxicology with patch/ pill counts (may give extra reserve, with the patient instructed to bring in pill bottle to verify extra doses)
  (routine or random) every 1-3 months, or more often if inconsistencies
- Recovery program/ psychotherapy/ NA/ AA with sponsor
- Consultative care with psychiatry or addictionologist if necessary
- Opioid agreement with strict monitoring
- (Ten Universal Precautions: Heit & Gourlay)

3.Informed Consent.
4. Treatment Agreement (NOT A CONTRACT)

- The healthcare professional must discuss the proposed treatment plan with patients and answer any questions that they may have about its anticipated benefits and foreseeable risks for **both** receiving a proposed treatment or not receiving a potential treatment
- The expectations and obligations of both the patient and the treating practitioner need to be clearly set forth in writing or by verbal agreement. Combined with informed consent (but may not be protective for medical negligence cases), the treatment agreement forms the basis of the therapeutic trial. A carefully worded treatment agreement (i.e. "may, could" instead of "must, shall" will help to clarify appropriately set boundary limits making possible early identification and intervention around aberrant behaviors

Contracts/Agreements/Consents

PURPOSE:

- Educational and informational, articulating rationale and risks of treatment
- Articulates monitoring (pill counts, etc.) and action plans for aberrant medication taking behavior
- Takes "pressure" off provider to make individual decisions (Our clinic policy is…)
- Prototype http://www.painedu.org

LIMITATIONS:

- Efficacy not well established
- No standard or validated form
- No evidence they are detrimental

Fishman SM, Kreis PG. Clin J Pain 2002; Arnold RM et al. Am J of Medicine 2006

Opioid agreements

- If having patients sign an agreement is viewed as just another administrative task, it misses the important opportunity to educate them about safe opioid use.
- Presenting agreements as tools to keep patients safe and to clarify expectations and responsibilities should be the goal.
- Due to variations in patient health literacy, agreements may need to be written at a sixth-grade reading level
- Methods such as "teach-back" should be used to confirm comprehension.
- In 1 study, fewer than 20% of patients who signed a pain agreement consistently remembered having done so.
- Review periodically (at least annually)

For patients with at least an English 8th grade reading level "Chronic Opioid Agreement" by M. Cloeren, MD see http://my.quantiamd.com/player/yeaeihfny

Standard Opioid Agreement form:

Pain Treatment With Opioid Medications: Patient Agreement

I, _____, understand and voluntarily agree that (initial each statement after reviewing):

_____ I will keep (and be on time for) all my scheduled appointments with the doctor and other members of the treatment team.

_____ I will participate in all other types of treatment that I am asked to participate in.

_____ I will keep the medicine safe, secure, and out of the reach of children. If the medicine is lost or stolen, I understand it will not be replaced until my next appointment, and may not be replaced at all.

_____ I will take my medication as instructed and not change the way I take it without first talking to the doctor or other member of the treatment team.

_____ I will not call between appointments, or at night or on the weekends looking for refills. I understand that prescriptions will be filled only during scheduled office visits with the treatment team.

_____ I will make sure I have an appointment for refills. If I am having trouble making an appointment, I will tell a member of the treatment team immediately.

_____ I will treat the staff at the office respectfully at all times. I understand that if I am disrespectful to staff or disrupt the care of other patients my treatment will be stopped.

_____ I will not sell this medicine or share it with others. I understand that if I do, my treatment will be stopped.

_____ I will sign a release form to let the doctor speak to all other doctors or providers that I see.

_____ I will tell the doctor all other medicines that I take, and let him/her know right away if I have a prescription for a new medicine.

_____ I will use only one pharmacy to get all of my medicines:

_____
Pharmacy name/phone#

_____ I will not get any opioid pain medicines or other medicines that can be addictive, such as benzodiazepines (Klonopin, Xanax, Valium) or stimulants (Ritalin, amphetamine), without telling a member of the treatment team ***before I fill that prescription***. I understand that the only exception to this is if I need pain medicine for an emergency at night or on the weekends.

_____ I will not use illegal drugs, such as heroin, cocaine, marijuana, or amphetamines. I understand that if I do, my treatment may be stopped.

_____ I will come in for drug testing and counting of my pills within 24 hours of being called. I understand that I must make sure the office has current contact information in order to reach me, and that any missed tests will be considered positive for drugs.

_____ I will keep up to date with any bills from the office and tell the doctor or a member of the treatment team immediately if I lose my insurance or can't pay for treatment anymore.

_____ I understand that I may lose my right to treatment in this office if I break any part of this agreement.

Pain Treatment Program Statement

We here at _____ are making a commitment to work with you in your efforts to get better. To help you in this work, we agree that:

We will help you schedule regular appointments for medicine refills. If we have to cancel or change your appointment for any reason, we will make sure you have enough medication to last until your next appointment.

We will make sure that this treatment is as safe as possible. We will check regularly to make sure you are not having bad side effects.

We will keep track of your prescriptions and test for drug use regularly to help you feel like you are being monitored well.

We will help connect you with other forms of treatment to help you with your condition.

We will help set treatment goals and monitor your progress in achieving those goals.

We will work with any other doctors or providers you are seeing so that they can treat you safely and effectively.

We will work with your medical insurance providers to make sure you do not go without medicine because of paperwork or other things they may ask for.

If you become addicted to these medications, we will help you get treatment and get off of the medications that are causing you problems safely, without getting sick.

Patient signature _____

Patient name printed _____

Date _____

Provider signature _____

Provider name printed _____

Date _____

Source: National Institute on Drug Abuse; National Institutes of Health; US Department of Health & Human Services

OPIOID LIABILITIES & Side effects (up to 80%)

- DEATH, overdose, difficulty breathing, sedation, altered alertness & memory, heart attack, falls, fractures, hypotension, itching & rash, constipation, nausea, vomiting, impaired GI motility, weight or appetite changes, dry mouth, sweats, reduced libido (androgen deficiency), infertility, mood changes, fatigue, dizziness or orthostasis, headache, insomnia, swelling, urinary retention, jerky movements, pancreatitis, biliary spasm, immunity, seizures, arrhythmias (QTc prolongation), serotonin syndrome, adrenal insufficiency & other unknown harms.
- Nausea can be the most common side effect, attributed to opioid binding in the brainstem, or as the first perceived symptom of constipation
- In some cases, the continued use of opioids may affect prognosis with wound healing, post-operative recovery, or contribute to additional medical complications.

Opioid adverse effects

- Class precautions include relative contraindications with paralytic ileus, or intestinal obstruction, and head injury with elevated intracranial pressure
- Standard Black box warnings for Schedule II drugs
- This can be reported: 1-800-FDA-1088 www.fda.gov/Safety/MedWatch/default.htm

Review package insert/ med guides by pharmacist for storage disposal & safety with other prescribed medications

Be proactive and ask about SEs including bowel or sexual functioning

Opioid risk/ adverse events

- Continued opioid use (< 25%) may result in a Substance use disorder (misuse), abuse & Addiction (8%) (compulsive use of drugs despite harm, causing permanent psychological distress & cravings)
- Pseudo-addiction may also occur (due to inadequate analgesia)
- Chronic use &/ or high doses can cause Physical dependency withdrawal symptoms with med changes or abrupt dose reduction
- Tolerance or habituation (more meds required for the same pain relief which may require periodic reduction or rotation of opioids) FDA defined ≥ 60 mg/d MME for 1 week
- "Opioid induced hyperalgesia" (increased pain sensitivity, which may require detoxification)

Opioid withdrawal syndrome

- Abrupt reduction of opioids may result in an abstinence (physical withdrawal) syndrome, which may include sweating, dilated pupils, irritability, insomnia, GI upset, goosebumps, bone & muscle aches
- Rarely may result in serious problems, including heart attacks or strokes.
- Withdrawal seizures can occur from other meds

(i.e. benzos, barbiturates, anticonvulsants, baclofen & alcohol).

A chemical dependency program including hospitalization/ day program for detoxification/ tapering from CS (including opioids) may be required, including medication assisted treatment (MAT)

Medication adherence & titration

- Patient must take meds exactly as prescribed including dose, time, interval, frequency & route. Exact quantities may be prescribed until the next appt interval, but may choose to take less, in order to build up a "reserve". Instructed not take previously prescribed/ dispensed CS/ meds, unless pre-arranged. Covering providers have the discretion to change dosing or quantities based on their clinical judgment.
- Adjustments to meds will be considered only during an OV based on their pain control, function, compliance including logs, tolerance & medical stability.
- If functionality is consistently limited (i.e. freq bedrest), then considerations may be made for tapering of opioids.
- Dose reductions will be considered for nonadherence of this agreement.
- Dose increases are usually based on legitimate need & demonstrated improvements in function/ pain.

Patient disclosures

- Pregnant (or suspected) or nursing, in conjunction with an obstetrician (or pediatrician) because CS or other meds can cause birth defects or other prenatal problems. At birth, the baby may become physically dependent, with a "neonatal opioid withdrawal syndrome". Naloxone may be teratogenic
- Notify providers if in a hospice, buprenorphine, methadone maintenance drug rehabilitation, Native American or VA medical programs (not part of PDMP)
- **Any changes** in medical condition including surgery (preop dose reductions are recommended), dental, new medical events (injury, symptoms, or loss of consciousness), & particularly, if any med changes are recommended by other providers.
- Medical record releases should be obtained concurrently by other providers at the time of service.

Dosing adjustments

- Dose reductions may be required to minimize drug interactions, in part due to age, gender, body habitus, genetic or metabolic factors, or with chronic kidney &/ or liver disease (initiate at 50% of the usual starting dose for adults)
- Dose reductions may occur for untreated or suspected sleep apnea (often associated with emphysema & obesity) or respiratory compromise
- During ACUTE medical conditions: cardiovascular (angina, low blood pressure or congestive heart failure), respiratory (asthma, pneumonia or flu), liver failure (hepatitis), blood loss, dehydration, abdominal cramping with constipation or vomiting, mentation changes, head injury, kidney failure or other **life threatening events** immediately & voluntarily reduce current dose of opioids by <80% & promptly seek urgent care
- Pain or other symptoms from an acute illness (i.e. angina) can be masked while taking my CS/ meds.
- Additional diagnostic testing & closer monitoring may be required

Precautions

- Avoid using alcohol while taking prescribed CS (opioids) due to "dose dumping" or with other sedating meds due to dangerous combined synergistic effects.
- Alcohol & Cannabis use may require more freq tox testing.
- Medical cannabis use for "therapeutic benefit" or symptom control must be disclosed with a valid MD certificate from registered providers for recommendations of approved conditions. Opioid dose reduction may be considered.
- **Tobacco**/ nicotine **cessation** is strongly recommended since it may adversely affect health, pain control, & has been associated with increased risk of a substance use disorder.

Precautions

- **Caution while (or refrain from) driving**, operating machinery or any other important tasks when taking any CS/ meds which can impair judgment & fine motor skills, particularly when combined with other CS (**opioids, benzos, sedating, sleeping meds), cannabis or alcohol.**
- Release of legal liability for prosecution of "drugged driving" or other violations related to the legitimate use of my meds.
- Patient advised to take newly prescribed med at home first to monitor for any possible side effects before using them while driving, operating equipment or work.
- Do not drive following seizures (except if medical cleared >90 days), if confused, with acute or serious medical events or < 7 hours after taking a hypnotic sleeping pill.
- http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/ucm107902.pdf

Opioid Balancing

- Once a stable opioid analgesic regimen is reached, patients with no significant cognitive/psychomotor impairments should be allowed to drive or operate machinery
- Caution if concomitant sedatives given
- Risk of pain directly contributing to impaired concentration, coordination and judgment

Emergency & Safety

- Call 911 for any emergency, or poison control (1-800-222-1222) for any overdoses or if CS/ meds are taken by others (unauthorized).
- If home naloxone injection or nasal mist is used for a suspected drug overdose, a significant other will immediately call 911 after administration & the patient will not take any additional opioids unless cleared by a medical provider.
- Dispose of any unused CS in a safe manner, usually by flushing down the toilet for most oral opioids, mail back, at a pharmacy, Drug Take Back Day, or through approved disposal locations with dates noted on DEA website: http://www.deadiversion.usdoj.gov/drug_disposal/takeback/index.html
- Discard all other expired meds per state law (cat litter or coffee grounds).
- FDA guidelines for safe use & disposal of meds: http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm186187.htm

Prescription accountability

- Verify scripts for accuracy, including name, address, birth-date, diagnostic codes (ICD-10), stamps and signatures & arrange for preauthorization (may take at least 72 hrs).
- The pharmacist must dispense the correct med & proper quantities. Most CS (Sch. II) requires original scripts. CS may also have limited availability.
- Can use post-dated scripts for my med safety, compliance & management
- Advise patient to have a reserve of meds available for me to use in the event of unexpected circumstances (i.e. weather or transportation) or supply problems.
- If the patient runs out of meds/CS due to interrupted care, they may be seen more often & restarted at lower dosages.
- Keep unused scripts & prescribed meds (including unused meds) for verification/ pill counts. Do not discard unused meds or scripts until cleared by provider.

Medication safety & security

- Safely store, protect & secure scripts & meds (especially with children & pets) *as if they are "$1000 cash & a loaded gun"*. Lock boxes are recommended.
- Significant others are encouraged to assist.
- Notify providers if there are any changes in social or living situation that might affect meds security, or ability to take meds exactly as prescribed.
- Lost meds/scripts will be only replaced by provider discretion (if stolen, a police report or proof of loss is required).
- Regardless of any explanation, more freq OV with tox testing, lower pill quantities &/ or a change in meds will likely occur, along with compliance classes/ counseling.

Opioid prescriptions while traveling

- Do not mix CS/ meds together in bottle (some newer bottles have a "timer cap" to prevent inadvertent overuse)
- Store meds in their original containers (don't place in checked baggage) & carry the original label
- Letter of explanation (with Dx, & current meds)
- Extra security (lock boxes) are recommended
- The provider may require travel itinerary/ receipts
- May require vacation over-ride approvals for early refills

Pharmacy arrangements

- The scripts will be filled by ONE local, in-state pharmacy **except if noted:** mail order, out of state, or other (specify) & prescriptions must be paid for by the pharmacy benefit plan, **except if:** self pay / other (specify)
- One pharm will dispense all CS/ meds with address updates required. An alternate pharmacy may be used, if prior arrangements have been made (i.e. travel or due to unavailability of meds).
- **Communication with** other designated health care providers including pharmacists, mental health, diagnostic testing, prescription drug monitoring program (PDMP) from any state or pharmacy requests for medical information and drug profiles, as well as my health insurance/ pharmacy benefit carriers (including pharmacy profiles) to assist with preauthorization or coordination of care.
- Mental health providers are highly recommended for prescribing, &/ or coordination any psycho-active/tropic meds, especially if they are CS

5. Pre- or Post-Intervention Assessment of Pain Level and Function.

- It must be emphasized that any treatment plan must begin with a trial of therapy. This is particularly true when controlled substances are contemplated or used. Without a documented assessment of pre-intervention pain scores and level of function, it will be difficult to assess success in any medication trial. The ongoing assessment and documentation of successfully met clinical goals will support the continuation of any mode of therapy. Failure to meet these goals will necessitate re-evaluation and possible change in the treatment plan. Pain diaries can be helpful.

Balance Goals of Treatment…

with Practical Solutions

SMART - Goals

- S= specific
- M= measurable
- A= attainable
- R= realistic
- T= timely

50% reduction in VAS

- "very meaningful" to patient
- Realistic Goal:
- **20-30% reduction in VAS or improved function which is "meaningful" to patient**

Mutual treatment goals for the patient- provider

- **Minimize and manage pain adequately (? least important)**
- **Improve or maintain function or activity tolerance, including safe mobility, ADL's, work, vocational retraining, homemaking, school, recreational, avocational, volunteer, bowel, bladder care, sexual activity, Improve physical attributes including flexibility, strength, stamina, endurance, balance, independent home exercises**
- **Improve quality of life including sleep, mood (hedonia), anxiety, pain coping strategies, mental agility and concentration**
- **Reduce medication dependence or adverse effects** by **tapering or detoxification,**
- **Prevent complications,** worsening of condition or deterioration from effects of **deconditioning, osteoporosis, or recurring pain and disability,**
- **Avoid additional medical care (including emergency department visits, hospitalizations, ill advised surgery, procedures or diagnostic tests),**
- **Prevent institutionalization, or palliation** (limited options refractory to other care),
- **Unsuccessful attempts at weaning opioid dosing with opioid sparing options,**
- **Alternative options of care have been deemed to be riskier, and less effective than opioids**

Managing the difficult patient

- Are the “addicted and drug-seeking” patients in severe pain appropriately “pain–relief seeking,” or is it a combination of both, can be difficult to sort out.
- Clinicians must base complex treatment decisions on a brief subjective assessment of whether there is sufficient benefit to justify continued therapy or whether harm is occurring to sufficient justify discontinuation.
- The provider's approach may be at odds with the patient's request.
- Although it is intended to keep the patient safe, such an approach may threaten the collaborative relationship that clinicians work hard to develop (affecting patient -centered care).
- FIRST DO NO HARM versus Listen to the patient?

Managing the difficult patient

- To optimize and individualize effective dose for any given patient that both maximizes benefit and minimizes harm is hard to predict.
- Dose-limit recommendations are based on low-quality evidence that focuses on associations between dose and overdose risk but could result in some patients being denied treatment despite apparent benefit
- Despite not being the guideline's intent, there is concern that the “recommended” dose thresholds will lead insurers to deny coverage for patients receiving high-dose opioids.
- To try to avoid arbitrary dose reductions for patients already receiving high doses, the guideline specifically recommends that we “reevaluate high dosages” in established patients rather than automatically decreasing them.

Difficult patient

- Need to build mutual trust by empathically validating symptoms, suffering, and fear and by emphasizing that success requires collaboration. "MAGIC MOMENTS"
- Discussion of polypharmacy, which, although probably started and titrated with good intentions, is not providing adequate benefits and is putting the patient's health at risk (for example, overdose, falls).
- Using shared decision making, the clinician and patient need to determine which medications are least beneficial and can be tapered first versus JUST SAY NO
- Patient may leave their physician before completing the taper and transitioning to new treatments. WHAT IS THE OUTCOME?
- Provider should not discount the importance of a therapeutic relationship even in the absence of effective treatment.
- Some patients benefit simply from being listened to and having their symptoms validated by an empathic, caring, compassionate provider, with improvement of patient satisfaction scores

Assessing and managing chronic pain in those with histories of interpersonal trauma, mood disorders and co-morbid addiction is complex (dual diagnosis)

- Chronic pain can have incapacitating effects on an individual especially if their pain is not well managed or treated holistically, including mind, body, spirit
- Poor management of a patient's pain is often related to clinicians' attitudes and knowledge about pain and addiction and the impact of stigma, gender, and how patients view their pain
- Clinician barriers to effective pain treatment include misinformation and fears of addiction
- Administering medication for pain becomes challenging when the clinician believes that the patient's request is purely a symptom of substance dependence
- In those with mental illness who also experiences physical pain, clinicians do not take their pain seriously; pain may not be fully investigated contributing to suboptimal care
- Providers need to listen to the patient's subjective experience and that their practice is evidence-informed, which includes an understanding of the complex nature between chronic pain, addiction, and mental illness
- DSM has reinforced a belief that there is a linear relationship between stress and pain perception
- Gender can impact whether or not a patient's disclosure of pain is believed by clinicians;
- Women are perceived as being more emotional, lazy, having a lower threshold for pain, or that their pain is psychological
- With mental illness, such as depression, patients may not understand where their pain is coming from. As a result, the patients may begin self-medicating with prescription opioids for pain and/or non-pain symptoms, such as unresolved emotional and social distress & chemical coping
- Interventions: (1) acknowledgement that pain is complex; (2) powerlessness, external locus of control, anger & belief system; (3) the therapeutic relationship by validating the patient's emotional and physical experience in a trusting milieu; and (4) pain coping through self-management & problem solving empowerment, adaptations, mindfulness, cognitive behavioral & acceptance therapies

6. Appropriate Trial of Opioid Therapy With or Without Adjunctive Medication.

- Pharmacologic regimens must be individualized on the basis of subjective as well as objective clinical findings.
- Need more thorough documentation if mainly subjective symptoms (i.e. headache, abdominal pain) including logs
- The appropriate combination of agents, including opioids and adjunctive medications, may be seen as "rational pharmacotherapy" and provide a stable therapeutic platform from which to base treatment changes.
- **7. Reassessment of Pain Score and Level of Function.** Regular reassessment of the patient combined with corroborative support from family or other knowledgeable third parties will help document the rationale to continue or modify the current therapeutic trial

8. Regularly Assess the "4 A's" of Pain Medicine - Routine assessment of:

- Analgesia: Effective pain control, with Appropriate dosing for the specific pain generator
  pain scale, ranges, fluctuations, comparison to prev. appt.
- Activity (ADLs): Physical functioning to justify the benefit of opioids, pain diaries
- Adverse effects: complaint of side effects which may limit dosing, patient's tolerance for continued use despite adverse events.
- Over time, SE's tend to diminish, but those with initial significant SE's were correlated with greater activity interference, negative affect, catastrophizing, with higher opioid misuse scores
  Proactively ask about GI SEs (i.e. constipation, nausea)
- Aberrant behaviors: Ambiguous drug-related or pain behaviors and adherence to opioid medication will help to direct therapy and support pharmacologic options taken; maladaptive behaviors

Passik

Patient Assessment and Documentation Tool (PADT) = 4 - A's (plus 2 A's) Passik

- Affect: Assess psychological status including family or social supports, Anxiety and mood.
- Adherence monitoring; Use opioid risk stratification scales (i.e. Opioid Risk Tool) in conjunction with drug toxicology testing of prescribed medications, prescription drug monitoring programs (PDMP), and pill counts.

- 3S's: monitor medication safety, including storage, security, and disposal

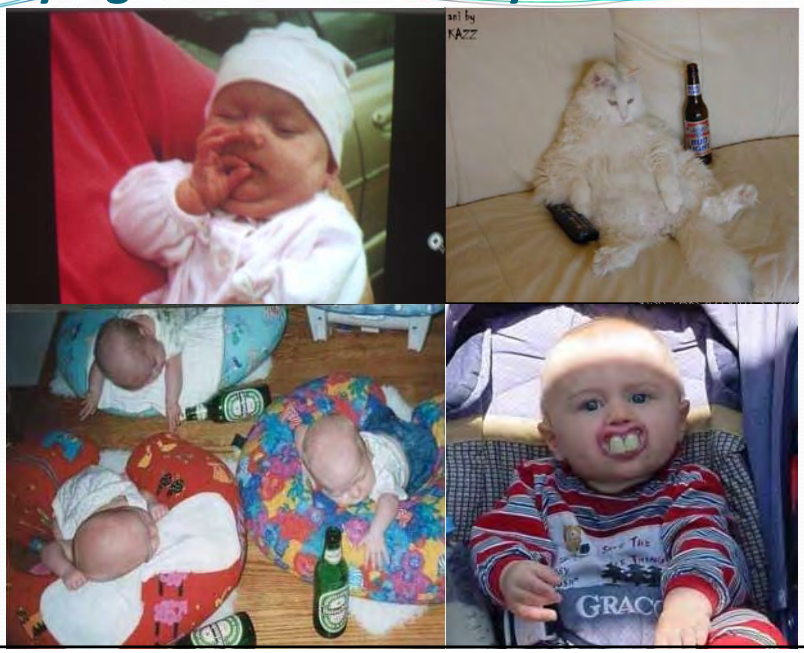
Positive Outcomes in Pain Management: Analgesia and Activities of Daily Living

- Document pain status:
  - Use 1 – 10 Numerical Pain Relief Scale (NPS)
  - Visual Analog Scale for Pain Intensity (VAS)
- Set goals related to ADLs:
  - Physical functioning
  - Mood
  - Family relationships
  - Social relationships
  - Sleep patterns
  - Overall functioning

- Document BOTH pain relief and progress toward ADL goals

(Passik, 1998)

Early signs of vulnerability to addiction



Assess the Risk of Iatrogenic Addiction or Aberrant Behavior in Each Patient

The potential for addiction is in the patient, not the opioid.

Substance addiction 6-10%, 15% Alcoholism, 9% cannabis
25% Nicotine dependency of US population

~ 45%
HIGH
Long-term exposure to opioids in addicts[2]

<1%
LOW
Short-term exposure to opioids in non-addict[1]

Opioid addiction through meta-analysis :
Incidence from 0 to 24% (median 0.5%)
Prevalence of up to 31% (median 3.7 - 4.5%)

Where is your patient?

“”Opioid misuse” averaged between 21% and 29%,
Rates of **“addiction” averaged between 8% and 12%**; iatrogenic 0.27- 2% (using strict def)
(1. Porter, 1980; 2. Dunbar,1996; 3. Adapted from Passik,1998)

Differential Diagnosis of Aberrant Drug-Taking Attitudes and Behavior

- Addiction (out of control, compulsive drug use)
- Pseudo-addiction (inadequate analgesia)
- Other psychiatric diagnosis
- Organic Mental Syndrome (confused, stereotyped drug-taking)
- Personality Disorder (impulsive, entitled, chemical-coping behavior)
- Chemical Coping (drug overly central)
- Depression/Anxiety/Situational stressors (self-medication)
- Criminal Intent (diversion)

(Passik & Portenoy 1996)

The Vast Middle Ground: The "Chemical Coper"

❖ Opioid use characterized by:
- –Being overly drug focused
- –Always on the fringes of appropriate drug taking
- –Not progressing towards goals

❖ Related characteristics:
- –Somatization
- –Alexithymia
- –"Accidental" overmedication

❖ Decentralize pain medication –focus on rehabilitation and psych interventions

Other traits:

- Kinesiophobia, PTSD, panic, anxiety related disorders
- Catastrophising

Pseudo-opioid resistance

- Some patients with adequate pain relief believe it is not in their best interest to report pain relief
  - Fear that care would be reduced
  - Fear that physician may decrease efforts to diagnose problem

Evers GC. Support Care Cancer. 1997

Red Flags

- Appears intoxicated at office visits or at pharmacy
- Repeated resistance to change in therapy despite evidence of adverse drug effects
- Repeated failure to keep appointments, or frequently stating they are “in a hurry” for their appointments
- Involvement with the law (MVCs, DWI, arrests, etc) including drug diversion, violence and illicit drug usage

"You're fired, Jack. The lab results just came back, and you tested positive for Coke."

Signs of Potential Abuse and Diversion (DEA)

- Request appointment toward end-of-office hours
- Arrive without appointment
- Telephone/arrive after office hours when staff are anxious to leave
- Reluctant to have thorough physical exam, diagnostic tests, or referrals
- Fail to keep appointments
- Unwilling to provide past medical records or names of HCPs
- Unusual stories
- However, emergencies happen: not every person in a hurry is an abuser/diverter

Drug Enforcement Administration. Don't be Scammed by a Drug Abuser. 1999. Cole BE. Fam Pract Manage. 2001;8:37-41.

Red Flags for pharmacists

Red Flags

- Males less than 30 years, single
- No health insurance, indigent, pays cash
- Limited educational background
- Travels greater than 30 miles for doctor or pharmacy, or pharmacy in same location as physician's office
- Doctor shopping using multiple providers and pharmacies (monitor by PDMP)
- Similar meds cocktail, esp benzos, carisoprodol ("Holy Trinity") or psycho-stimulants from same provider or prescribed to multiple patients/ family at same address
- Patient has a diagnosis of "nonspecific" back pain
- Requests branded short acting, or non ADF opioids
- Higher quantity pills dispensed

Exit Plan: Stopping Opioid Analgesics

- Consider tapering or weaning off opioids when patients engage in serious or repeated aberrant drug-related behaviors or diversion, experience intolerable adverse effects, or make no progress toward meeting therapeutic goals
- May consider conversion to buprenorphine, methadone for pain, or referral to a methadone maintenance program
- The provider usually sends the patient a registered letter informing him/her of discharge with 30 days notice, and lists at least three referrals for alternative care.
- The provider is under no obligation to actually prescribe 4 weeks for medication for the impending discharge, and may dispense limit quantities with more frequent office visits during this transitional period.
- Risks for difficulty weaning patients: higher & longer duration opioid dose, polypharmacy, including SSRIs or SNRIs, psychologic disorders, females, older, medical co-morbidities
- Consider transition to LAOs with ADF properties, without provisions for breakthrough SAOs in at risk patients

Not Enough Benefit?

- Reassess factors affecting pain
- Re-attempt to treat underlying disease and co-morbidities
- Consider escalating dose as a “test”
- No effect = no benefit, hence benefit cannot outweigh risks – so STOP opioids (Ok to taper and reassess)
- S Stop
- T Think
- A Act
- R Review

Source: Christina Nicolaidis, MD, MPH, Oregon Health & Science University. SGIM 2008 precourse

Too Much Risk?

- **Differential dx for aberrant medication – taking behavior, then match action to cause**:
  - Miscommunication of expectations – Patient education
  - Unrelieved pain – Change of dosage or medication
  - Addiction – Referral to addiction treatment
  - Diversion – STOP medication

    (caution with patient/ family reprisals)

Source: Christina Nicolaidis, MD, MPH, Oregon Health & Science University. SGIM 2008 precourse

Discussing Lack of Benefit

- Stress how much you believe/empathize with patient's pain severity and impact
- Express frustration re: lack of good pill to fix it
- Focus on patient's strengths
- Encourage therapies for "coping with" pain
- Show commitment to continue caring about patient and pain, even without opioid rx
- Schedule close follow-ups during and after taper
- Time commitment to address multimodal therapy
- Listening "lending an ear" improves patient satisfaction scores

Opioid tapering for detox

- Patient is not improving and may have opioid-resistant pain (i.e. central sensitization or hyperalgesia) (consider Lamotrigine for central pain)
- Patient may have a new problem – opioid chemical dependency (by DSM) = addiction by pain medicine specialists, and may need substance abuse treatment or chemical dependency program
- Providers continue to work on pain management using non-opioid therapy
- Taper patient slowly to prevent opioid withdrawal; Need 75-80% of the previous day's opioid dose to prevent withdrawal symptoms. Approaches to weaning range from a slow 10% dose reduction every 1-4 wks followed by 5% monthly thereafter after a total of 2/3 dosing achieved (for patients on chronic, high dose, resistant to tapering) to a more rapid 20% to 50% reduction (for lower dose patients) per wk. Decrease dose to lowest unit, then increase intervals. (Berna C et al Mayo Clin Proc 2015;90:828-842)
- May use clonidine, NSAIDs, muscle relaxants (tizanidine, methocarbamol), APAP, loperamide, anti-emetics, diphenydramine, hydroxyzine, anticonvulsants, tramadol, antidepressants (trazadone), topicals, dicyclomine, bismuth, buprenor ketamine, ibogaine, cannabis
- Improvements in psych well-being, quality of life, function & pain may occur with therapeutic detoxification when chronic opioids are stopped, especially with psych co-morbidity using intensive (inpatient or day) interdisciplinary care programs

Periodically Review Pain Diagnosis and Comorbid Conditions, Including Addictive Disorders

- Underlying illnesses evolve. Diagnostic tests change with time. As a result, treatment focus may need to change over the course of time. If an addictive disorder predominates, aggressive treatment of an underlying pain problem will likely fail if not coordinated with treatment for the concurrent addictive disorder in conjunction with mental health counselor/ psychologist/ psychiatrist/ addictionologist. The input of specialty consultative care (specific for the painful generator or the diagnoses treated) on an annual basis may be helpful.
- Consider pain management second opinion regarding opioid therapy, especially with higher dosing, psych problems, aberrancy or mainly subjective complaints

Documentation

- Careful and complete recording of the initial evaluation and each follow-up is both medicolegally indicated and in the best interest of all parties. Thorough documentation combined with an appropriate doctor (provider)-patient relationship will reduce medicolegal exposure and risk of regulatory sanction
- Documentation of the above, rationale for care, decision making and consequences of behaviors is paramount to pain management therapies especially with higher opioid doses, subjective symptoms or frequent aberrant behaviors.
- 5 Ds of physician Downfalls: Dated, Disabled, Defiant, Dishonest, Duped, Medication mania, Hypertrophied enabling, Confrontation phobia
- 7 Ds of Defensive medicine: Diagnoses, Documentation, Death, Discrimination (risk stratification), Disability Related to Medication Use, Diversion, Recreational Use, Unauthorized Medication Use, DEA and State Regulations

Health Insurance Opioid Policies are quickly changing

Proposals by many programs, including Medicare Part D (pharmacy plans) to have a **"ceiling" dose of opioids** and **limited duration of prescribed amounts**, based on CDC pain management guidelines.

- National Medicare proposal to penalize providers for the number of patients that require $\geq$ 120 mg/day MME (MACRA). This includes mandatory pre-authorizations, and other time consuming documentation for total daily doses MME $\geq$ 90mg/d, including **formulations with abuse deterrent properties (which can reduce the risk of misuse, and deter diversion for both the patient and others living in the household**).
- For improved access, Maryland law (SB 606) now allows for the option of two abuse deterrent opioids, specified by the insurance carrier, to be approved at parity cost (compared to generic alternatives) to the patient based on the provider's determination of risk.
- limited formulary coverage for specific drug options, quantity limits per month, or limits on the number of prescriptions written per month of any controlled substance (which is a disincentive to allow a patient to pace him/her self).
- Mandatory CME for providers (MD state 1 hr per renewal) FDA REMS for LAOs/ SAOs & pain management, considering mandatory CMEs of 3-6 hrs)
- Settlements & pending litigation for opioid distributors and pharm companies
- Pharmacy quotas, limited availability of opioids, pharmacist education/ liability

Barriers to opioid sparing care

- Providers who recommend opioid sparing treatments are limited in implementing them, as long as copays for generic medications (even opioids) are inexpensive, and their proposed alternatives will be met with resistance by the patient due to our societal bias for drugs with immediate gratification.
- Adverse effects of opioid sparing medications (i.e. NSAIDs, anticonvulsants, antidepressants, muscle relaxants). Warning letters from pharmacy benefit plans on the risks of combining these medications, even if the patient has tolerated this combination for years.
- No specific pain interventions available that has demonstrated or proven continued or improved outcome efficacy sustained over time (i.e. greater than one year).
- Insurance disincentives: preauthorizations for dose reductions, quantity limits for small increments of reduction, # scripts/ mo copays. More quantity limits on opioid sparing meds than opioids, "step therapy" requiring Sch II opioids before Sch III or IV

Advice to avoid physician discipline of opioid therapy

- Legitimate purpose with usual course of medical practice: no diversion or unapproved use of opioids including misuse, avoid "over-prescribing" (exact quantities, close monitoring)
- Providers whose prosperity/ rankings make them an "outlier"
- The more procedures/ tests performed, the less likely any one procedure will be "medically reasonable & necessary"
- Draw boundaries: Do not give prescription drugs for favors or Prescribing outside of office setting (i.e. friends or relatives)
- Avoid dispensing controlled substances from your office
- Consultative / consensus care with other peers
- Remain professionally objective, incorporate staff loyalty
- No conflict of interest or self-referral/ patient steering
- Informed consent / treatment agreements
- Stratify Risks: UDT, pill count, PDMP, patient profiles
- Meticulous documentation with proper ICD-10 & E/ M coding
- Prompt response to inquiries from Boards, insurance requests
- Remain cooperative with investigations
- Do not voluntarily relinquish DEA license by coercion during investigation phase (wait for hearing)
- Legal representation ("med –guard" insurance policies)

What is the Physician's Role?

VS.

Summary of opioid therapies

- Opioids for pain continues to require a careful balance of efficacy, including assessment of benefit/ risk, and safety concerns for the patient and society.
- Analgesics for pain management can be utilized effectively in a patient centered way, if the provider allows adequate time, thorough monitoring, and strict precautions, with appropriate documentation, which optimizes outcomes and manages risks.
- Opioid therapy should be prescribed in the context of "art" of multidisciplinary pain management including rational polypharmacy, with inclusion of nonopioid analgesics and adjuvants as well as nonpharmacologic options
- The treatment must be dynamic, defensible, rational and compassionate
- Advocacy for balanced pain management approaches

Art of medicine and/ or evidence based approach

Creativity is allowing oneself to make mistakes

Art is knowing which ones to keep

"Practicing" Pain Medicine

Experience is a wonderful thing. It enables you to recognize a mistake when you make it again.

"Isn't it a bit unnerving that doctors call what they do "practice"?"

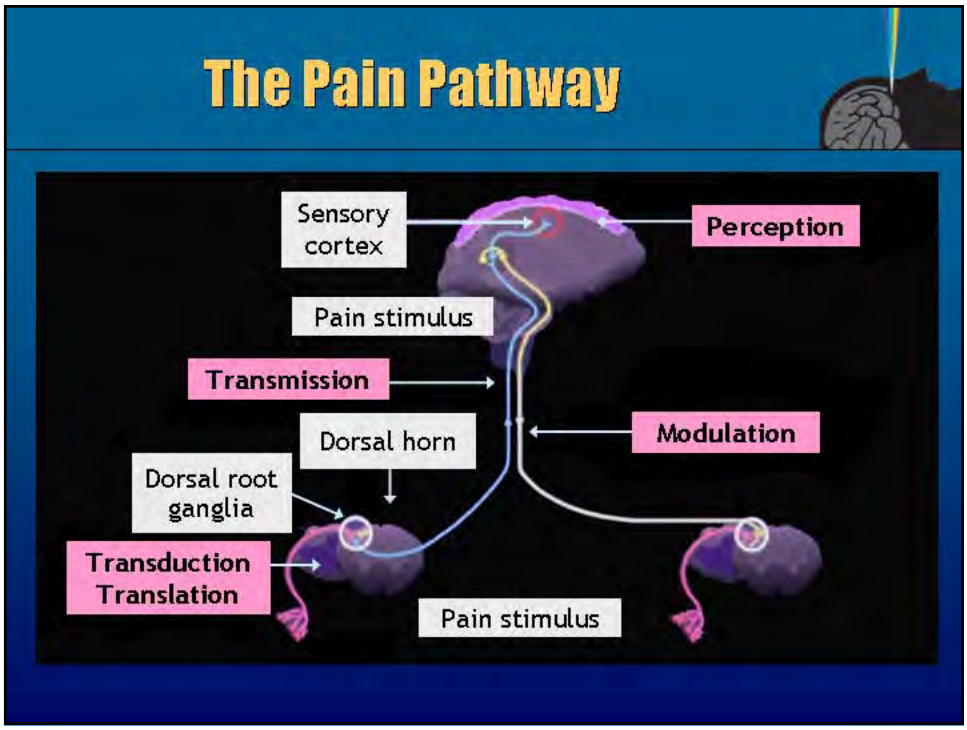
- George Carlin

Thanks to Rachel Boyer for coordinating this conference

.....and it does take practice!!!!!

Addendum Slide supplements – Extra info

- Pain pathophysiology
- Acute pain pre-emptive analgesia
- Objective pain measures
- Pain assessment/ temporal characteristics
- Opioid receptor type and locations
- Opioid Use disorder def/ statistics
- Withdrawal syndrome definition
- Levels of Scientific Evidence
- Respiratory depression risk scale
- Opiophobia
- Chemical coping
- PROP(physicians for responsible opioid prescribing)
- Burden by providers
- CDC critique
- Pain and addiction
- Current MD MMA opioid coverage
- High risk programs
- Risk screening tools
- Urine toxicology
- Treatment agreement
- Informed consent
- Office policies
- Short and long acting opioids
- Methadone consideration
- Breakthrough pain TIRF fentanyl (cancer related or "off label")
- Illicit drug taking activities
- Aberrant behaviors red/ yellow flags
- Governmental policies
- Insurance disincentives
- Prescription safety recommendations
- Provider conduct
- ABCDE/ COMPLIANCE / ABCDQRST



Classification by Pathophysiology

Nociceptive pain - may be somatic or visceral

Commensurate with identifiable tissue damage with inflammatory transmitters causing primary hyperalgesia (reduced pain threshold) and activation of "silent" nociceptors

Neuropathic pain - caused by dysfunction in peripheral or central nervous system (ectopic firing by both the injured and intact sensory axons)

Allodynia - sensitization of the A - beta fibers

Secondary Hyperalgesia - increased NMDA activation through peripheral and spinal cord transmitters

Preemptive analgesia may inhibit the development of neuropathic pain

- Idiopathic pain
- Psychogenic pain
- Combinations of above

Stress Response to acute or postop pain

Increased Cortisol, ACTH, GH, NE, EPI, Interleukins, Glucagon, with decreased Insulin resulting in:

- Increase Catabolism, reduced Anabolism, Hypercoagulability
- Immunosuppression
- Sympathomimetic tachyarrhythmia, hypertension, tachypnea, ischemia, vasoconstriction, piloerection
- May be suppressed by pre - emptive analgesia including peripheral and spinal anesthetic blockade, opioids, and COX -2 selective agents (to minimize bleeding)
- Acute pain is a stimulus for respiration, and once pain is abolished, the opioid induced respiratory narcosis contributes to apnea (slippery slope) & is less responsive to pCO_2
- But the patient can develop a tolerance to this effect
- Perioperative pain paradox: opioids cause impaired function, ADLs with sedation & GI SEs, but severe uncontrolled pain affects healing, sleep, & behavior – use multimodal pain mgmt

Objective Pain Assessment for Chronic Pain

Mainly a subjective experience

Static and dynamic quantitative sensory testing (QST) has the potential to be useful in the prediction of the response to opioid treatment

Thermal and mechanical pressure threshold testing

Functional MRI or PET scans can show increased metabolism of the brain with perceived pain

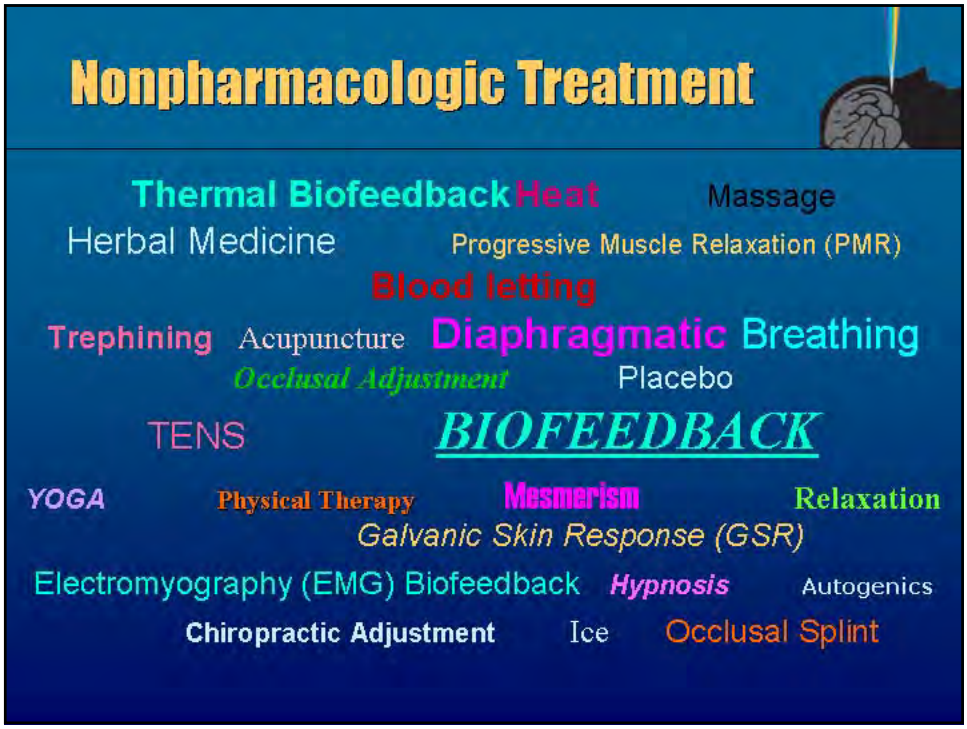
Autonomic (Adrenergic) responses including labile hypertension

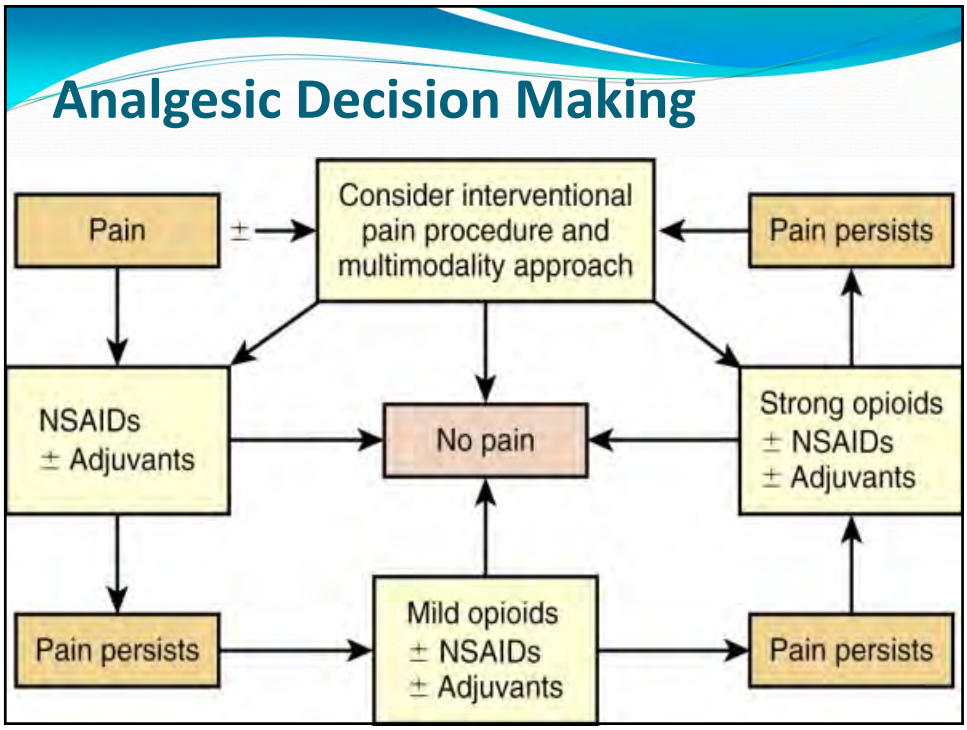
Positional relief, sensory avoidance, and pain distraction that modulate pain complaints

Replicatable physical exam findings including spasm, neurologic, restrictions of motion, postural changes

Pain Assessment Tools: Temporal Nature of Pain

- Intensity of persistent and breakthrough pain
- Number of episodes of breakthrough pain
- Timing of breakthrough pain relative to Around The Clock (ATC) dosing interval
- Location of breakthrough pain relative to persistent pain
- Efficacy of analgesia for persistent pain
- Efficacy of analgesia for breakthrough pain
- Acute: 0-6 wks, subacute: 6-12 wks, chronic: >3 mos


Nonpharmacologic Treatment
Thermal Biofeedback
Heat
Massage
Herbal Medicine
Progressive Muscle Relaxation (PMR)
Blood letting
Trephining
Acupuncture
Diaphragmatic Breathing
Occlusal Adjustment
Placebo
TENS
BIOFEEDBACK
YOGA
Physical Therapy
Mesmerism
Relaxation
Galvanic Skin Response (GSR)
Electromyography (EMG) Biofeedback
Hypnosis
Autogenics
Chiropractic Adjustment
Ice
Occlusal Splint


Analgesic Decision Making
Pain
±
Consider interventional pain procedure and multimodality approach
Pain persists
NSAIDs ± Adjuvants
No pain
Strong opioids ± NSAIDs ± Adjuvants
Pain persists
Mild opioids ± NSAIDs ± Adjuvants
Pain persists

Opioid receptor locations

MOR-2 receptor: Inhibits Smooth muscle contraction of the Intestinal tract, especially the small intestine (constipation), CNS

MOR-1 receptor: Granulocytes, macrophages/ monocytes, lymphocytes and plasma cells which are up-regulated in patients with inflammatory conditions

PNS: nociceptive sensory dendrites (A delta and c fibers), DRG

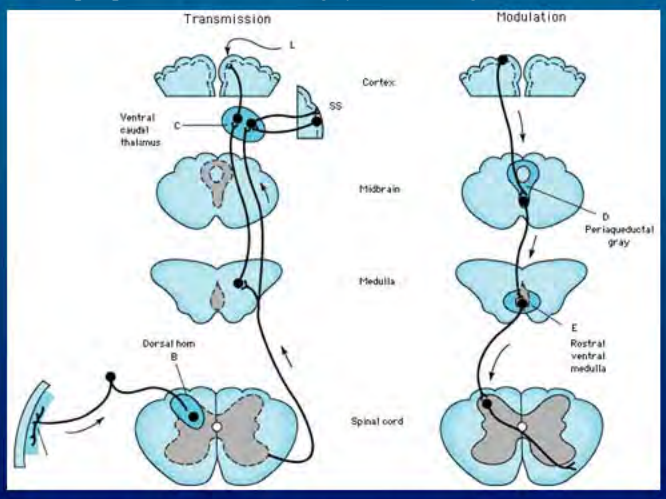
CNS: Dorsal horn cells, spinal sensory neurons (especially lamina I and II), Brainstem (peri-aqueductal grey, reticular formation, locus ceruleus, and the rostral ventromedial medulla), Hypothalamus, olfactory bulb, Medial thalamic, amygdala , striatum, nucleus accumbens, solitary tract, Cerebral cortex.

DOR receptors: Dilation: Vascular, Cardiac (negative inotropic), GI, Respiratory (inhibits bronchoconstriction via vagal sensory nerve endings, Vas deferens, Skeletal muscle metabolism and vasodilation (animals)

Peripheral binding of opioids do not result in a tolerance effect

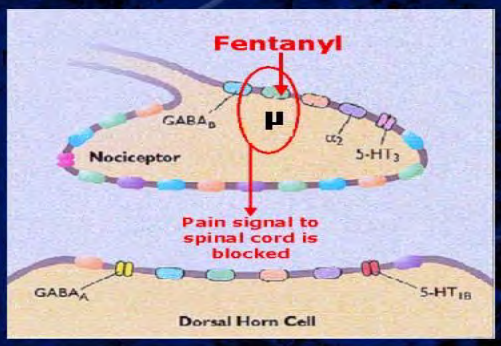
Opioid Analgesics: Sites of Action

Opioid receptors found in GI, CNS (brain and spinal cord) and peripheral tissue including synovial lining



Katzung BG, ed. *Basic and Clinical Pharmacology*. 8th ed. Lange Publishers, 2001.

Duragesic®: Pain Relief and Opioid Receptors



- Fentanyl from the Duragesic patch binds to mu opioid receptors on pain-sensing nerve cells
- Transmission of pain signals to the dorsal horn of the spinal cord is blocked

(Brookoff, 2000, Illustration by Seward Hung)

- **u (23 subtypes) & d receptors binding: increases adenylyl cyclase which increases K+ conductance and opens K+ channels with hyperpolarization, resulting in direct analgesia**
- **u receptors have different affinities based on the drug and individual variation resulting in variable analgesic properties (supraspinal analgesia) and side effects (respiratory depression, euphoria, physical dependence)**
- **K+ receptors inhibit Ca+2 entry closing Ca+2 channels, diminishing ascending transmission of impulses resulting in reduced pain perception and modulates visceral pain, spinal analgesia, miosis and sedation (oxycodone has a greater affinity).**

Breakthrough pain

- Transient and sudden increase in pain (67% prevalence in outpatients with Cancer)
- Rapid onset, short duration (<3min in 43%)
- Rises to moderate to severe intensity

Incident or respondent (i.e. wt bearing, sneeze)
Spont onset (ie neuropathic shocklike, colic)
End of dose failure (med interval assessment)
20-90% prevalence, esp with long acting meds

- Try to limit "rescue" medications to ≤4 episodes/ day
- Caution in using short acting opioids in those pain patients with suspected drug aberrancy behavior
- May result in a relative physical withdrawal state due to trough levels, perpetuating opioid usage to minimize symptoms with an anxiety reaction vs. euphoric state of fast onset, higher peak short acting opioids, perpetuating usage for recreational use

OUD comorbidities

- Genetic factors play a particularly important role (60%) both directly (OPM(K,D)R1, PENK, COMT, FKBP5, MC2R genes) and indirectly, greater risk with lower socioeconomic status, but over time, OUD is seen more often among white middle-class individuals, especially females
- Often associated with other SUD, especially those involving tobacco, alcohol, cannabis, stimulants, and benzodiazepines, which are often taken to reduce symptoms of opioid withdrawal or craving for opioids, or to enhance the effects of administered opioids
- High risk of medical comorbidities from SUD including infections esp from injections, physical trauma including nasal or from intoxication, or adverse effects from opioids (dry mouth, GI, pupillary, sexual dysfunction, i.e. ED or infertility)
- Psychiatric disorders: Depressive disorders, Posttraumatic stress disorder, Antisocial personality disorder, Conduct disorder in childhood
- Heightened risk for self-harms including suicides or attempts

Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression (RIOSORD)

More accurate predictability than other available scales **Score**

In the past 6 months, has the patient had a **health care visit** (outpatient, inpatient, or ED) involving:

Opioid dependence?	15
Chronic **hepatitis** or cirrhosis?	9
Bipolar disorder or schizophrenia?	7
Chronic **pulmonary** disease? (e.g., emphysema, chronic bronchitis, asthma, pneumoconiosis, asbestosis)	5
Chronic **kidney** disease with renal impairment?	5
Active traumatic **injury**, excluding burns? (e.g., fracture, dislocation, contusion, laceration, wound)	4
Sleep apnea?	3

Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression (RIOSORD)

Description	Y/N	Score
Does the patient consume:		
• An **extended-release or long-acting (ER/LA) formulation** of any prescription opioid or opioid with long and/or variable half-life? (e.g., OxyContin, Oramorph-SR, methadone, fentanyl patch, levorphanol)		9
EXTRA RISK IF PRESCRIBED:		
• **Methadone**? (Methadone is a long-acting opioid, so also write Y for "ER/LA formulation")		9
• **Oxycodone**? (If it has an ER/LA formulation [e.g., OxyContin], also write Y for "ER/LA formulation") (but not fentanyl)		3
• A prescription **antidepressant**? (e.g., fluoxetine, citalopram, venlafaxine, amitriptyline) related to altered effect on CNS pCO2 drive		7
• A prescription **benzodiazepine**? (e.g., diazepam, alprazolam)		4
Is the patient's current maximum prescribed opioid dose (MME):		
• **>100 mg morphine** equivalents per day?		16
• **50-100 mg morphine** equivalents per day?		9
• **20-50 mg morphine** equivalents per day?		5
In the past 6 months, has the patient:		
• Had 1 or more **ED** visits?		11
• Been **hospitalized** for 1 or more days?		8
Total MAXIMUM Score		**115**

Opioid Use disorder DSM-5 (2013) within past 12 mos

- 1. Opioids are often taken in larger amounts or over a longer period than was intended.
- 2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
- 3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
- 4. Craving, or a strong desire or urge to use opioids.
- 5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
- 6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
- 7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
- 8. Recurrent opioid use in situations in which it is physically hazardous.
- 9. Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.

OUD (2) FOR Tolerance and withdrawal: This criterion is not considered to be met for those taking opioids solely under appropriate medical supervision.
Specify if: In early, sustained remission, maintenance therapy, or in a controlled environment

- 10.Tolerance, as defined by either of the following:
- a. A need for markedly increased amounts of opioids to achieve intoxication or desired effect.
- b. A markedly diminished effect with continued use of the same amount of an opioid.
- 11.Withdrawal, as manifested by either of the following:
- a. The characteristic opioid withdrawal syndrome (refer to Criteria A and B of the criteria set for opioid withdrawal).
- b. Opioids (or a closely related substance) are taken to relieve or avoid withdrawal symptoms.
- Severity of OUD and coding:
- 305.50 (F11.10) Mild: Presence of 2–3 symptoms
- 304.00 (F11.20) Moderate: Presence of 4–5 symptoms
- 304.00 (F11.20) Severe: Presence of 6 or more symptoms
- Differential Dx: Opioid induced mental disorders (i.e. depression, F11.24), other intoxication or withdrawal substance (opioid) use (changes the 4th integer of the ICD-10 codes)

DSM 5 Criteria for Opioid Withdrawal

- A. **Either** of the following: cessation of (or reduction in) opioid use that has been heavy and prolonged (several weeks or longer) or administration of an opioid antagonist after a period of opioid use
- B. **Three (or more)** of the following, developing within minutes to several days after Criterion A: dysphoric mood, nausea or vomiting, muscle aches, lacrimation or rhinorrhea, pupillary dilation, piloerection, or sweating, diarrhea yawning, fever, insomnia
- C. The signs or symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- D. The signs or symptoms are not due to another medical condition and are not better accounted for by another mental disorder, including intoxication or withdrawal from another substance.
- ICD-10-CM code with moderate of severe opioid use disorder is F11.23.
- (Do not use withdrawal code with mild opioid use disorder.)
- Clinical Opioid Withdrawal Syndrome (COWS)
- Grade 1: lacrimation, rhinorrhea, diaphoresis, yawning, restless, insomnia within 8-24 hrs
- Grade 2: mydriasis, piloerection, muscle twitch, myo/arthralgia, abd pain
- Grade 3: tachycardia/pnea, hypertension, fever, anorexia, nausea, restlessness after 1-3 days
- Grade 4: diarrhea, vomiting, dehydration, hyperglycemia, hypotension, curled up
- Safety concerns: unstable cardiac ischemia or arrhythmia, labile hypertension (esp with pain), DM, anxiety, PTSD, panic, Depression with suicidal/ harmful thoughts

Physicians for Responsible Opioid Prescribing (PROP)

With addiction medicine backgrounds, opine that safe opioid prescribing requires a drastic reduction in opioid dosing and duration of treatment for all **adult patients with non-cancer chronic pain**, or those with cancer, in remission, statistics that indicate there has been a dramatic increase in prescribed opioid utilization for pain control (with commercialization from the pharmaceutical industry), combined with an epidemic of opioid overdose deaths from all causes. The harms are generally dose dependent.

- Safety trumps efficacy
- Based on **limited medical evidence** that over the **long term, there are greater harms (particularly with higher dosing), than benefits for opioid** therapy, in which efficacy is determined by functional outcomes, and not based on any reduction in pain intensity. Recommending safety over efficacy.
- Paradoxical effect over time, in some patients on chronic opioids, in which there is a diminished effectiveness of the pain relieving effect, sometimes with the "spread" of pain complaints (possibly due to "opioid induced hyperalgesia", "central sensitization" or dynamic changes in the brain's neurotransmitters, pain pathways and hormones from pain itself), along with reduced function
- Particularly in those with **headaches, non-specific low back pain, fibromyalgia, visceral (internal or abdominal organ) & polyneuropathy pain** syndromes.

Levels of scientific evidence (SE)

- 18% of all clinical decisions are based on patient oriented high level evidence
- Level IA SE obtained from meta-analyses of randomized clinical trials.
- Ib SE obtained from at least one randomized clinical trial
- IIa SE obtained from at least one well-designed, non-randomized controlled prospective study
- IIb SE obtained from at least one well-designed, quasi-experimental study
- III SE obtained from well-designed observational studies, such as comparative studies, correlation study or case-control studies.
- IV SE obtained from documents or opinions of experts committees and/or clinical experiences of renowned opinion leaders

Grades of recommendation from SE

- A (Levels of SE Ia, Ib) It requires at least one randomized clinical trial as part of the scientific evidence with overall good quality and consistency in terms of the specific recommendation
- B (Levels of SE IIa, IIb, III) It requires methodologically correct clinical trials that are not randomized clinical trials on the topic of recommendation. It includes studies that do not meet A or C criteria.
- C (Level of SE IV) It requires documents or opinions of experts committees and/or clinical experiences of renowned opinion leaders. It indicates the absence of high quality, directly applicable clinical studies

Burden by providers

- Clinical burnout – high demands, low support, fear of scrutiny, reimbursements, time commitments, 30-40% lifetime risk due to emotional exhaustion and depersonalization
- Many provider recommendations require approvals for preauthorization, often performed without reimbursement, for other non-opioid adjunctive medications, even for generic products (ironically, the actual cost of generic opioids is low), counseling, injections, adaptive equipment and physical medicine therapies that could potentially decrease pain.
- Limited benefits for opioid sparing proposed treatments are "investigational or experimental", including acupuncture, biofeedback, massage, some chiropractic and physical therapy modalities, electrical stimulation devices (i.e. transcutaneous electrical stimulation for low back pain, peripheral nerve stimulators, and limitations on spinal or brain stimulators), certain injections (including limited approval for trigger point injections, interventional blocks and IV ketamine) and regenerative medicine (i.e. stem cells, prolotherapy, and viscosupplementation, except for knees).
- Plans do not cover certain durable medical / adaptive equipment including heating pads or cold packs, seating for rollators, shower chairs, nutritional supplements, and other alternative/ complementary medical approaches.
- Barriers to care may actually may cost our society more in the long run (including cost shifting), resulting in complications, including increased risk of falls, prolonged impairments with reduced outcomes and disability, additional suffering, or "forcing" patients to consider riskier procedures or surgery.

Argoff - CDC critique (cont)

At least 40% take opioid without incident

Primary care providers are fearful to continue prescribing opioids even if the patients have benefited without adverse effects (opioidphobia)

Pain management needs to be provided by providers that have appropriate training and educational backgrounds

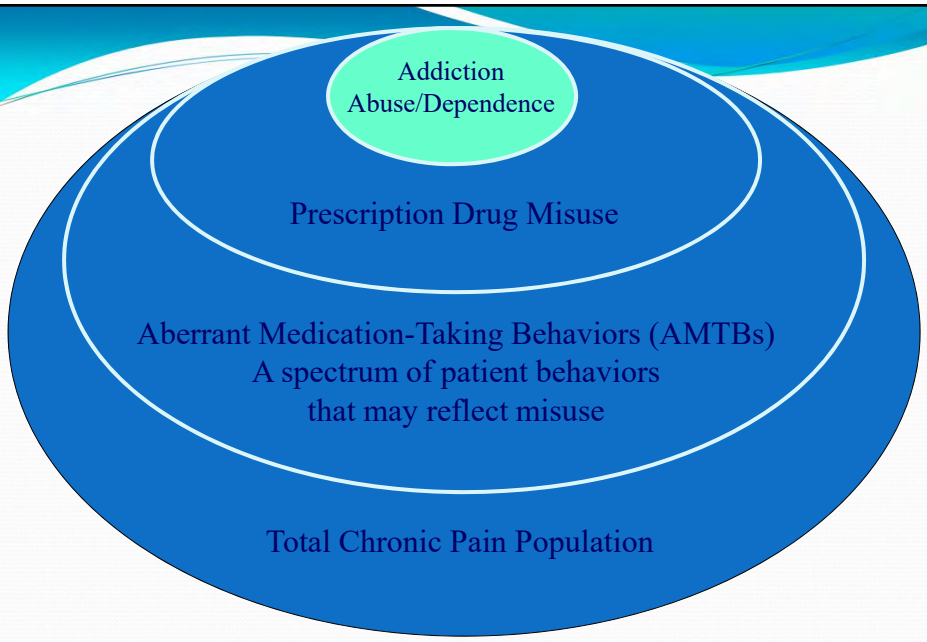
Not enough pain trained providers, too few training programs with multidisciplinary care

Economic incentives encourage unimodal interventional, procedures, and not spent doing cognitive care

Hopefully, the pendulum will swing back to allow primary providers to have the proper resources to competently manage pain

Chronic pain and addiction

- is a bio-psychosocial illness, involving biological, genetic, psychological, and environmental factors.
- When pain is accompanied by comorbidities, impaired function, or psychological disturbances, chronic opioid therapy should be utilized in conjunction with comprehensive multidisciplinary pain management
- including non-pharmacologic approaches, patient education for responsible and proper use of all medications
- Adaptive (coping) vs maladaptive pain (catastrophising)
- Chronic pain classified as a separate “disease”



Adapted from Steve Passik. APS Resident Course, 2007

50% of patients are undertreated

Why do some physicians under-prescribe? "Opiophobia"

- Overestimate potency and duration of action
- Fear of being scammed
- Often prescribed with too small a dose and too long a dosing interval
- Exaggerated fear of addiction potential

Morgan, J. Adv Alcohol Subst Abuse, 1985

Application: Stratification Tool for Opioid Risk Mitigation (STORM) for vets

- Developed by VA that reflects a holistic approach and facilitates patient identification for proactive monitoring and application of risk mitigation interventions (i.e. opioid dose, substance use disorders) and risk mitigation interventions (e.g., urine drug screening, psychosocial treatment). STORM prioritizes patients for review and intervention according to their modeled risk for overdose/suicide-related events (80% variance accounted for) and displays risk factors and risk mitigation interventions obtained from VA electronic medical record (EMR)-data extracts. The risk for an overdose/suicide-related death event for Vets in 2011 was 2.1%

Pain Assessment

History of Present Illness

Medical history—may be affected by pain therapies

A. Coexisting diseases

B. Medications and allergies

C. Substance abuse history and habits (tobacco)

D. Other constitutional symptoms (i.e., anorexia, fatigue, sedation and other changes in mental status, nausea, vomiting, dysphagia, dyspnea, constipation, urinary and sexual function, depression, dry mouth, ability to take medications by mouth, presence of a central venous catheter) Psychiatric symptoms may be similar to pain symptoms

- Patient expectations and goals

Pain Assessment

Personal and social history

A. Background: age, educational, employment, marital, residential, religious, cultural, ethnic

B. Current status: functional status, caregivers and their health and availability, support system

Physical examination detailed M-S exam including posture, gait, ROM, inspection, palpation, mentation

Review of additional information

A. Medical records, radiologic/laboratory studies

Degree of Pathology/ diagnostic or objective findings do not always correlate with pain generator intensity

B. Family members and physicians and/or nurses who know the patient and his or her illness

Differential diagnosis including pain generator(s)

Recommendations regarding workup and therapy

Reassessment

Basics of Pain Management - ABCDE

ASK about pain regularly.

ASSESS pain systematically.

BELIEVE the patient and family in their reports of pain and what relieves it.

CHOOSE pain control options appropriate for the patient, family and setting.

DELIVER interventions in a timely, logical, and coordinated fashion.

EMPOWER patients and their families.

ENABLE them to control their course to the greatest extent possible.

Current Opioid Misuse Measure (COMM™)

- 17 item self-report for **ongoing** risk assessment
- Questions based on 6 primary concepts underlying medication misuse
- Helps to identify patients at high risk for **current** aberrant medication-taking behavior
- A high score raises concern for Prescription Drug Abuse, but is NOT diagnostic

Butler et al. Pain. 2007

Urine drug testing (UDT)

- "Opiate" immunoassays detect morphine and codeine – Do not detect synthetic opioids such as Methadone or Fentanyl – Do not reliably detect semisynthetic opioids such as Oxycodone, Hydrocodone, Hydromorphone, buprenorphine, levorphanol, tramadol or tapentadol
- GC/MS will identify these medications (may limited with levorphanol, which cross-reacts with dextromethorphan)
- Cross reaction of oxycodone (by IA) with oxymorphone
- Codeine metabolizes into morphine, which in turn can metabolize into hydromorphone
- Hydrocodone can metabolize into hydromorphone
- FDA purity of pharmaceuticals +/- 1%; may have hydrocodone in oxycodone, codeine or even 6MAM in morphine, codeine in hydrocodone detected by G/LC-MS (usually at higher doses)

Patient / Provider *Medications* & Treatment Adherence Agreement, with INFORMED CONSENT, Education, Office Policies & Code of Conduct

- ***Education:*** Based on FDA, all opioids (some with abuse deterrent properties) prescribed for a legitimate medical purpose "should be reserved in patients with pain severe enough (**intractable** or of at least **moderate intensity)** to require opioid treatment & for which *alternative treatment options* are inadequate or not tolerated". Opioids may be continued, in good faith, on a trial basis, based on a beneficial & meaningful therapeutic responses with specific goals (**not** for total relief or cure), using clinical judgment, "to prescribe the lowest effective dose of an opioid that is no greater than the quantity needed for the expected duration of pain (if acute) based on evidence-based clinical guidelines that is appropriate for a patient's health care status", increased **function,** maintenance or palliation in refractory conditions & with tolerable side effects.

Types of opioids

- *Short acting opioids (**SAO**)* are used for acute or episodic pain, & selectively, for chronic pain, as pre-meds prior to activities &/or following functional tasks, & are generally limited to several times per day.
- *Long acting opioids (**LAO**)* are prescribed to improve around the clock control of baseline pain & possibly compliance, to reduce pill taking behaviors, better sleep (but may worsen sleep apnea) in chronic pain. LAO are usually taken on a scheduled basis, one pill at a time, cannot be altered in any way & are taken without alcohol. LAO must be taken on a scheduled basis, cannot be altered in any way & are taken without alcohol. (For LAO patches: avoid taking hot baths, do not cut or apply a heating pad nearby; metallic patches must be removed prior to MRI scan).
- SAO combined with LAO, are often used in those with persisting pain that have daily episodic fluctuations.

Close Opioid Dosing Monitoring

- Overall function & compliance with strict accountability, are closely monitored for the pain management response, overall function & compliance with strict accountability, including freq office visits (**OV**), pain logs & questionnaires (PEG = Pain intensity, Enjoyment & General activity), exams & screening for substance use disorders. If any CS/ meds have intolerable side effects, ineffective, or result in a substance use disorder, prescribed CS /meds be reduced or discontinued, utilize alternative treatments, or be referred for consultative care.
- Combine drug therapy with comprehensive multidisciplinary pain management *with non-pharmacologic approaches (i.e. injections, acupuncture, psychological counseling, adaptive equipment, mobilization/chiropractic/physical therapy exercises & home modalities)* & pharmacologic (which may include non-habituating alternative "opioid sparing" adjunctive meds)

Office Policies and Code of Conduct

- Forthcoming & honest to communicate all my medical diagnoses including my pain complaints & how it affects my function including activities, sleep & mood to my providers.

Clinical vignette: A provider cannot treat appropriately if there is dishonesty

- Complete medical & psychiatry records available at the first appt
- Full disclosure of all meds must be given to all providers (including MD, DO, RN, NP, PA, optometrist, dentist & podiatrist prescribers), hospitals or emergency situations.
- Completion of paperwork & pain logs with accurate demographics & contact info with Photo identification & verify employment
- Appropriate hygiene & attire for a physical exam; NO disruptive behavior, or intoxication or impaired by drugs. Arrive on time
- Financial responsibility for all office charges including drug *toxicology (**tox**)* tests & verify coverage
- All patient care including prescribing my CS (opioids) will occur during a scheduled OV unless otherwise specified
- Primary care providers & dentists are highly recommended. Specialty consultative care may also be required.
- Covering providers may change meds &/or quantities prescribed at their discretion.

Medical Care Milieu – Treatment Agreement

- Medical care is based on accurate information with disclosure of current & previous med/ drugs (including intrathecal pumps, OTC, supplements) usage
- Work history (including governmental)
- Any legal or disciplinary issues that pertain to opioid treatment may obtain judicial searches
- Previous medical history
- Prior difficulties with substance use disorders, abuse, alcohol, smoking, withdrawal symptoms, & family history of such
- Impaired driving, work activities & relevant thinking/ judgment
- Psychiatric problems (including disturbing or suicidal thoughts).
- CS will be limited or denied if there is suspicion of drug diversion, substance misuse, Driving While Intoxicated, incarcerated for violent crimes, or active use of alcohol/ illicit drugs.
- If there are any concerns for a high risk of non-adherence, then a chemical dependency, addictionologist, &/ or psychological evaluation may be required while using CS.

Mnemonic: ABCDPQRS provides a way to remember precautions with opioid therapy

- Alcohol affects judgment and memory, and impairs respiration.
- Benzodiazepines and Other Drug Use concurrently with opioids increases the risk of oversedation, overdose and trauma. Habitual Marijuana consumption warrant more careful monitoring when prescribing opioids.
- Cocaine use has been associated with increased risk of diversion of opioids, and any patient with a substance use disorder should be educated carefully about the risks of combining drugs and overusing opioids. Clinicians may choose to prescribe fewer pills, use smaller doses and follow up within three to five days. Clearance and Metabolism of the Drug; Many opioids require renal clearance of active metabolites. Morphine and meperidine are toxic in renal insufficiency (GFR < 60). Hepatic impairment, if severe, can affect the metabolism of many opioids. A dosage adjustment or change of dosing interval may be necessary for morphine, hydrocodone and oxycodone. For patients with impaired liver function, consider lowering the dose of acetaminophen or, preferably, avoiding the use of acetaminophen/opioid combination medication altogether.

Mnemonic: ABCDPQRS provides a way to remember precautions with opioid therapy

- Delirium, Dementia and Falls Risk Patients on acute dosing of opioids or geriatric are at an increased risk from falls and other accidental trauma. Other CNS depressants such as anticholinergic medications, alpha adrenergic blockers and benzodiazepines will compound the risk of falls and fractures in patients on opioids. Opioids can precipitate delirium in some patients particularly in those with cognitive impairments, polypharmacy, advanced liver or kidney disease;
- Psychiatric Comorbidities: comorbid anxiety or depressive disorder Opioids should be regarded as having powerful anxiolytic properties as well as analgesic properties. Psychic distress may exacerbate nociceptive (physical) pain or be confused for physical pain. Post-traumatic stress disorder and childhood sexual trauma increase the risk of opioid-related adverse events tenfold. Depression and anxiety disorders (including generalized anxiety disorder, social anxiety disorder and obsessive compulsive disorder) are known to increase the risk of opioid misuse and harm, as well. Childhood attention deficit hyperactivity disorder is a risk for later pharmaceutical misuse. Opioid withdrawal can exacerbate psychotic symptoms an assessment of suicide risk is wise.

Mnemonic: ABCDPQRS provides a way to remember precautions with opioid therapy

- Query a prescription monitoring program (PMP) when prescribing opioids for pain. In greater than 50% of acute pain visits, the patient has already received an opioid for that pain within one month, from a different clinician. Verify PMP before making a final determination of aberrancy, by querying a pharmacy profile or the pharmacy benefit plan printout. This can be supplemented by requesting the medical records of all the providers involved, including dentists, podiatrists, nurse practitioners and physician assistants.
- Respiratory Insufficiency and Sleep Apnea: Common risk factors include sleep apnea, chronic obstructive pulmonary disease, congestive heart failure and concurrent use of benzodiazepines, alcohol or barbiturates. Sleep apnea is a commonly missed diagnosis, and the symptoms of this disease are often not readily apparent to the patient or physician. Opioids likely exacerbate both obstructive and central sleep apnea.
- Safe Driving, Work: Cautious use with CS while driving or operating machinery.
- Storage and Disposal: The FDA recommends that Schedule II medications be flushed down toilets due to safety concerns. Other pharmaceuticals can be combined with unpalatable substances (e.g., used coffee grounds) in a bag and thrown away. There are FDA take back programs where patients can dispose of unwanted pharmaceuticals at specific locations several times per year.

Off-label utilization of opioids

- "Off-label" based on the FDA recommendations with relative contraindications, pharmaceutical labeling precautions or "black box" warnings.
- Many meds can cause drug interactions (particularly with antidepressants) with unpredictable side effects, including death.
- The benefit/ risk of taking any such med(s) & its dosing is individualized & based on a mutual (medical provider/ patient) decision of the beneficial treatment effects

TIRF Indications / Precautions
Transmucosal Immediate Release Fentanyl

- FDA approved for breakthrough pain related to CANCER (may be in remission or related to any painful complication from a cancer related procedure), but consider "off label" use for acute, severe benign pain, exacerbations of chronic pain which might necessitate IV / IM analgesics, pre-procedural analgesia, wound and burn care, possibly useful for titration of long acting fentanyl, and for those with who cannot tolerate oral routes of administration of opioids
- Schedule II controlled substance and can be habit forming.
- Approved for Opioid tolerant adult patients only
- Scenario: Chronic pain opioid dependent patient with new onset cancer pain, which is uncontrolled
- Cannot interchange one product with another; start at lowest dose
- Consider in-office observation for dose titration
- Caution with pregnancy and nursing
- Caution with respiratory, head injury, or confusion
- Recommend naloxone for possible overdose risk

Special formulations – TIRF (fentanyl)

- If TIRF is given for **breakthrough** pain (BTP), then the patient MUST continue taking a prescribed around the clock opioids at current doses
- Avoid driving for 2 hrs after each use
- Not approved for use as a premedication of potential pain
- Must sign a *risk evaluation mitigation strategy* (TIRF-***REMS***) consent form for these products every 2 yrs (tel: 866-822-1483).
- Dose reductions should be considered due to Cytochrome P450 3A4 interactions: antimicrobials (i.e. erythromycin or ketoconazole), grapefruit juice

Contraindicated for acute headaches (unless for tumors), dental, ED, postop or acute pain (if opioid naive)

- Fentanyl "pop" (generics) contain sugar & cause dental decay

Special considerations: medications

Methadone (LAO), has a greater risk of drug interactions (5HT, Cyp 450), variable t ½ life, avoid linezolid for staph infections) variable responses, respiratory depression & death.

- Electrocardiograms every 6-12 months may be required to evaluate for cardiac arrhythmias (QTc interval).
- May cause dental decay by reducing saliva production.

Misusing **CS (opioids**)/**Buprenorphine** &/or mixing with other **sedatives** especially **benzos,** muscle relaxants, antihistamines, tranquilizers & **alcohol** may result in OVERDOSE, death, sedation, respiratory depression, reduced heart rate, impaired thinking, other dangerous side effects with pinpoint pupils.

Illicit activities

- Use of Illicit substances is prohibited & illegal. **Cannabis** is still considered illicit by the DEA, & may result in increased risk of substance use disorder, requiring closer monitoring. MD Medical cannabis has been legislatively approved, but awaiting implementation. **Code of MD – Criminal Law 5-601:**
- Fraud, deceit, misrepresentation, or concealment of a material fact including false Information that is communicated to a provider in an effort to obtain a CS; false name or address
- Counterfeiting or alteration of a prescription by written / verbal order;
- Altered or forged prescriptions will be confiscated.
- Illegal to trade, deal, obtain by internet, sell, divert or steal meds, or conduct any other illegal or disruptive activities
- Cannot share, loan, borrow, or give these meds to others, or take CS from other sources (including family members or friends). This is considered a **crime**.
- Law enforcement may be involved if there are illegal actions including "double dipping" or "doctor shopping" & diversion.

Illicit activities (cont.)

- If any criminal acts are suspected (by others), the patient has an obligation to inform law enforcement officers.
- May use anonymous confidential tips/ tel calls
- Make proactive efforts to prevent & avoid "prescription drug abuse or misuse".
- Health care providers & pharmacists will cooperate fully in any local, state or federal investigations regarding illegal activities including misuse, abuse, sale or diversion.
- HIPPA statutes allow full disclosure of med records, pharm profiles & PDMP for suspected criminal events related to medical care, or assist law enforcement investigations regarding CS/ meds including any illegal activities.

Adherence policies

- **Urine toxicology: urine specimen will be required PRIOR TO USING THE REST ROOM, or up to 2 hrs to void**.
- Urine, saliva or blood **tox** tests (with **observed specimens at the practice's discretion**) are obtained routinely or **randomly**.
- Inconsistent tox confirmations with unexplained or unauthorized CS, drugs/ substances present, or lack thereof, may result in closer monitoring &/or discharge from care.
- Avoid using Poppy seeds, Hemp, Vick's inhalant/ decongestants or Cough syrup (alcohol) for 48 hrs prior to OV.
- **Pill counts** (may be random) **or on demand**, to be available within 6 hrs of notification (or to a local pharmacy if limited access).
- If requested, for my OV, the patient will bring in all meds in their original bottles, any unused scripts, used packaging or wrappings for patches, pharmacy receipts or pill bottles from other providers.
- If the patient fails to comply, or have inconsistencies in my predicted pill quantities then he/ she will be subjected to closer monitoring, med changes, compliances classes &/ or discharge.

Informed consent enforcement

- Contacts given for significant others to be involved in monitoring & assessing the response to treatment & may be contacted by the pain med prescribers.
- Policies will be enforced, & non-compliance may result in consequences including more freq visits with dose changes or smaller quantities prescribed &/ or discharge from the practice with a 30 day written or verbal notice. A signed discharge letter will include at least 3 referrals for pain management, addictionologists &/ or psychiatrists
- A discharge may be selectively rescinded if the patient shows immediate compliance & remorsefulness
- Otherwise the CS/ meds may be reduced (or discontinued) & close monitoring to ensure safe tapering & transition to alternative treatments along with case management

Acknowledgment of contents

- The patient has reviewed the document and is familiar with the contents of this engagement agreement including a code of conduct. This establishes expectations for a patient centered, individualized care plan to enhance communication & avoid misunderstandings for proper & safe treatment including Risk evaluation and mitigation strategy (REMS) & with active participation. Any questions (particularly with the potential benefits & risks of meds/ CS) or alternative therapies have been satisfactorily answered.
- With voluntary informed consent, to abide to the best of by his/ her abilities by the above contents, & this consent will be enforced by the practice, with periodic reviews (at least annually) &/ or if there are significant changes to the prescribed CS/ meds or pharmacy.
- If the patient has been adversely impacted by this agreement, then he/ she can submit a written appeal explaining my concerns.
- This document shall be in compliance with state & federal regulations including HIPPA & FTC “red flag” rules

Chemical Coper theory & Treatment Strategies

- **Fusion of the emotional and physical pain responses**
- **? Endorphin deficiency**
- **Bears resemblance to addiction with regard to centrality of drugs and drug procurement**
- **Responds to a highly structured environment** with psych input, and opioid sparing drug treatments with **operant conditioning and cognitive -behavioral modification to decentralize the significance of pain medicine to** undo conditioning, undo socialization – accomplished through pain-related psychotherapy and prudent drug selection
- **Individual and family counseling**
- **Prudent drug selection to minimize drug taking behaviors (i.e. may prefer using transdermal time contingent medications such as fentanyl patch)**

Based on Passik

4th "A" - Aberrant Drug-related Behavior

Adverse consequences possibly resulting from drug use

Change or Decline in physical, psychological & social function,
Purposeful over sedation, Negative mood, Appearing intoxicated,
Increasingly unkempt or impaired, Involvement in MVA,
Worrisome drug effects ("Getting High"), Contact with street culture,
Engages in sale of sex to obtain drugs, Engages in staff splitting,
Does not comply with other recommended treatments,
Reports no effects of other medications,
Misses appointments except for medication renewal,
Requests frequent early renewals, Reports lost or stolen prescription, Requests higher doses in worrisome manner,
Changes route of administration, Abusing alcohol and street drugs,
Patient arrested or detained by police, Patient a victim of abuse,
Associate(s) arrested or detained by police

Aberrant Drug-taking Behaviors

Yellow Flags

- 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

- Passik and Portenoy, 1998

POTENTIAL RISK FACTORS FOR OPIOID MISUSE and BEHAVIORAL ABERRANCY

Red Flags

RED FLAGS predictive:

- Selling Rx drugs / Prescription forgery
- Stealing drugs from others
- Adulterating or Injecting oral formulations
- Obtaining Rx drugs from non-medical sources
- Concurrent abuse of alcohol or illicit drugs (especially cocaine)
- Repeated dose escalation or other non-compliance despite multiple warnings
- Repeated visits to other EDs or healthcare providers (may include dentists and podiatrists) without advising prescribers
- Drug-related deterioration in function at work, in the family or socially
- Repeated “losses” of medication / requests for early refills

Red Flags

Red Flags

- History of adverse childhood experiences (ACE) – Neglect or Physical, emotional, sexual abuse (particularly if there is pre-adolescent sexual abuse in females)
- Family history of drug abuse or alcoholism
- Psychiatric/ Mental illness especially PTSD, panic, agoraphobia, social phobia, bipolar, depression, ADHD, histrionic, sociopathic, schizophrenic, borderline personality disorder, suicidal/ homicidal, malingerer
- Psychological stress (chemical coping)
- Polypharmacy with CS especially benzodiazepines
- Tobacco/ nicotine dependency (may also affect pain responses to opioids, with drug interactions)
- Nicotine, as a stimulant, it may potentiate analgesics
- Multiple tattoos (especially “offensive ones”) and piercings

Red Flags (cont)

Red Flags

- History of compulsive behaviors: sexual, gambling, eating disorders (particularly with weight reduction procedures)
- Prefers a “cocktail” of medications including benzodiazepines and carisoprodol (“Holy Trinity”), with higher doses and quantities prescribed, given in a “factory-like” manner (ie pill mill)
- Inconsistent intervals of medication refills based on previous quantities given
- Patient calls their medications by their “street” name
- Patient appears to be in withdrawal (dilated pupils) with irritability or lethargic
- Same addresses for several clients for the same pharmacy with similar medications

Provider Prescription script recommendations

- Keep all prescription blanks in a safe place where they cannot be stolen; minimize the number of prescription pads in use. Use tamper-resistant prescription pads, including ink, watermark paper, serial numbers, pad assignments with accountability for unused scripts
- Write out the actual amount prescribed in addition to giving a number to discourage alterations of the prescription order.
- Use prescription blanks only for writing a prescription order and not for notes.
- Avoid signing prescription blanks in advance, with legible handwriting
- Assist the pharmacist when they telephone to verify information about a prescription order; a corresponding responsibility rests with the pharmacist who dispenses the prescription order to ensure the accuracy of the prescription.
- Contact the nearest DEA field office or law enforcement to obtain or to furnish information regarding suspicious prescription activities.
- E- prescribe with encryption software; may result in less prescribing errors, reduced risk for altered scripts; may be coupled with electronic health records to include drug interactions, prior authorizations, doctor shopping and PDMP
- Use DEA, NPI and ICD-10 codes for Schedule II scripts, patient address, DOB
- Specify the PRN reason, may use "maximum ____ tablets per day"
- Long acting opioids should not be used PRN;
- For methadone, state "for chronic pain"

Chronic opioid therapy (COT) Summary:

- Use of opioids may be appropriate – Pathology that fits the problem – Improved level of function and increased ADLs – Decreased pain – Manageable side effects
- Balanced multimodal care – Use of opioids as part of complete pain care – Anticipation and management of side effects
- Maintain standard of care with adequate documentation and reassessments – H&P, F/U, PRN referral, functional outcomes

Mnemonic COMPLIANCE summarizes the meticulous care required for pain management

- Often Assessed The patient is seen often enough to assess analgesia level, activity level, adverse reactions and aberrant behavior (e.g. “the Four A’s)
- Medical Records are accurate, legible, complete, and accessible.
- Plan of treatment has objectives and goals to determine functional status.
- Legitimate diagnosis of a recognized chronic painful condition.
- Informed Consent with Treatment Agreement
- Addiction risk assessment (e.g. alcohol and drug questionnaire: CAGE =cut down, annoyed, guilty, eye opener, past and current use, family history, psychological and social issues).
- Non-habituating medications have proven inadequate or unacceptable (either through clinical trial or review of medical history).
- Consultation(s) have been obtained when necessary and other health care concerns are addressed.
- Evaluation is thorough (history and physical) is consistent with the complexity of the case.

Governmental policies strategies and disincentives

- Need health insurance incentives to promote opioid sparing treatments.
- Federal agencies are recommending these alternatives, but at the same time, governmental and many private health insurances have limitations and/or no coverage for TENS for chronic low back pain, acupuncture, biofeedback, yoga, “mindfulness” (meditation), as well as caps for physical and occupational therapies, limited chiropractic, soft tissue injections or interventional blocks, and restricted magnetic or electrical stimulation procedures, ketamine infusions, and topical creams, which are all labeled as "experimental or investigational".
- Interdisciplinary care is most effective for chronic pain, but there are limited outpatient or inpatient treatment options or coverage for such integrated programs.
- “Elective" surgical procedures with nebulous outcomes are readily covered (i.e. knee arthroscopy and arthroplasty), with additional iatrogenic risks for worsening of the chronic painful conditions resulting in greater opioid dependency. Opioid dependency worsens outcome for many elective surgeries (i.e. lumbar surgery) and wound care.
- FDA could require end-to-end tracking of every opioid medication. The ability to track from the manufacturer plant to the distribution center, then to pharmacy and patient pick-up, would significantly decrease the diversion of opioids to the illicit market. They can limit marketing of opioid products, require additional studies of longer duration for newly developed opioids, and potentially remove products from the market (if there is evidence of a safety issue)

FDA REMS for opioids mandatory provider training to promote non-pharmacologic options:

- Mandatory physician training does not improve the patient access to these alternatives, unless the insurance plans promote or incentivize the participation by the patient, and societal values need to be redirected based on "entitlements" for health insurance benefits, with a greater responsibility placed on the patient to achieve the desired outcomes.
- "Accountable care" paradigms may achieve this goal, but these programs must also include in their analysis, providers who choose not the commit to the care of complex pain patients (and "take off the top" low complexity patients to achieve a desirable profile by insurance carriers), because they have not committed their professional resources to comprehensively manage these individuals, and in many cases, this is based on financial incentives of performing unimodal procedures, as reimbursed by health insurance carriers.

Maryland Medical Assistance Opioid Policies July 1, 2017
Treatment Act in Maryland

Require prior authorization for long-acting opioids, fentanyl products, methadone for pain, and any opioid prescription that result in a patient exceeding 90 morphine milligram equivalents per day, with a standard 30-day quantity limit for all opioids set at $\leq$ 90 milligram equivalents per day

HealthChoice Opioid Response Recommendations

- According to the Centers for Disease Control and Prevention, inappropriate prescribing practices and opioid prescribing rates are substantially higher among Medicaid patients than among privately insured patients.
- In one study based on 2010 data, 40 percent of Medicaid participants with prescriptions for pain relievers had at least one indicator of potentially inappropriate use or overlapping prescriptions for pain relievers, overlapping pain reliever and benzodiazepine or extended release prescription pain relievers for acute pain, and high daily doses.
- With more than 20 percent of Marylanders enrolled in the HealthChoice program and six of eight managed care organizations being integrated provider and payer networks, Maryland Medicaid's HealthChoice managed care organizations are a critical partner in helping achieve maximum results in combatting the opioid epidemic.
- Maryland Medicaid is moving to implement policy changes recommended by the Centers for Disease Control and Prevention for both Medicaid fee-for-service and all HealthChoice managed care organizations that will:

Maryland Medical Assistance Opioid Policies July 1, 2017

a. Prevent medical and non-medical opioid misuse, abuse, and addiction from developing;
b. Identify and treat opioid dependence early in the course of the disease;
c. Prevent overdose deaths, medical complications, psychosocial deterioration, transition to injection drug use, and injection-related disease; and
d. Use data to monitor and evaluate activities.

http://bha.dhmh.maryland.gov/OVERDOSE_PREVENTION/Pages/Index.aspx
https://mmcp.dhmh.maryland.gov/healthchoice/opioid-dur-workgroup/Pages/healthchoice-opioid-response.aspx

Heroin and Opioid Prevention Effort (HOPE) 2017

- Funding, Real time surveillance for tracking of OD trends
- Making drug dealers culpable for overdose deaths

Prior authorization will, at a minimum, require the following items:

- a. Attestation of a patient-provider agreement;
- b. A medical justification for high-dose and/or long-acting opioid prescription (may include treatment goals);
- c. Attestation of screen patient with random drug screen(s) before and during treatment; and
- d. Attestation that a naloxone prescription was given or offered to the patient/patient's household member.
- Patients with sickle cell anemia or patients in Hospice are excluded from the prior authorization process, but should also be kept on the lowest effective dose of opioids for the shortest required duration to minimize risk of harm.
- Health Choice managed care organizations may choose to implement additional requirements or limitations beyond the State's policy; more information is forthcoming.

Maryland Medical Assistance Opioid Policies July 1, 2017

As such, Maryland Medicaid recommends to following:

1. Consider non-opioids first-line treatment for chronic pain.

- The Centers for Disease Control and Prevention recommends expanding first-line treatment options for non-opioid pain therapies. To address this recommendation, non-steroidal anti-inflammatory drugs, duloxetine (for chronic pain), diclofenac topical; and certain first-line non-pharmacological treatment options (e.g., physical therapy) are all available for prescription within the HealthChoice program.

2. Require prior authorization for long-acting opioids, fentanyl products, methadone for pain, and any opioid prescription that result in a patient ≥ 90 MME per day, with a standard 30-day quantity limit for all opioids set at ≤ 90 milligram equivalents per day.

- Providers must obtain a prior authorization every six months to prescribe long-acting opioids, fentanyl products, methadone for pain and opioids ≥ 90 milligram equivalents (MME) per day.

3. Screen patients for Substance Use Disorder

- Providers should always use caution in prescribing opioids for any patients who are identified as having any type of or history of substance use disorder. Providers should refer any patient identified as having a substance use disorder to a substance use treatment program.
- Before prescribing an opioid or any controlled substance, providers should use standardized tool(s) to screen for substance use. Screening, Brief Intervention and Referral to Treatment (SBIRT) is an evidence-based practice used to identify, reduce, and prevent problematic use, abuse and dependence on alcohol and drugs. SBIRT enables providers to systematically screen and assist people who may not be seeking help for a substance use problem, but whose drinking or drug use may cause or complicate their ability to successfully handle health, work or family issues. Medicare reimbursements available since 2011. The provision of SBIRT is a billable service under Medicaid. with brief training. SBIRT involvement includes health care providers, PA, NP, social workers and clinical professional counselors. Billable codes, W7000-7022 (3-20 minutes) are through medical Maryland Medicaid coverage (not Beacon) ranging from $5-22, with a frequency of 1 initial screening assessment and 4 interventions annually.

Proven Benefits: Single most effective method after analyzing 40 types of programs;

Reduces Healthcare costs 3.8-5.6: 1 ratio by Injury (trauma, MVA), Cost and frequency of medical care, including ED, office, hospitals, Criminal episodes;

Reduces Severity of drug or alcohol use, identifies SUD; facilitates chemical dependency referrals

Reduces Risk of emotional or physical trauma

4. Refer patients identified as having Substance Use Disorder to substance use treatment

- Maryland Medicaid administers specialty behavioral health services through a single Administrative Services Organization: Beacon Health Options. Referrals for behavioral health treatment resources are available through Beacon Health Options.

5. Prescribe Naloxone to patients who meet certain risk factors.

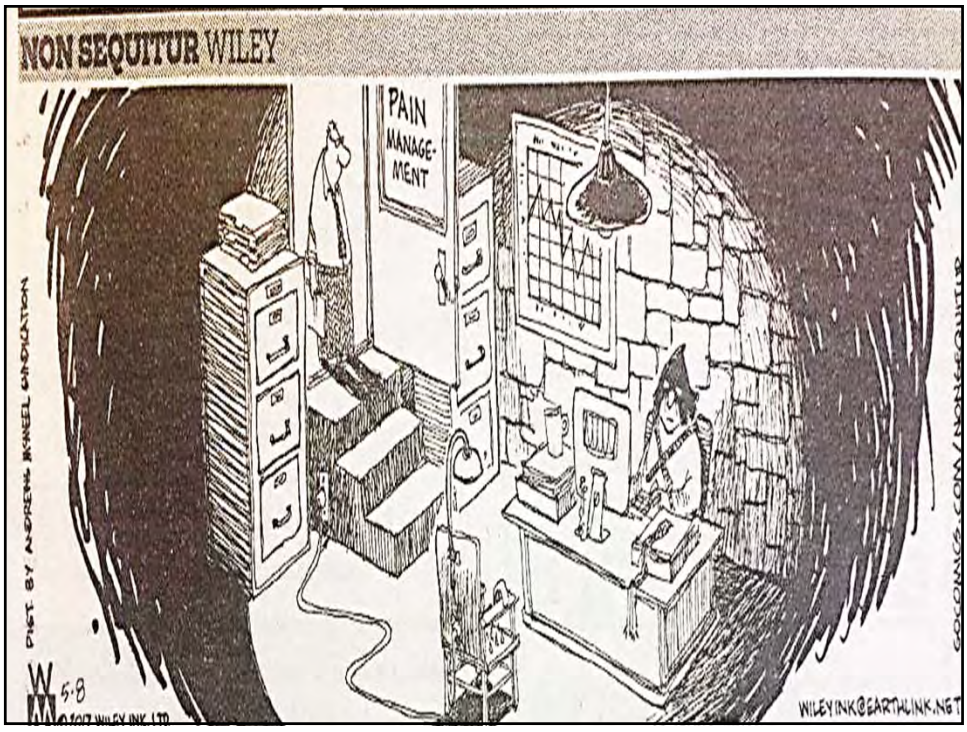
- Both the Centers for Disease Control and Prevention and the Centers for Medicare and Medicaid Services emphasize that clinicians should incorporate strategies to mitigate the risk of overdose when prescribing opioids. We encourage providers to prescribe naloxone - an opioid antagonist used to reverse opioid overdose - if any of the following risk factors are present:
- a. History of substance use disorder (SUD);
- b. High dose or cumulative prescription that result in ≥ 50 milligram equivalents per day (MME);
- c. prescriptions for both opioids and benzodiazepine or non-benzodiazepine sedative hypnotics; or
- d. other factors, such as drug-using friends/family.

6. Use the Prescription Drug Monitoring Program for all Controlled Dangerous Substance prescriptions.

- Administered by the Department of Health and Mental Hygiene, the Prescription Drug Monitoring Program gives health care providers access to their patients' complete Controlled Dangerous Substance prescription profile. Practitioners can access Prescription Drug Monitoring Program at no cost through the Chesapeake Regional Information System for Our Patients (CRISP) health information exchange. Providers who register with CRISP get access to a powerful virtual health record that includes patient hospital admission, discharge and transfer records, laboratory and radiology reports, clinical documents, as well as Prescription Drug Monitoring Program data.
- If you are not already a registered CRISP user, you can register for free. The Prescription Drug Monitoring Program usage is highly encouraged for all Controlled Dangerous Substance prescribers and will become mandatory (by law) on July 1, 2018.
- All providers for CS privileges need CRISP user # after July 1, 2017

The Rules!

- Cannot Rx Schedule II or III for family members
- Can provide samples of unscheduled drugs for family, but MUST document in a medical record
- Cannot Rx for anyone in a current sexual relationship, EVER
- Cannot Rx opioids for yourself, EVER
- Cannot Rx opioids to anyone (including friends) if you have not documented their H& P and have a current chart on file (must use the usual course of clinical care)
- Proper office disposal of controlled substances with witnesses



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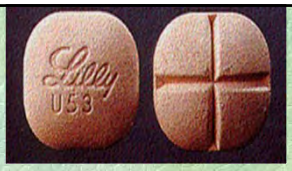
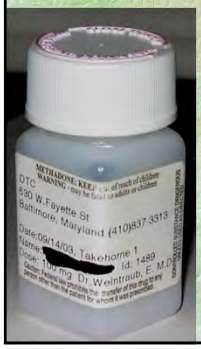


MAINTENANCE TREATMENTS FOR OPIOID USE DISORDER



MDH & Maryland Medicaid
Pharmacy Program Conference
St. Agnes Hospital
October 14, 2017

Christopher Welsh M.D.

UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE

I have no financial conflicts of interest.

I will not be discussing off-label use of medications.

OUTLINE

- Definitions
- Medication Assisted Treatment- General
- Methadone
- Buprenorphine
- Naltrexone
- Choice of Medication
- Patient Monitoring
- Special Situations- Pain, Pregnancy

SOME TERMS

- Use
- Misuse
- Abuse
- Risky/At risk Use
- Problematic Use
- Non-medical Use
- Non-prescribed Use
- Illicit Use
- Illicit Use of a Licit Substance

ADDICTION (ASAM)

- 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.
- This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.
- Characterized by behaviors that include:
  - inability to consistently abstain
  - impairment in behavioral control
  - craving
  - diminished recognition of significant problems with one's behaviors interpersonal relationships

PHYSIOLOGIC DEPENDENCE

- **The state of the body as a result of the ongoing exposure to a substance.**
- **It is present if the person displays tolerance and/or withdrawal.**

TOLERANCE

- A diminished biological or behavioral response to repeated administration of the same amount of a substance

or

- The need for increasing amounts of a substance to achieve the same effect.

WITHDRAWAL

- The physical and/or psychological disturbances that occur after the cessation of use of a substance to which the body has developed tolerance

SUBSTANCE DEPENDENCE

- **A maladaptive pattern of substance use leading to significant impairment or distress.**
- **A chronic, progressive, relapsing disorder (disease?) of continued substance use despite negative consequences**
- **Synonymous with "*addiction*."**

DSM IV DEPENDENCE

-Still used in ICD-10

-A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period:

1. Tolerance

2. **Withdrawal**

3. The substance is often **taken in larger amounts** or **over a longer period** than was intended

DSM IV DEPENDENCE

4. There is a persistent **desire or unsuccessful efforts to cut down** or control substance use
5. A **great deal of time is spent** in activities necessary to obtain the substance, use the substance, or recover from its effects
6. Important social, occupational, or recreational **activities are given up or reduced** because of substance use
7. The substance use is **continued despite knowledge of having a persistent or recurrent physical or psychological problem** that is likely to have been caused or exacerbated by the substance

SUBSTANCE USE DISORDERS (DSM-5)

- **Mild=2*-3; Moderate=4-5; Severe=6 or more**
- **A maladaptive pattern of substance use leading to clinically significant impairment or distress:**
  - **-Tolerance***
  - **-Withdrawal***
  - **-Often taken in larger amounts or over a longer period than intended**
  - **-Inability to cut down/control use**
  - **-Considerable time spent using/obtaining/recovering**
  - **-Important activities given up/reduced**
  - **-Use despite negative consequences**
  - **-Failure to fulfill role obligations**
  - **-Craving or strong desire to use**
  - **-Recurrent use in hazardous situations**
  - **-Recurrent use despite persistent, related social/interpersonal problems**

PHYSICAL DEPENDENCE & ADDICTION

PSEUDOADDICTION

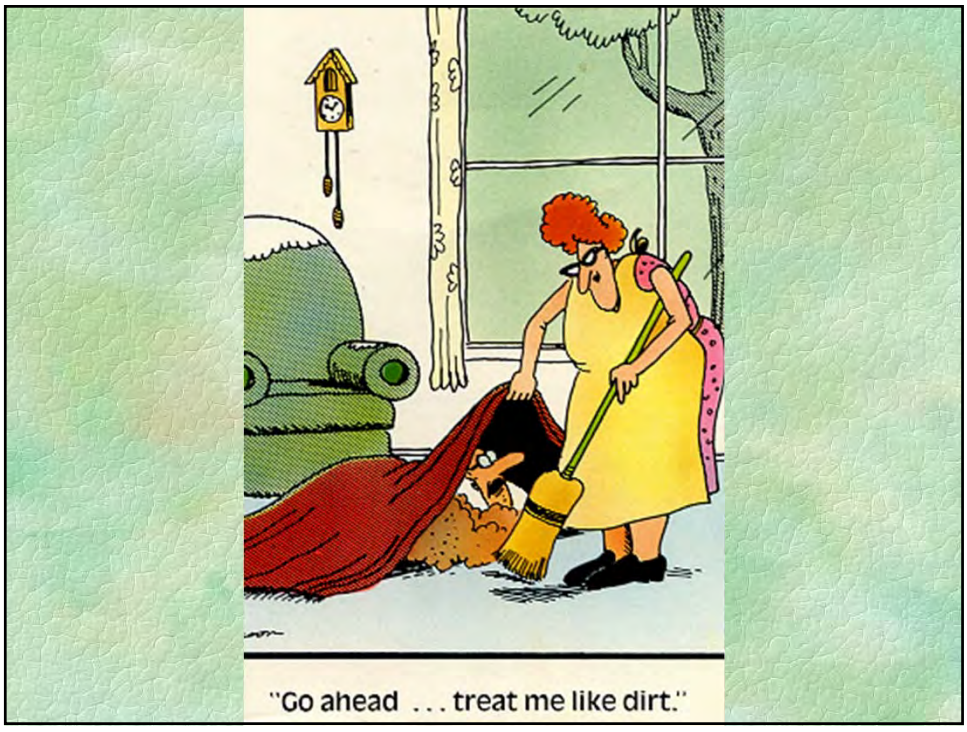
- An iatrogenic misinterpretation of relief-seeking behaviors caused by under-treatment of pain that is identified by the clinician as inappropriate drug-seeking behavior
- Behaviors cease when adequate pain relief is provided
- Not a diagnosis, rather a description of a clinical interaction

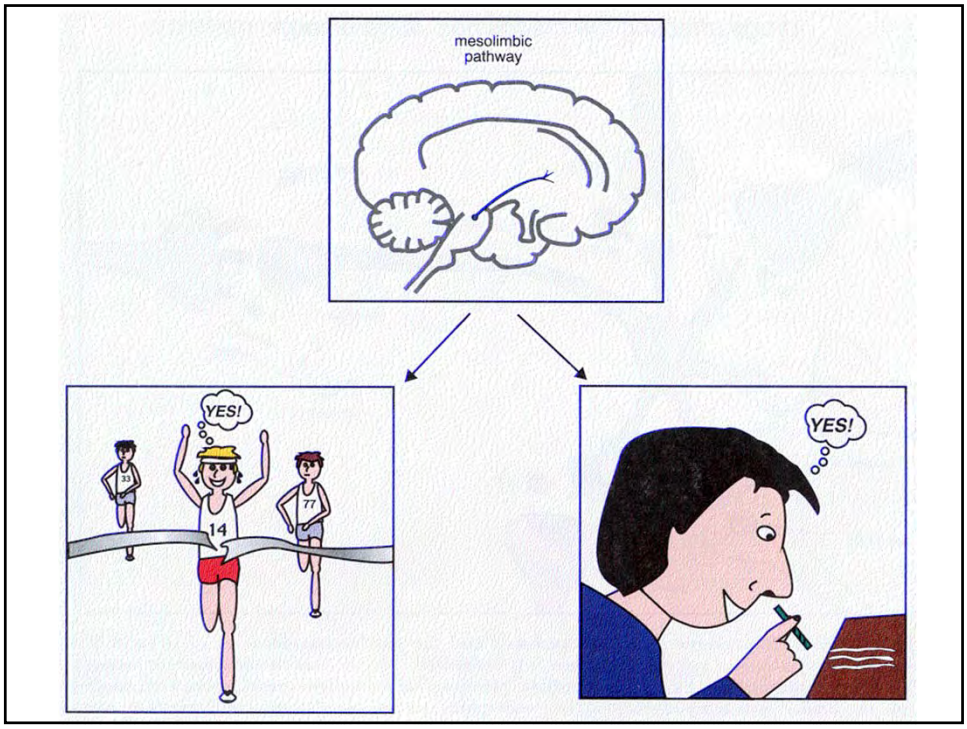
PSEUDOTOLERANCE

- The need to increase medication dose due to reasons other than adaptation of the system.
  - Disease progression
  - New disease
  - Increased physical activity
  - Lack of compliance
  - Change in medication
  - Drug interaction

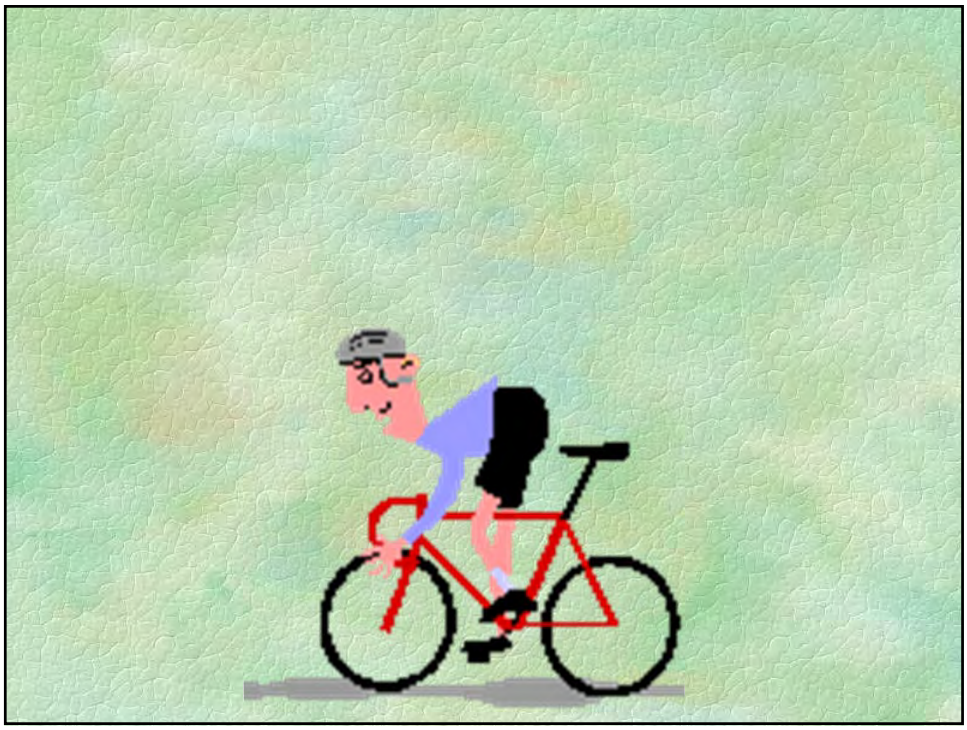
OTHER TERMS

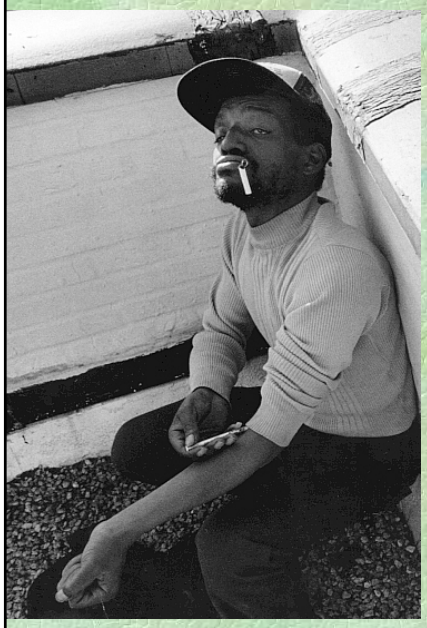

90
GREEN = TEMP/

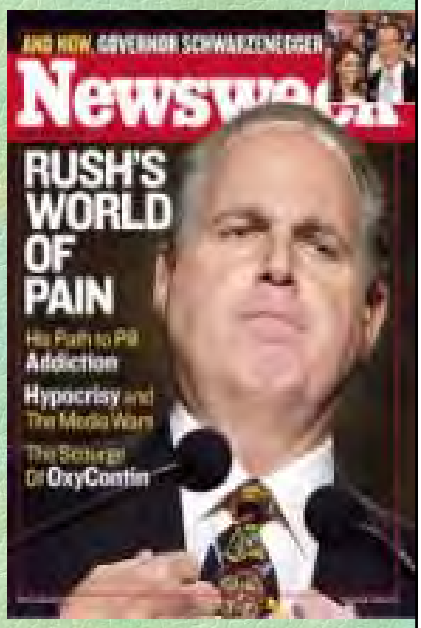

"Go ahead . . . treat me like dirt."


mesolimbic
pathway
YES!
14
YES!

"IF YOU'VE SEEN ONE PATIENT WITH ADDICTION, YOU'VE SEEN ONE PATIENT WITH ADDICTION."

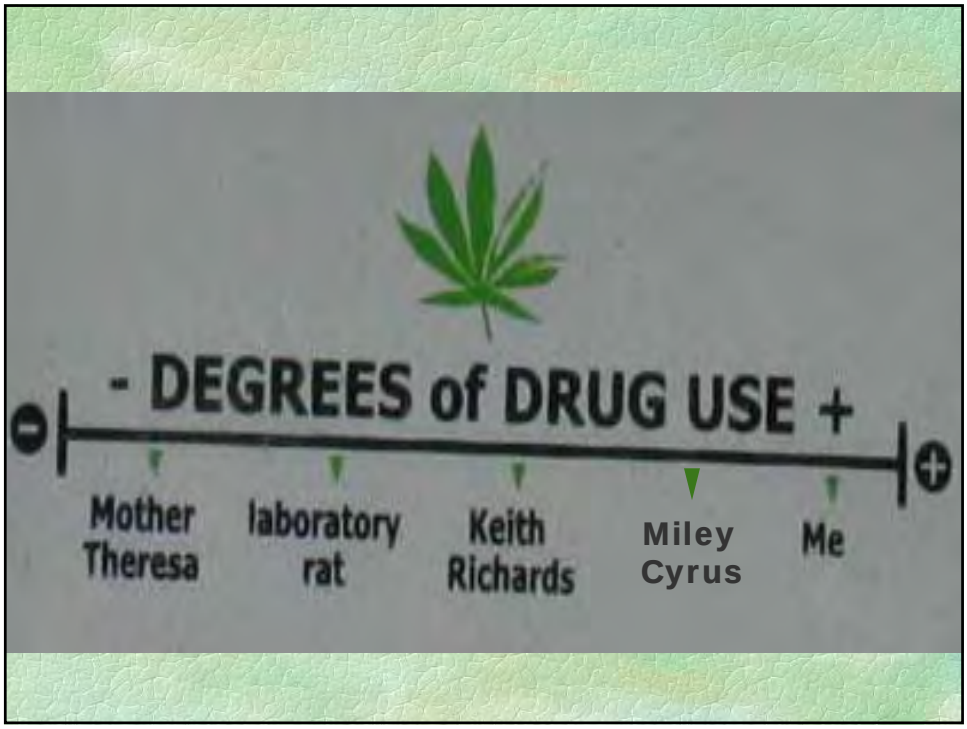






DETECTING SUBSTANCE USE/ABUSE

- Screening instruments – e.g., DAST-10
- Self-report of use, reason
- Multiple trauma
- Hospitalization
- Infections
- Body fluid testing (e.g., urine)
- PDMP



The DAST-10 survey: These questions refer to the past 12 months. One point is awarded for each "Yes" answer.	
1. Have you used drugs other than those required for medical reasons?	Yes / No
2. Do you abuse more than one drug at a time?	Yes / No
3. Are you unable to stop using drugs when you want to?	Yes / No
4. Have you ever had blackouts or flashbacks as a result of drug use?	Yes / No
5. Do you ever feel bad or guilty about your drug use?	Yes / No
6. Does your spouse (or parents) ever complain about your involvement with drugs?	Yes / No
7. Have you neglected your family because of your use of drugs?	Yes / No
8. Have you engaged in illegal activities in order to obtain drugs?	Yes / No
9. Have you ever experienced withdrawal symptoms (felt sick) when you stopped taking drugs?	Yes / No
10. Have you ever had medical problems as a result of your drug use (e.g., memory loss, hepatitis, convulsions, bleeding)?	Yes / No

Opioid Risk Tool

This tool should be administered to patients upon an initial visit prior to beginning opioid therapy for pain management. A score of 3 or lower indicates low risk for future opioid abuse, a score of 4 to 7 indicates moderate risk for opioid abuse, and a score of 8 or higher indicates a high risk for opioid abuse.

Mark each box that applies	Female	Male
Family history of substance abuse		
Alcohol	1	3
Illegal drugs	2	3
Rx drugs	4	4
Personal history of substance abuse		
Alcohol	3	3
Illegal drugs	4	4
Rx drugs	5	5
Age between 16—45 years	1	1
History of preadolescent sexual abuse	3	0
Psychological disease		
ADD, OCD, bipolar, schizophrenia	2	2
Depression	1	1
Scoring totals		

D.I.R.E. Score: Patient Selection for Chronic Opioid Analgesia

For each factor, rate the patient's score from 1-3 based on the explanations in the right hand column.

Score	Factor	Explanation
	Diagnosis	1 = Benign chronic condition with minimal objective findings or no definite medical diagnosis. Examples: fibromyalgia, migraine headaches, nonspecific back pain. 2 = Slowly progressive condition concordant with moderate pain, or fixed condition with moderate objective findings. Examples: failed back surgery syndrome, back pain with moderate degenerative changes, neuropathic pain. 3 = Advanced condition concordant with severe pain with objective findings. Examples: severe ischemic vascular disease, advanced neuropathy, severe spinal stenosis.
	Intractability	1 = Few therapies have been tried and the patient takes a passive role in his/her pain management process. 2 = Most customary treatments have been tried but the patient is not fully engaged in the pain management process, or barriers prevent (insurance, transportation, medical illness). 3 = Patient fully engaged in a spectrum of appropriate treatments but with inadequate response.
	Risk	(R = Total of P + C + R + S below)
	Psychological:	1 = Serious personality dysfunction or mental illness interfering with care. Example: personality disorder, severe affective disorder, significant personality issues. 2 = Personality or mental health interferes moderately. Example: depression or anxiety disorder. 3 = Good communication with clinic. No significant personality dysfunction or mental illness.
	Chemical Health:	1 = Active or very recent use of illicit drugs, excessive alcohol, or prescription drug abuse. 2 = Chemical coper (uses medications to cope with stress) or history of CD in remission. 3 = No CD history. Not drug-focused or chemically reliant.
	Reliability:	1 = History of numerous problems: medication misuse, missed appointments, rarely follows through. 2 = Occasional difficulties with compliance, but generally reliable. 3 = Highly reliable patient with meds, appointments & treatment.
	Social Support:	1 = Life in chaos. Little family support and few close relationships. Loss of most normal life roles. 2 = Reduction in some relationships and life roles. 3 = Supportive family/close relationships. Involved in work or school and no social isolation.
	Efficacy score	1 = Poor function or minimal pain relief despite moderate to high doses. 2 = Moderate benefit with function improved in a number of ways (or insufficient info – hasn't tried opioid yet or very low doses or too short of a trial). 3 = Good improvement in pain and function and quality of life with stable doses over time.

___ Total score = D + I + R + E

Score 7-13: Not a suitable candidate for long-term opioid analgesia
Score 14-21: May be a candidate for long-term opioid analgesia

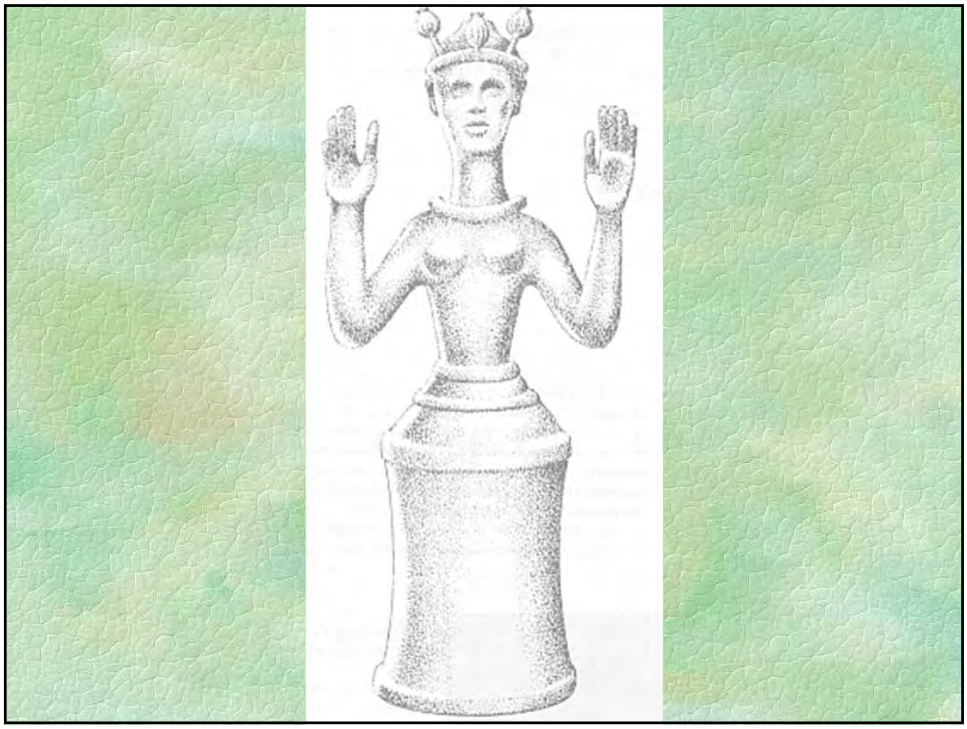
ADDICTION IS TREATABLE!!!

SUD TREATMENT GENERAL PRINCIPLES

1) **Agonist** ("substitution", "maintenance", "replacement")
   methadone, buprenorphine, nicotine
2) **Antagonist**
   naltrexone (for opioids)
3) **Aversive**
   disulfiram
4) **Reduction in reinforcement**
   naltrexone (for alcohol)
5) **Increase in metabolism or clearance**
   butyrylcholinesterase
6) **"Vaccines" or "peripheral blockers"**

OPIOIDS

- **FDA Approved**
  - **Methadone** (Methadose; Dolophine)
  - **levo-alpha-acetylmethadol** (ORLAAM)
  - **Buprenorphine**(Suboxone; Suboxone Film; Subutex; Bunavail; Zubsolv)
  - **Naltrexone** (Trexan; Vivitrol)
- **Experimental/Not Approved**
  - **Ibogaine**
  - **Heroin**



MORPHINE, OPIUM, COCAINE

AND ALL OTHER DRUG HABITS

PERMANENTLY CURED IN 10 TO 15 DAYS!

NO HYPODERMICS USED.

OUR cure antidotes and eliminates all Narcotic Poisons from the system, revives and restores the dormant nerve cells, clears and strengthens the mind, and the broken-down and debilitated patient is reinvigorated and rebuilt into a strong and healthy being again.

Magnetic Springs Sanitarium, Eureka Springs, Arkansas

UNDER our treatment patients eat and sleep well from the time of beginning. They are under no restraint whatever, being at perfect liberty at all times to visit the various springs, roam over the mountains and enjoy the beauties which nature has provided here so bountifully.

We *positively guarantee* to cure any case of Morphine, Opium, Codine, Chloroform, Chloral, Cocaine or other Drug habit, in from ten to fifteen days, without causing the patient the slightest sickness or pain. *Patients need not pay one cent until satisfied in their own minds that they are cured.*

LIQUOR HABIT—DRUNKENNESS—CURED IN ONE WEEK

NO HYPODERMICS USED

We positively guarantee to cure the Liquor Habit or Drunkenness in one week, without the least sickness, confinement or any bad after-effects. Our cure consists of a specific which is absolutely harmless, yet speedy and certain in its action, and is *the only cure known to medical science* which permanently removes all need, craving or desire for whiskey, beer, wine or other alcoholic stimulants. It builds up the shattered nerves, increases and strengthens the sexual powers and leaves the patient in perfect health, physically and mentally. After a cure has been effected the *smell* of liquor becomes *extremely offensive* and the *taste sickening* and obnoxious.

SUPERIOR TO ALL OTHER TREATMENTS.

Dr. Norton Bishaw, who was formerly on the staff of physicians of Dr. Leslie E. Keeley of Dwight, Ill., and who has made a careful study of the methods and treatment for the Drug and Liquor Habit at the various leading sanitariums of the country, writes as follows of the cure administered at the Magnetic Springs Sanitarium:

Special round trip tickets to Eureka Springs, Ark., can be purchased from any point in the United States via the Frisco System at greatly reduced rates, which places this wonderful cure within the reach of all.

YOU NEED NOT PAY ONE CENT UNTIL CURED.

Patients visiting the Magnetic Springs Sanitarium for treatment for the liquor habit or any drug habit are *not required to pay one cent until satisfied in their own mind that they are cured.* In case of failure to effect a cure in any case we agree to refund all railway fares from the place of residence to Eureka Springs and return, and charge nothing for the treatment. The Sanitarium is a handsome and commodious building with every modern improvement and convenience. A competent staff of physicians is always in attendance under the direction of Dr. C. A. Reed, President of the Sanitarium. Full information concerning the treatment, terms, etc., can be obtained by addressing

MAGNETIC SPRINGS SANITARIUM

C. A. REED, M. D., Medical Director, Box 616, EUREKA SPRINGS, ARKANSAS.

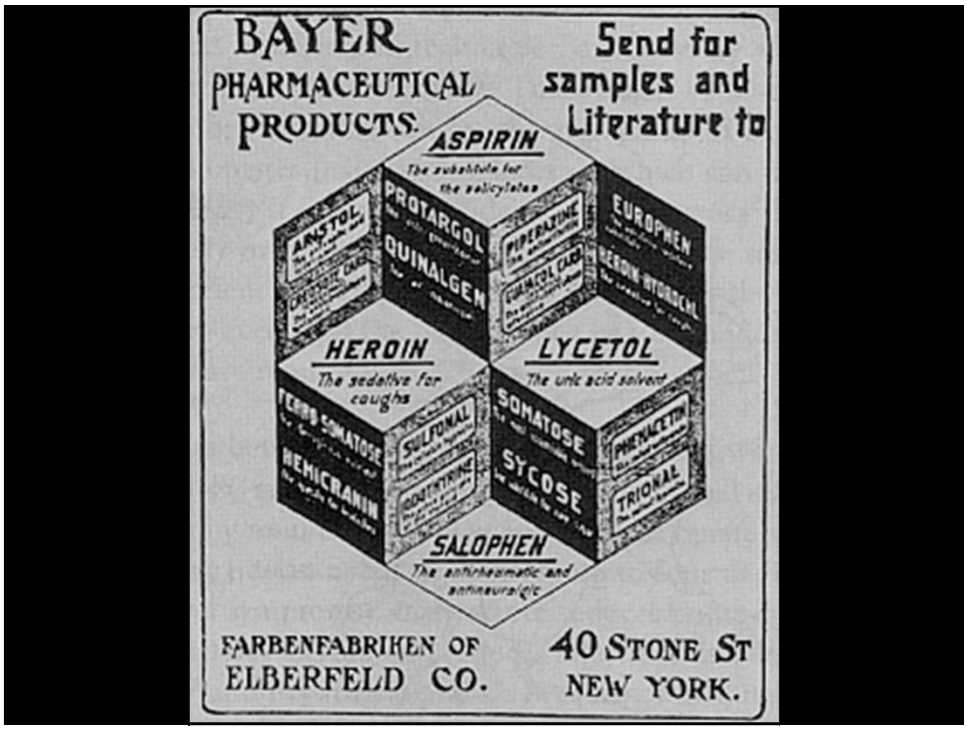
1904

"I received a note from her when she had used this. She was much encouraged and had ordered two pounds more… I saw her recently when she assured me that she had no desire for morphine."

Dr. W.H. Bentley

Detroit Therapeutic Gazette, 1880

(about a woman for whom he had prescribed one pound of cocaine for morphine addiction)



Harrison Narcotics Tax Act, 1914

Full text of the Act.

Public Acts of the Sixty-Third Congress of the United States

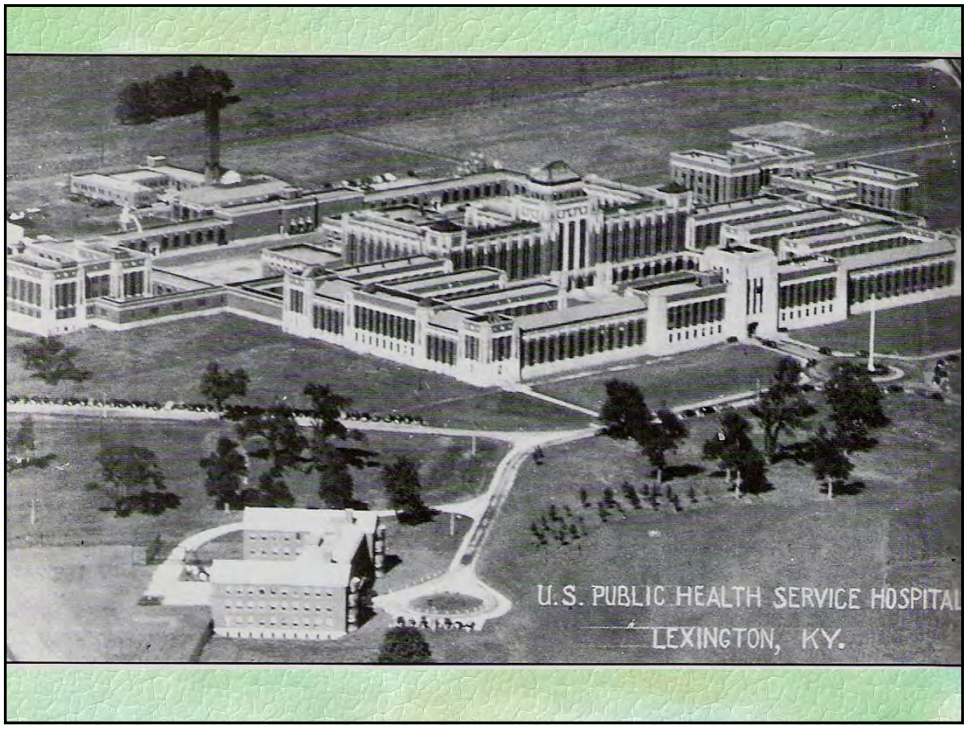
Woodrow Wilson, President; Thomas R. Marshall, Vice-President; James P. Clarke, President of the Senate pro tempore; Claude A. Swanson, Acting President of the Senate pro tempore, December 21 to 23, 29 to 31, 1914, and January 2, 1915; Nathan P. Bryan, Acting President of the Senate pro tempore, January 22, 1915; Champ Clark, Speaker of the House of Representatives

Chap 1. - An Act To provide for the registration of, with collectors of internal revenue, and to impose a special tax on all persons who produce, import, manufacture, compound, deal in, dispense, sell, distribute, or give away opium or coca leaves, their salts, derivatives, or preparations, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, that on and after the first day of March, nineteen hundred and fifteen, every person who produces, imports, manufactures, compounds, deals in, dispenses, distributes, or gives away opium or coca leaves or any compound, manufacture, salt, derivative, or preparation thereof, shall register with the collector of internal revenue of the district, his name or style, place

"The shallow pretense that drug addiction is "a disease" which the specialist must be allowed to "treat," which pretended treatment consists of supplying victims with the drug has caused their physical and moral debauchery…"

American Medical Association
***Report of the Committee on the Narcotic Drug Situation,* 1920**



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A Medical Treatment for Diacetylmorphine (Heroin) Addiction

A Clinical Trial With Methadone Hydrochloride

Vincent P. Dole, MD, and Marie Nyswander, MD

A group of 22 patients, previously addicted to diacetylmorphine (heroin), have been stabilized with oral methadone hydrochloride. This medication appears to have two useful effects: (1) relief of narcotic hunger, and (2) induction of sufficient tolerance to block the euphoric effect of an average illegal dose of diacetylmorphine. With this medication, and a comprehensive program of rehabilitation, patients have shown marked improvement; they have returned to school, obtained jobs, and have become reconciled with their families. Medical and psychometric tests have disclosed no signs of toxicity, apart from constipation. This treatment requires careful medical supervision and many social services. In our opinion, both the medication and the supporting program are essential.

The question of "maintenance treatment" of addicts is one that is often argued but seldom clearly defined. If this procedure is conceived as no more than an unsupervised distribution of narcotic drugs to addicts for self-administration of doses and at times of their choosing, then few physicians could accept it as proper medical practice. An uncontrolled supply of drugs would trap confirmed addicts in a closed world of drug taking, and tend to spread addiction. This procedure certainly would not qualify as "maintenance" in a medical sense. Uncontrolled distribution is mentioned here only to reject it, and to emphasize the distinction between distribution and medical prescription. The question at issue in the present study was whether a narcotic medicine, prescribed by physicians as part of a treatment program, could help in the return of addict patients to normal society.

No definitive study of medical maintenance has yet been reported. The Council on Mental Health of the American Medical Association, after a thorough review of evidence available in 1957,[1] concluded that "The advisability of establishing clinics or some equivalent system to dispense opiates to addicts cannot be settled on the basis of objective facts. Any position taken is necessarily based in part on opinion, and on this question opinions are divided." With respect to previous trials of maintenance treatment, the Council found that "Assessment of the operations of the narcotic dispensaries between 1919 and 1923 is difficult because of the paucity of published material. Much of the small amount of data that is available is not sufficiently objective to be of great value in formulating any clear-cut opinion of the purpose of the clinics, the way in which they operated, or the results attained." No new studies bearing on the question of maintenance treatment have appeared in the eight years since this report was published. Meanwhile, various medical and legal committees have called for additional research.[2]

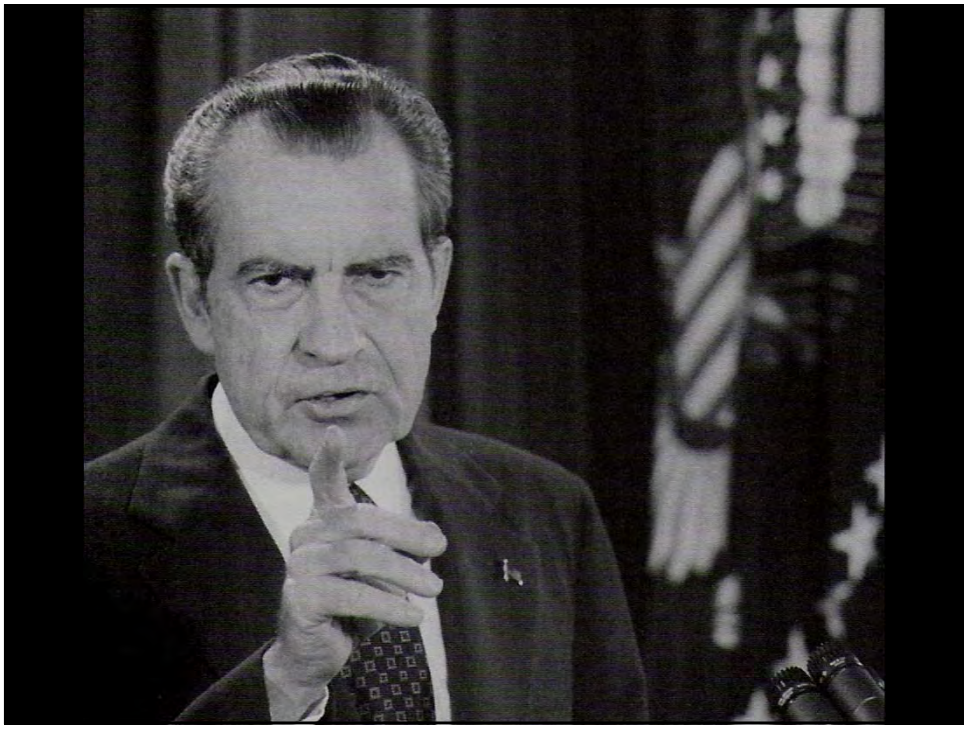
See also page 673.

The present study, conducted under the auspices of the departments of health and hospitals, New York city, has yielded encouraging results; patients who before treatment appeared hopelessly addicted are now engaged in useful occupations and are not using diacetylmorphine (heroin). As measured by social performance, these patients have ceased to be addicts. It must be emphasized that this paper is only a progress report, based on treatment of 22 patients for periods of 1 to 15 months. Such limited study obviously does not establish a new treatment for general application. The results, however, appear sufficiently promising to justify further trial of the procedure on a larger scale.

Procedure

The patients admitted to the program to date were men, aged 19 to 37, "mainline" diacetylmorphine users for several years with history of failures

From the Rockefeller Institute, and Manhattan General Division of Beth Israel Hospital, New York.
Reprint requests to Rockefeller Institute, New York 10021 (Dr. Dole).



THE NEW ERA

- **2000: Drug Abuse Treatment Act (DATA)**
  - **-Section 3502 of The Children's Health Act of 2000**
  - **-Schedule III, IV, and V medications (Buprenorphine) approved for detoxification and maintenance**
- **2002: FDA approved Subutex and Suboxone**
- **2003: Subutex and Suboxone available in pharmacies**

DRUG ABUSE TREATMENT ACT (DATA) OF 2000

Allows:

physicians to prescribe (in office-based setting)

&

pharmacists to dispense

"narcotics", specifically buprenorphine,

to treat opioid addiction

COMPREHENSIVE ADDICTION & RECOVERY ACT (CARA) 2016

Allows:

Nurse practitioners and physicians assistants to prescribe buprenorphine (requires extra training)

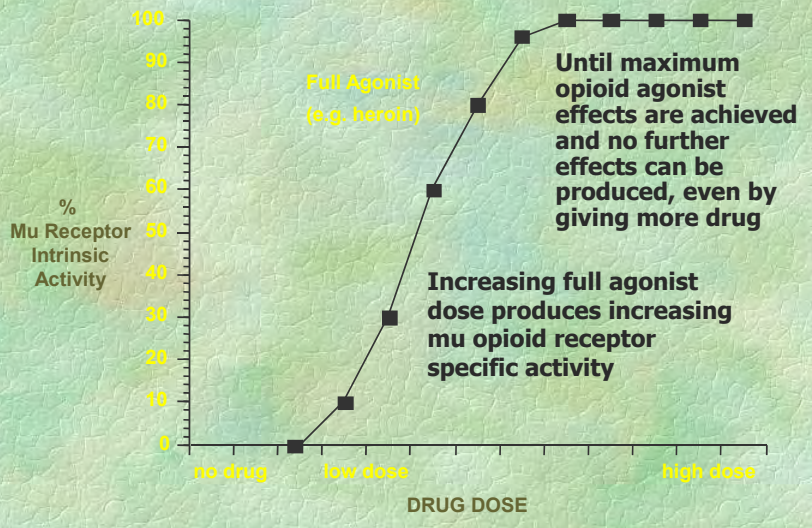
Allows certified addiction specialists to treat 275mg patients at a time

Function at Receptors
Full Agonists

Mu receptor ← **Full agonist binding …**

- **activates the mu receptor**
- **is highly reinforcing**
- **is the most abused opioid type**
- **includes heroin, methadone, & others**

Full Agonist Activity Levels



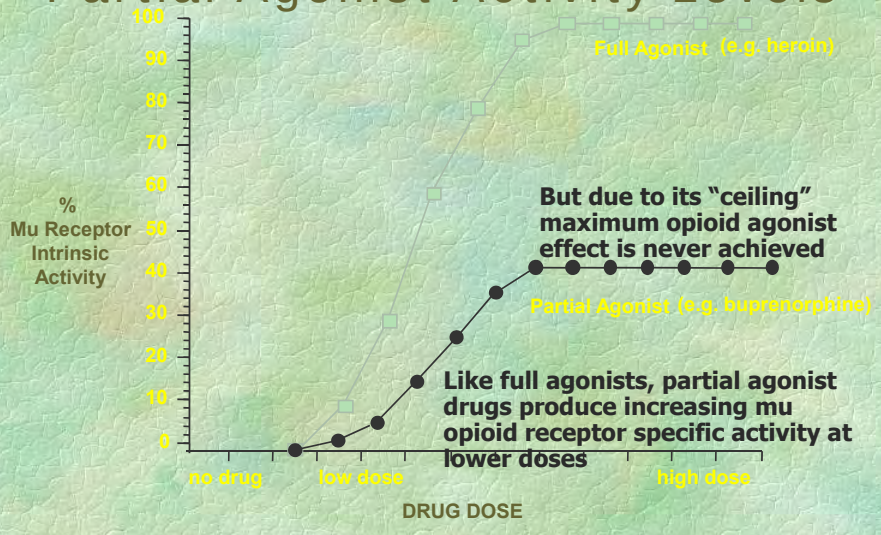
Function at Receptors
Partial Agonists

Mu receptor

Partial agonist binding ...

- **activates the receptor at lower levels**
- **is relatively less reinforcing**
- **is a less abused opioid type**
- **includes buprenorphine**

Partial Agonist Activity Levels



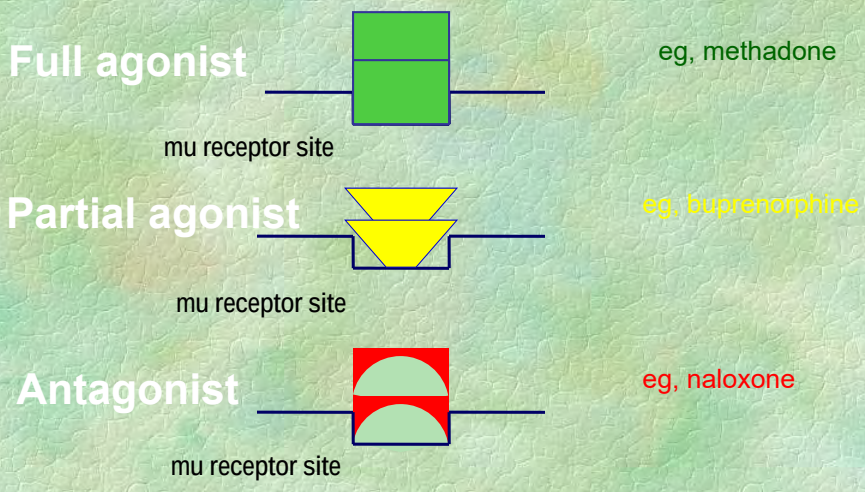
Function at Receptors: Antagonists

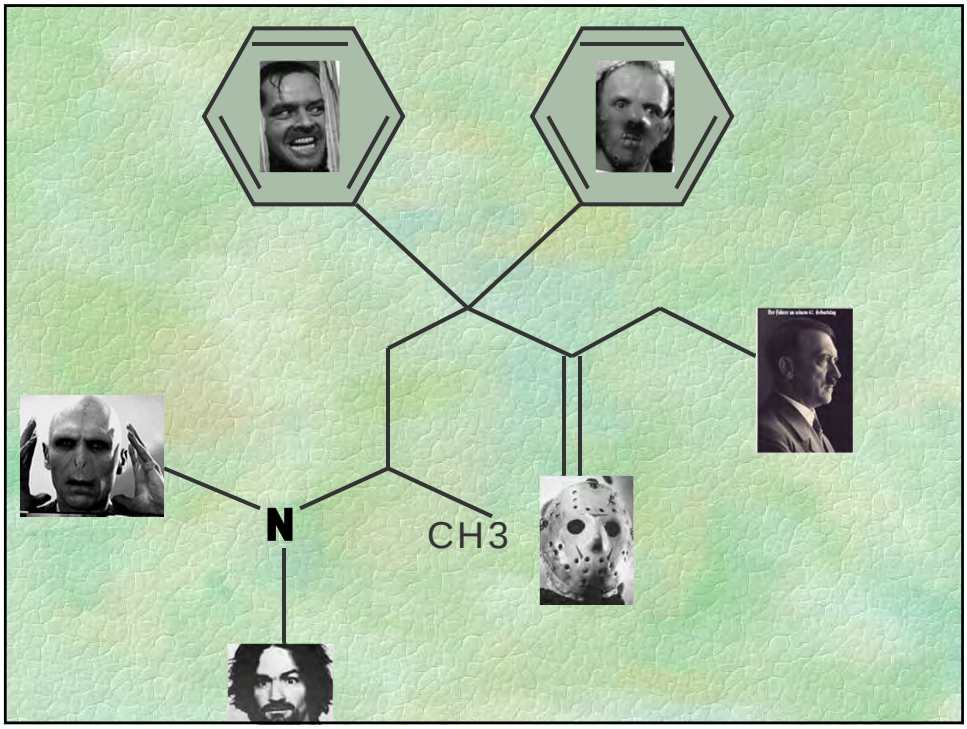
Mu receptor

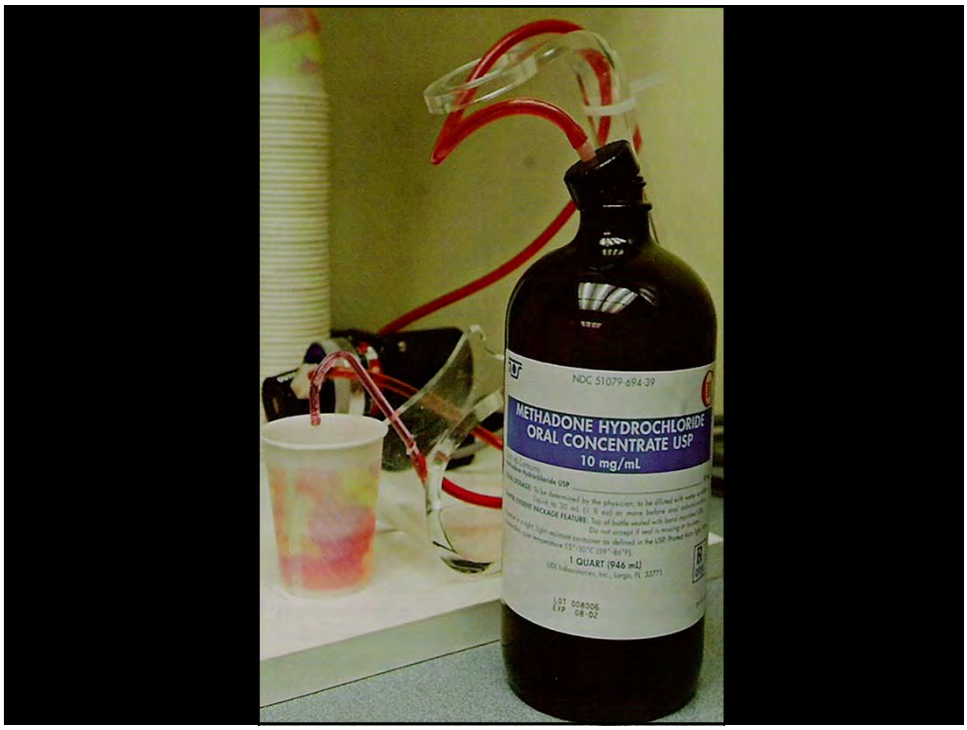
Antagonist binding …

- occupies without activating
- is not reinforcing
- blocks abused agonist opioid types
- includes naloxone and naltrexone

RECEPTOR ACTIVATION




N
CH3

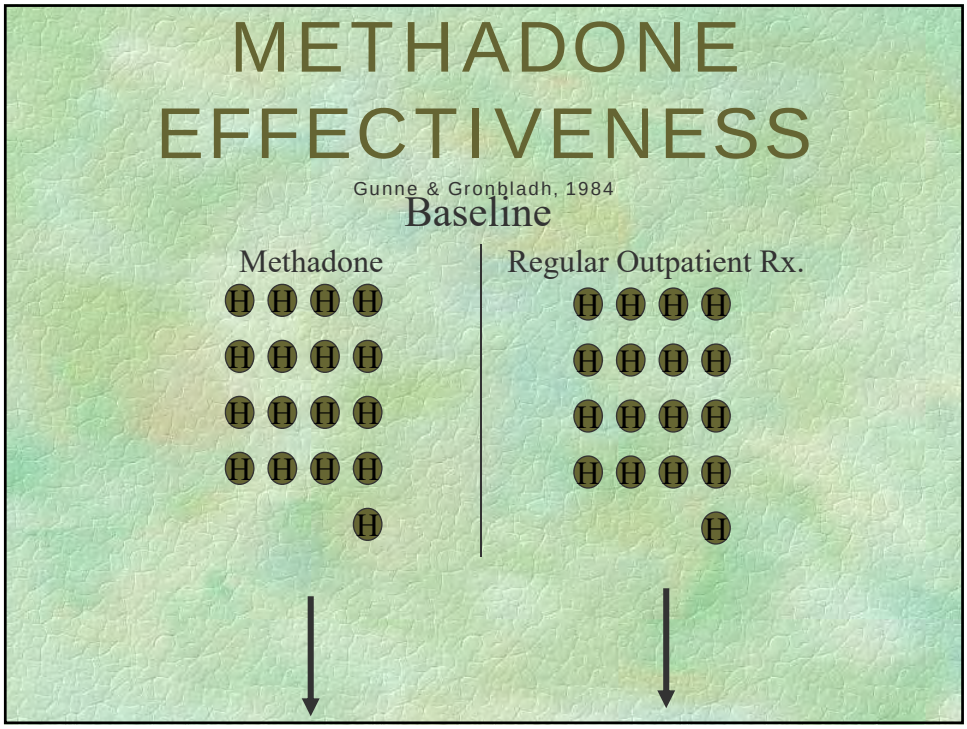

NDC 51079-694-39
METHADONE HYDROCHLORIDE
ORAL CONCENTRATE USP
10 mg/mL
1 QUART (946 mL)

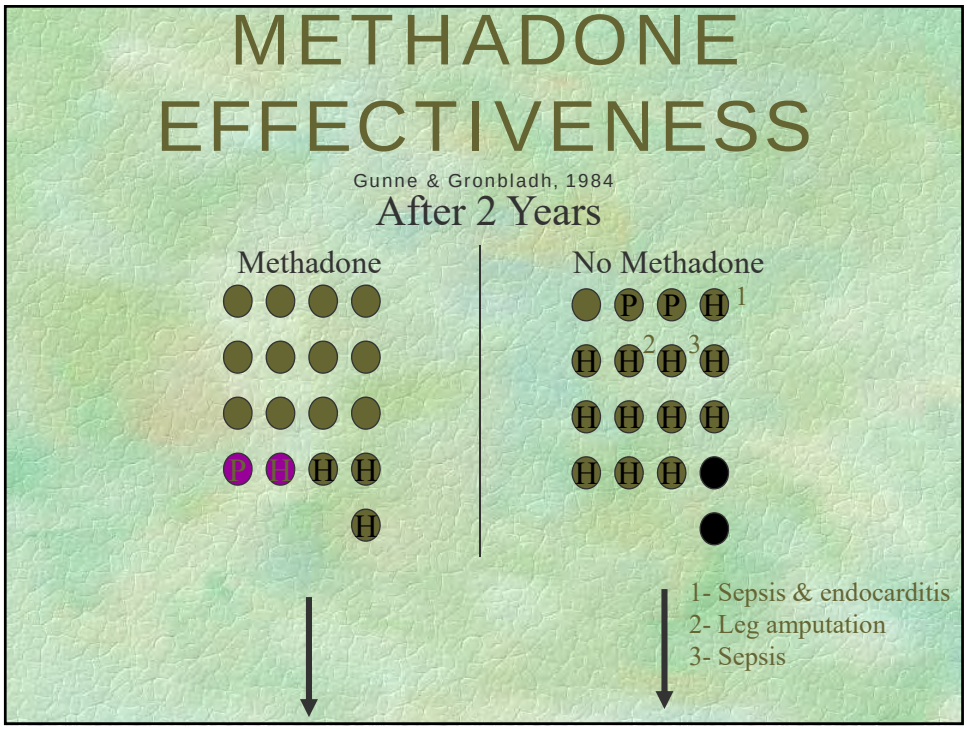
ADVANTAGES OF METHADONE

- Orally administered
- Gradual onset of action
- Long half-life
- Long duration of action
- Produces complete blockade of effects of heroin
- Minimal chronic problems

METHADONE MAINTENANCE BENEFITS

- Reduction in the use of illicit opioids
- Reduction in criminal activity
- Reduction in HIV and hepatitis infection rates and transmission
- Reduction in endocarditis, cellulitis, etc.
- Improvement in general health
- Improvement in productivity and "social health"

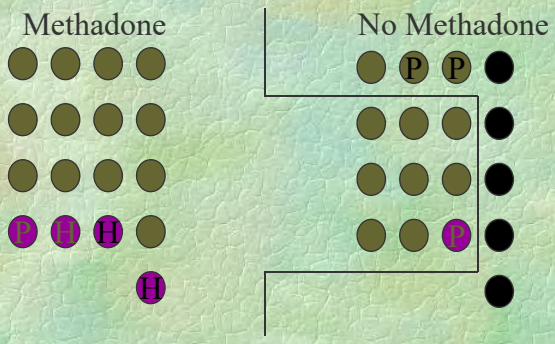

METHADONE EFFECTIVENESS
Gunne & Gronbladh, 1984
Baseline
Methadone
Regular Outpatient Rx.

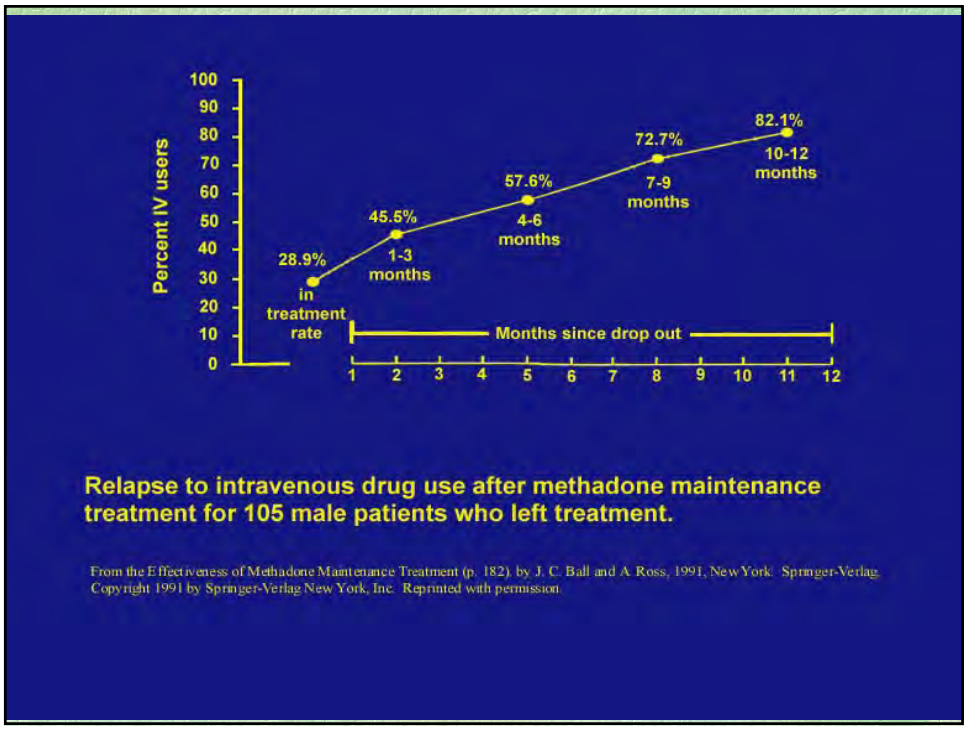

METHADONE EFFECTIVENESS
Gunne & Gronbladh, 1984
After 2 Years
Methadone
No Methadone
1- Sepsis & endocarditis
2- Leg amputation
3- Sepsis

METHADONE EFFECTIVENESS

Gunne & Gronbladh, 1984

After 5 Years





Relapse to intravenous drug use after methadone maintenance treatment for 105 male patients who left treatment.

From the Effectiveness of Methadone Maintenance Treatment (p. 182). by J. C. Ball and A. Ross, 1991, New York: Springer-Verlag. Copyright 1991 by Springer-Verlag New York, Inc. Reprinted with permission.

Benefits and Costs of Methadone Treatment

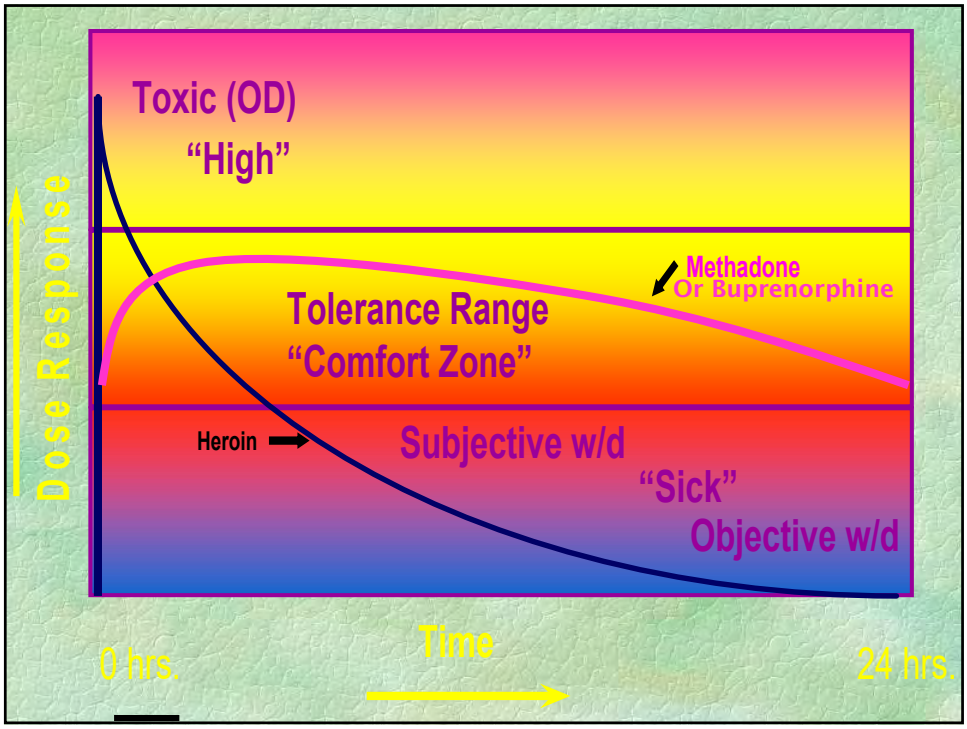
Methadone treatment saves money by reducing crime, increasing employment, improving access to health care. The first treatment episode costs $2699 but reaps $13,116 in economic benefits. Estimates based on single treatment episodes indicate every $1 spent on treatment yields $4.86 in benefits. However, treatment also has long-term benefits. Estimates based on ongoing methadone treatment indicate that every $1 spent on treatment yields almost $38 in benefits.

OUTCOME	
Crime	
Mean pre-treatment cost per month per individual	$2,707
Mean post-treatment cost per month per individual	$2,298
Employment	
Mean pre-treatment earnings per month per individual	$371
Mean post-treatment earnings per month per individual	$1,005
Health Care	
Mean pre-treatment costs per month per individual	$140
Mean post-treatment costs per month per individual	$89
Economic	
Mean pre-treatment monthly economic benefit per month per individual	<- $12,475>
Mean post-treatment monthly economic benefit per month per individual	<- $1,382>
Net economic benefit per first treatment episode	$13,116
Treatment cost per first treatment episode	$2,699
Benefit-cost ration (economic benefits per episode/treatment cost per episode)	$4.86

of OTPs In U.S.

Total # of programs > 1250 (@ 80 in Maryland)

Total # of patients treated> 300,000 (@30,000 in Maryland)



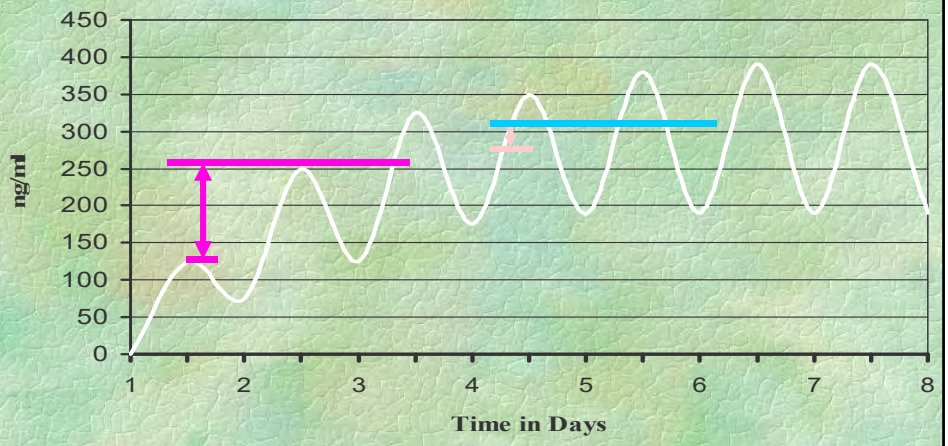
METHADONE DOSING

- **Prevent withdrawal symptoms**
  - **-usually 20-50mg/day**
- **Reduce drug craving**
  - **-usually 50-70mg/day**
- **Block the effects of other opioids**
  - **-usually >70mg/day**
- **Optimal blood levels 150-600ng/ml**
- **Higher dose (70-100mg/day) more effective than lower (40-60mg/day)**

Common Dosing Issues

- Induction
- Stabilization- After induction period
- Over sedation
- New onset of withdrawal in a previously stable patient
- Planned new medication
- Missed doses
- Vomited doses

INDUCTION & "STEADY STATE"

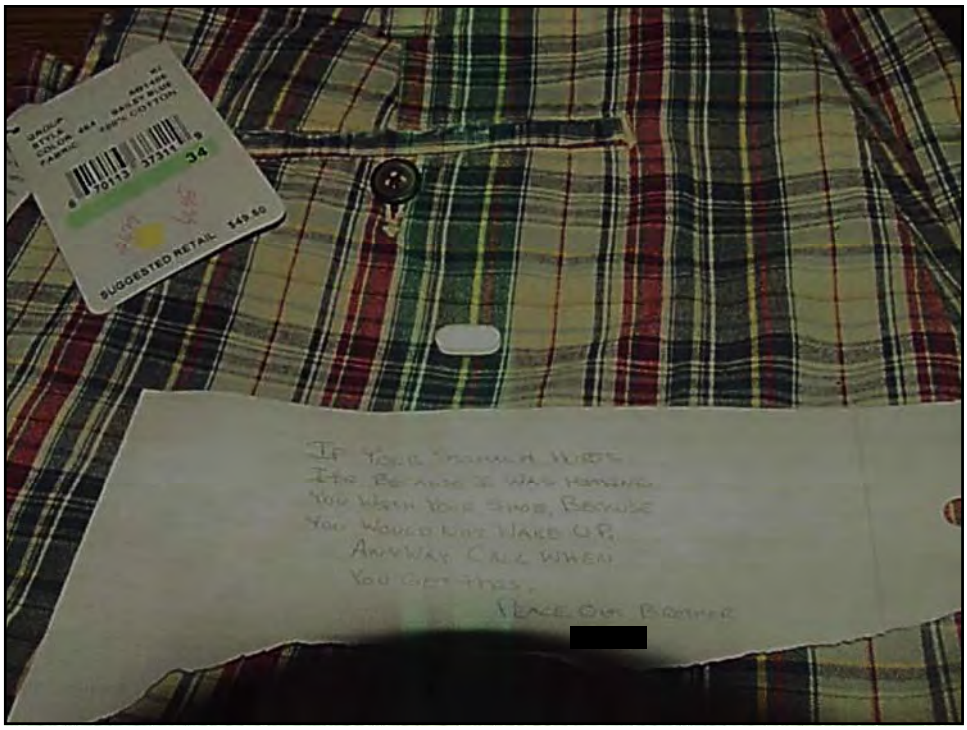


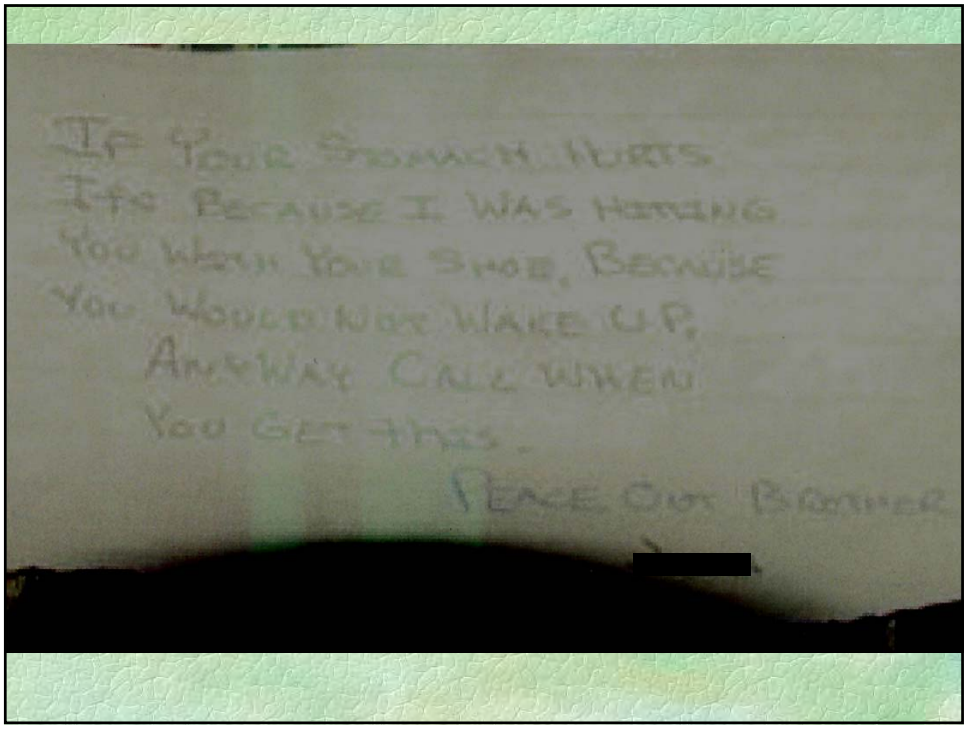
Days/ Half-lives- Methadone half-life = 24-36 hours. Build-up peak SMLs days 1,2, & 3 v. days 4,5, & 6. Dose remains at 30 mg daily. Peak levels increase daily for 5-7 days with NO increase in dose!

J. Thomas Payte MD

Chronic Medical Conditions That May Influence Dose

- **"Older Age"**
- **Cardiac/Syncope History**
- **Cirrhosis and Other Liver Disease**
- **Respiratory Problems and Lung Disease**
- **Endocrine Disorders**
  - **Male & Female patients**
- **Sleep Problems**
  - **Especially sleep apnea**
- **Disabilities**
- **Acute and Chronic Pain**





COMMON SIDE EFFECTS OF METHADONE

- **Generally go away in months:**
  - **-nausea**
  - **-drowsiness**
  - **-headache**
  - **-skin rash**
- **May persist for several years:**
  - **-constipation**
  - **-diaphoresis**
  - **-decreased libido**
  - **-appetite alterations**
  - **-insomnia/nightmares**

METHADONE METABOLISM

- Primarily by CYP3A4
- No active metabolites
- May be increased as a result of stress
- Some patients are “rapid metabolizers”

INCREASE METHADONE METABOLISM

- Rifampin/Rifabutin
- Phenytoin
- Phenobarbital
- Carbamazepine
- Nevirapine
- Sustiva
- Ethosuximide
- Ethanol (chronic)

DECREASE METHADONE METABOLISM

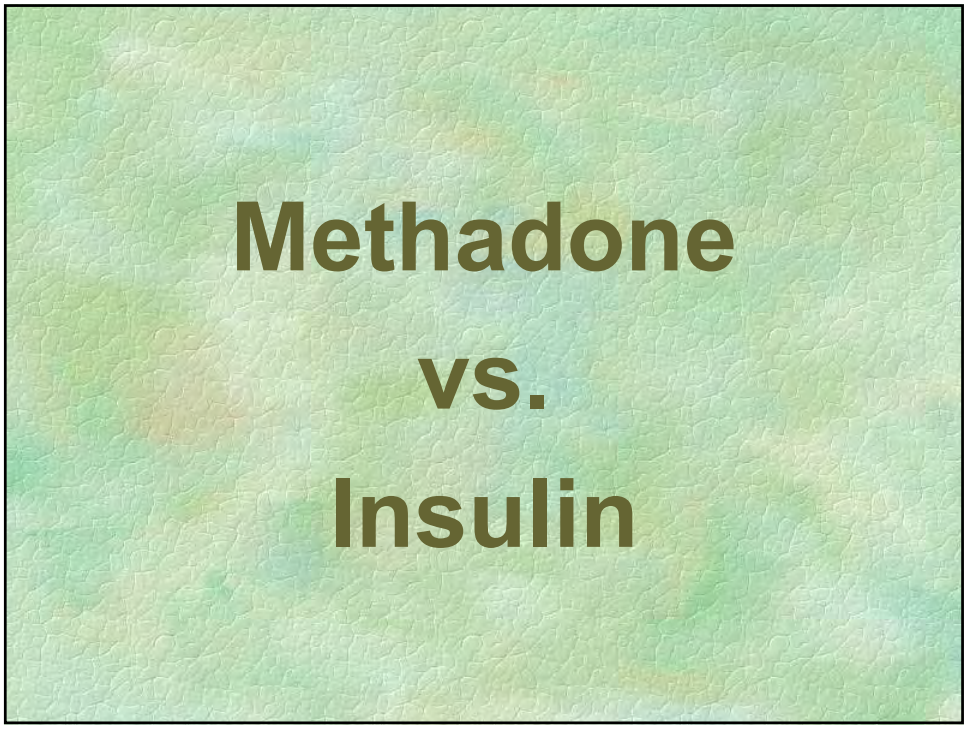
- Delaverdine
- Indinavir
- Ritonavir
- Saquinavir
- Fluconazole/Ketoconazole
- Omeprazole
- Metronidazole
- Erythromycin/Clarythromicin
- Ethanol (acute)

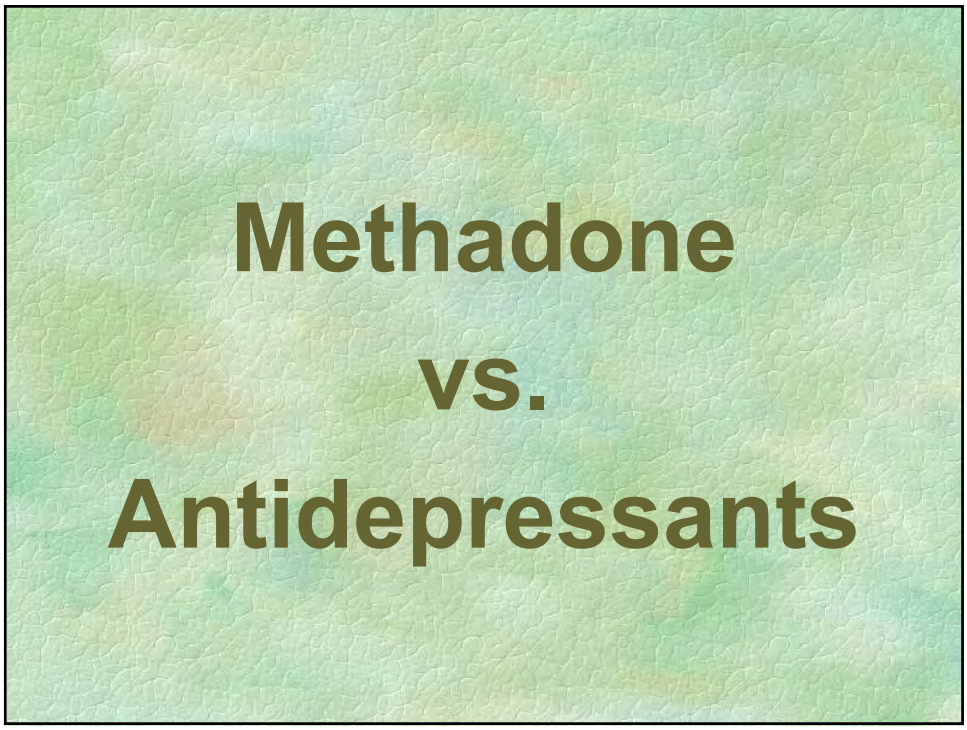
METHADONE DISADVANTAGES

- Fairly high abuse liability & street value
- Necessitates “take home” doses
- Overdose potential in non-tolerant people
- Detoxification from blocking dose may be difficult
- Poor public acceptability
- Very difficult to expand treatment capacity


1001
Active Duty
CARMEN IRIS CAPELES
TREATMENT CENTER
NEW LIFE
EVANGELICAL
BAPTIST CHURCH
"OPEN ACCESS" to Treatment - Opening Soon
IN and OUT - 15 Minutes !!!
Determined To Lift Up JESUS !
BH HEALTH SERVICES


WE ARE THE
10,000
WE ARE THE
10,000
WE ARE THE
10,000
A METHADONE
CLINIC DOES
NOT BELONG IN ANY
METHADONE CLINICS
IN FOCUS
NEIGHBORS CONCERNED ABOUT SATURATION
abc 2
HAPPENING NOW
METHADONE CLINIC BAD FOR BUSINESS?
HAMPDEN MERCHANTS WANT FACILITY TO MOVE
abc
6:04


Methadone
vs.
Insulin


Methadone
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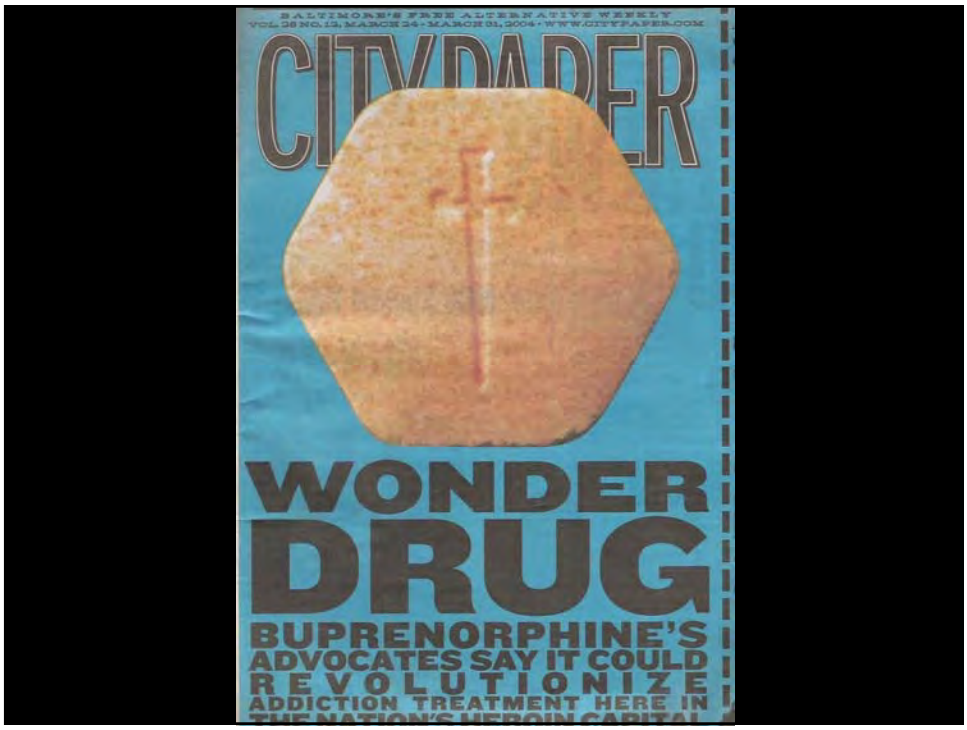
Antidepressants


CITYPAPER
WONDER
DRUG
BUPRENORPHINE'S
ADVOCATES SAY IT COULD
REVOLUTIONIZE
ADDICTION TREATMENT HERE IN

BUPRENORPHINE PHARMACOLOGY

- Extremely high affinity for opioid receptors
- Opioid antagonist effect equal to naloxone
- 0.3mg=10mg morphine in analgesic effects
- Absorption depends on route of administration
- Dissociates very slowly from receptors
- Duration of action independent of half-life
  - -analgesic effects up to 6 hours
  - -antagonist effects up to 30 hours

BUPRENORPHINE FORMULATIONS

Buprenex-for pain only

Butrans/Belbuca-for pain only

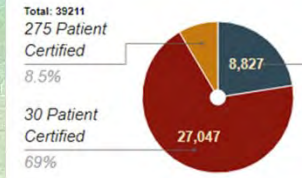
Subutex-for opioid addiction only

Suboxone-for opioid addiction only

-combination pill/film/buccal "patch" w/ naloxone

Bup Providers U.S.

Physician and Program Data



Learn how SAMHSA evaluates the buprenorphine waiver program under the Drug Addiction Treatment Act of 2000 (DATA 2000) and tracks the number of DATA-certified physicians.

Time Frame	30 Cert	%	100 Cert	%	275 Cert	%	Total
Past 30 days	1,319	84	147	9	106	7	1,572
Past 60 days	1,886	79	279	12	215	9	2,380
Past 90 days	3,354	83	393	10	318	8	4,065
Last Year	7,367	59	1,707	14	3,337	27	12,411
Current	27,047	69	8,827	23	3,337	9	39,211

As of July 31, 2017

SAMHSA

SUBOXONE PHARMACOLOGY

If taken under tongue, predominant buprenorphine effect

If opioid dependent person dissolves and injects, predominant naloxone effect (and precipitated withdrawal)

Naloxone will block buprenorphine's effects by the IV but not the sublingual route

Sublingual absorption:

buprenorphine @ 70%

naloxone @ 10%

SUBOXONE: CLINICAL IMPLICATIONS

- **Buprenorphine mono product produces pleasurable effects and would likely be purchased by illicit drug users**
- **Naloxone when combined with buprenorphine attenuates euphoric effect**
- **Buprenorphine/naloxone should decrease abuse liability in untreated opioid-dependent individuals**

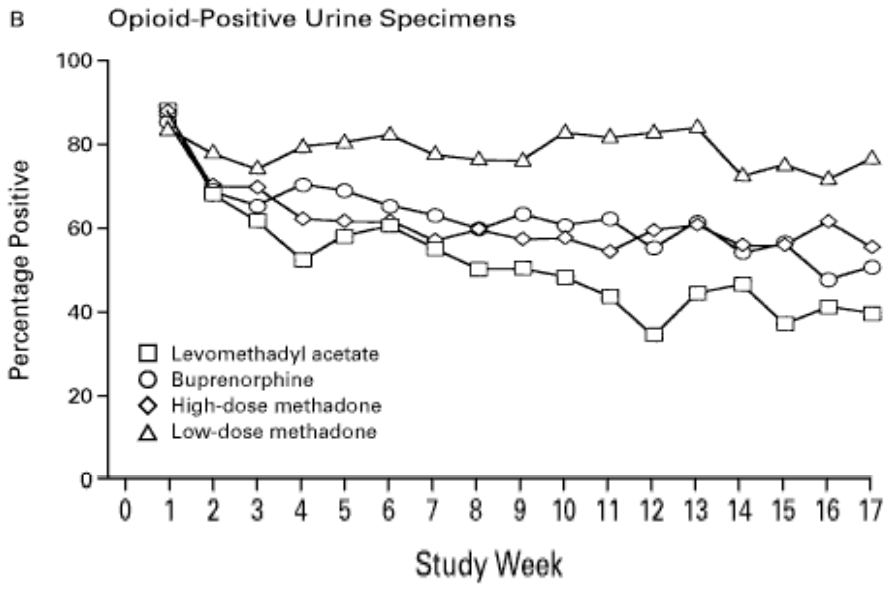
MAINTENANCE TREATMENT USING BUPRENORPHINE

- **Numerous outpatient clinical trials comparing efficacy of daily buprenorphine to placebo, and to methadone**

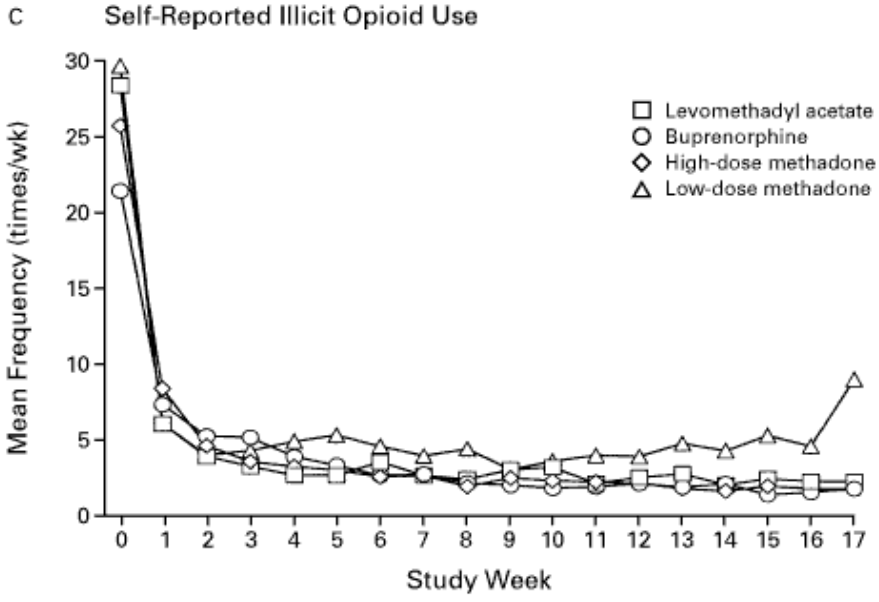
- **Consistently find:**

  Buprenorphine more effective than placebo

  Buprenorphine equally effective as moderate doses of methadone (e.g., 60 mg per day)



Johnson RE,et al.NEJM. (2000)



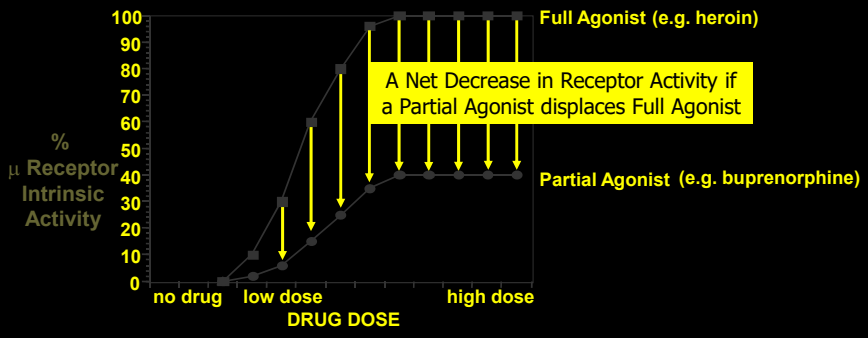
Johnson RE,et al.NEJM. (2000)

BUPRENORPHINE SAFETY

- Highly safe medication
- Primary side effects: like other mu agonist opioids but may be less severe
- No evidence of significant disruption in cognitive or psychomotor performance
- No evidence of organ damage with chronic dosing
- Possible mild increase in LFTs for patients with hepatitis

PRECIPTATED WITHDRAWAL

- Displaces full agonist off μ receptors



NALTREXONE

- ***mu*** **opioid receptor antagonist**
- **Only works if you take it!**
  - **-should be observed**
  - **-should be dispensed as part of a comprehensive treatment program**
  - **-works well with professionals & probationers**
- **Generally very well tolerated**
- **Allows patient to function without constraints of a clinic**
- **Long-acting injection now approved for opioid**
- **No abuse potential**

VIVITROL

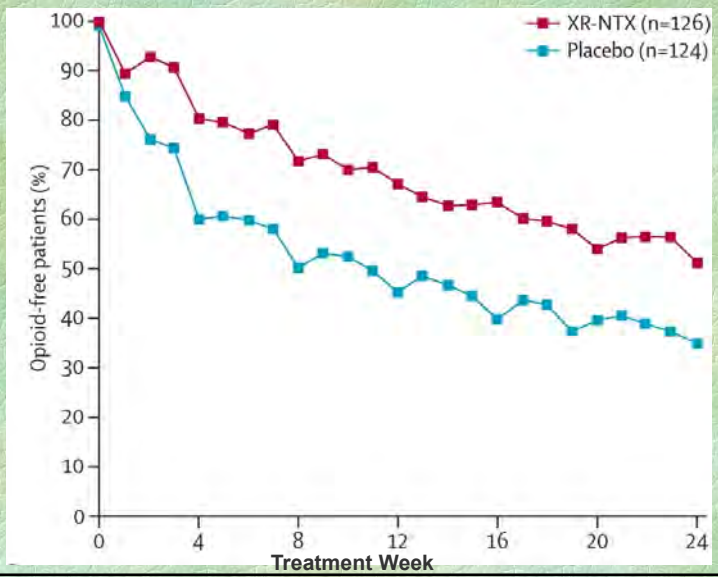
VIVITROL

VIVITROL (naltrexone for extended-release injectable suspension) is supplied in single use cartons.

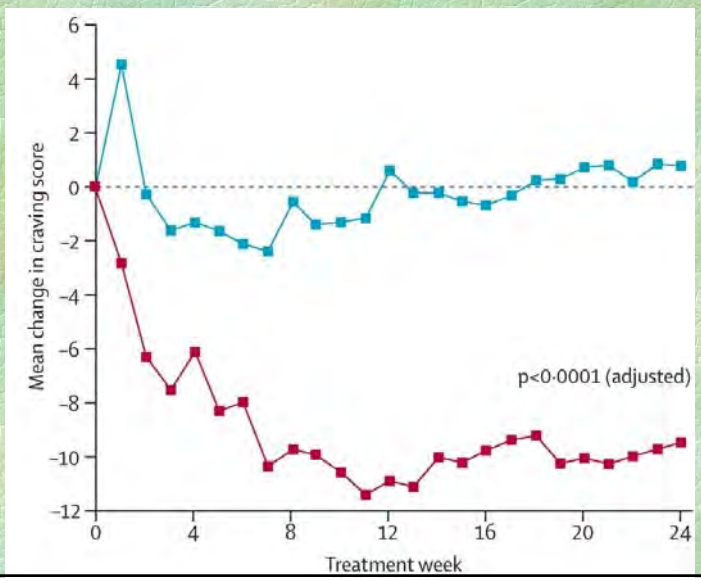
Carton Contents:

- 1 - Package Insert / Directions for Use
- 1 - Patient Package Insert
- 1 - Diluent for the Suspension of VIVITROL Microspheres
- 1 - Vial Containing VIVITROL Microspheres
- 1 - Prepackaged Syringe
- 2 - 1½ inch 20G Administration Needles with Safety Device [one spare]
- 1 - ½ inch 20G Preparation Needle [Not For Administration]

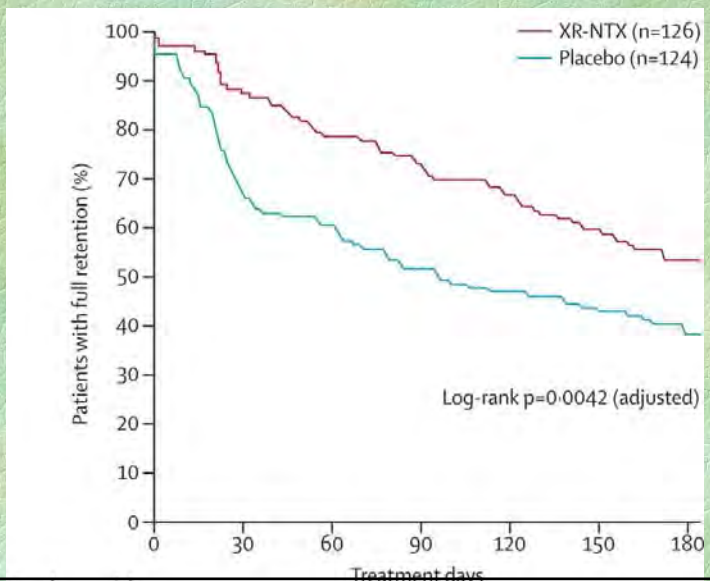
VIVITROL: EFFICACY



VIVITROL: EFFICACY



VIVITROL: EFFICACY



MONITORING FOR DIVERSION/ADHERANCE

- Checking PDMP
- Random call-backs with pill counts
- Urine toxicology
- Patient Agreements
- COORDINATION OF CARE

'So this is how he knows if we've been bad or good!...'

“Opiate” Screens

- Designed to detect heroin use, not adherence to therapeutic opioid regimen
- Heroin metabolized to 6-MAM, then morphine
  - Morphine in urine not proof of heroin use
    - Codeine metabolized to morphine
    - Morphine use or abuse
    - Morphine from poppy seeds addressed by cutoff change from 300 to 2000 ng/mL
  - 6-MAM is absolute proof of heroin use
- Street heroin often contaminated with codeine
- Heroin addicts occasionally abuse codeine

6-MAM=6-monoacetylmorphine


ANYTIME, ANYWHERE... LET IT FLOW!
ORIGINAL
The WHIZZINATOR 2000
•UNDETECTABLE!
•FOOLPROOF!
•RE-USABLE!
COMES IN NATURAL, LIFELIKE SKIN TONES
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FOR URINATOR PURCHASERS $10.00 EACH
THC TEST KITS $10.00
add $5.00 ground, $10.00 second day, $16.00 overnight

URINE TESTING

Why conduct urine drug testing?

- Drug abuse & dependence are chronic disorders relapse can occur
- Patients may deny or minimize use
- Urine testing an integral part of on-going evaluation and treatment planning
- **Not** to punish the patient

URINE TESTING

Different laboratory methods for drug testing

- Enzyme immunoassay (EIA)
- Gas chromatography/mass spectrometry

URINE TESTING

Urine toxicology detection time limits

Amphetamine	**2-4 days**
Benzodiazepines	**1-10 days**
Cocaine	**1-3 days**
Heroin/morphine	**1-3 days**
Methadone	**1-4 days**
Marijuana	**1-30 days**
PCP	**3-30 days**

INTERPRETATION OF UDT RESULTS

- Immunoassays report each sample as positive or negative for particular drug/class
  - Based on predetermined cutoffs
- Positive UDT results
  - Reflect recent drug use
  - Cannot determine exposure time, dose, or frequency of use

Wolff K, et al. *Addiction*. 1999;94:1279-98.
Vandevenne M, et al. *Acta Clinica Belgica*. 2000;55:323-33.

PRACTICAL MEDICATION ISSUES

- Remember that
  - Pts. With Opioid Use Disorder will have a higher tolerance and may require higher doses of opioids to control pain
  - Changes to the opioid system seen with chronic opioid use tend to make people more sensitive to pain
  - Attempt to get patient on appropriate standing dose of opioid and use limited prn's

PRACTICAL MEDICATION ISSUES

- If pt. is on a methadone program:
  - Remember that they are tolerant and will need opioid in addition to their regular methadone dose
  - Generally better to keep pt. on the regular methadone dose and add opioid to that to treat pain
  - Call the methadone program to confirm the dose and let them know the patient has been hospitalized

PRACTICAL MEDICATION ISSUES

- If patient is “in recovery”:
  - Remember the risk of relapse if patient is exposed to an opioid
  - Remember the risk of relapse if patient’s pain is inadequately treated

EXCEPTIONS TO THE CONTROLLED SUBSTANCES ACT

- **Pain Management Exception:**

  May administer or dispense narcotic drugs, including methadone, in a hospital for the management of pain. **The order/prescription must specify “FOR PAIN” and the dose must be split.**
- **Incidental Exception:**

  May administer or dispenses narcotic drugs in a hospital to maintain or detoxify a person” if such action is incidental adjunct to medical or surgical treatment of conditions other than addiction.”
- **Relief of Acute Withdrawal Symptom Exception:**

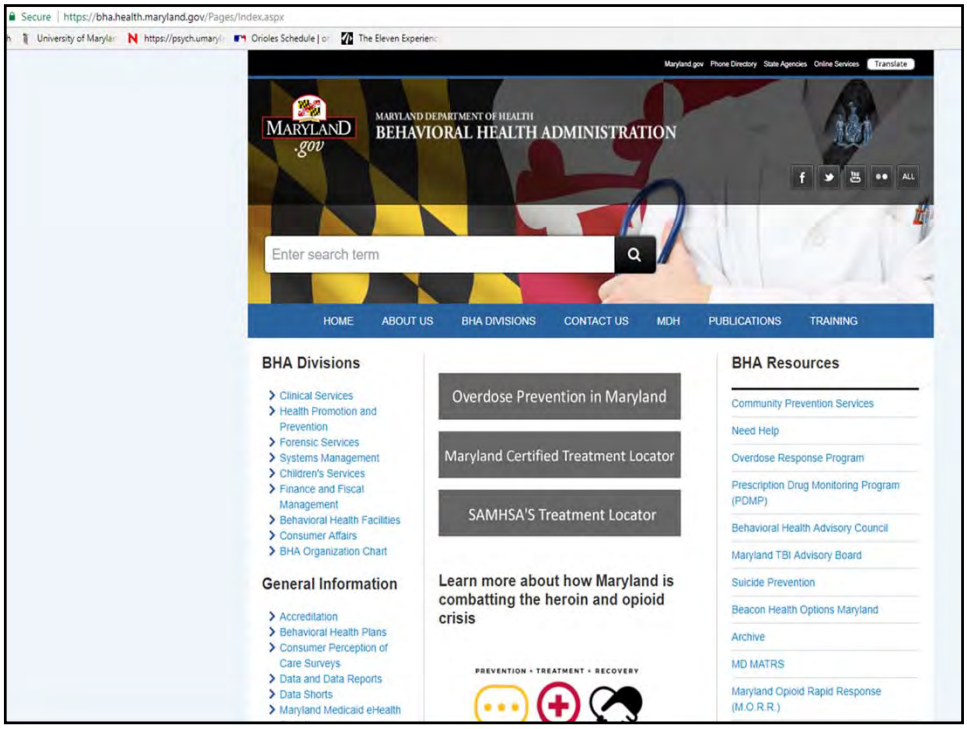
  May administer (<u>but not prescribe</u>) narcotic drugs “to a person for the purpose of relieving acute withdrawal symptoms when necessary while arrangements are being made for referral to treatment.”
  -no more than one day’s medication at one time
  -may not last for more than 3 days

  This exception applies in out-patient & Emergency Dept. settings.

METHADONE BUPRENORPHINE & PREGNANCY

- Less risk to the fetus than heroin
- Less adverse pregnancy outcomes
- Less adverse birth outcomes
- Less chance that mother will contract STDs, endocarditis, cellulitis, etc.
- Less chance that mother will get shot, stabbed, beaten, arrested, etc.
- Neonatal abstinence syndrome (NAS) is relatively easy to manage

Heroin Assisted Treatment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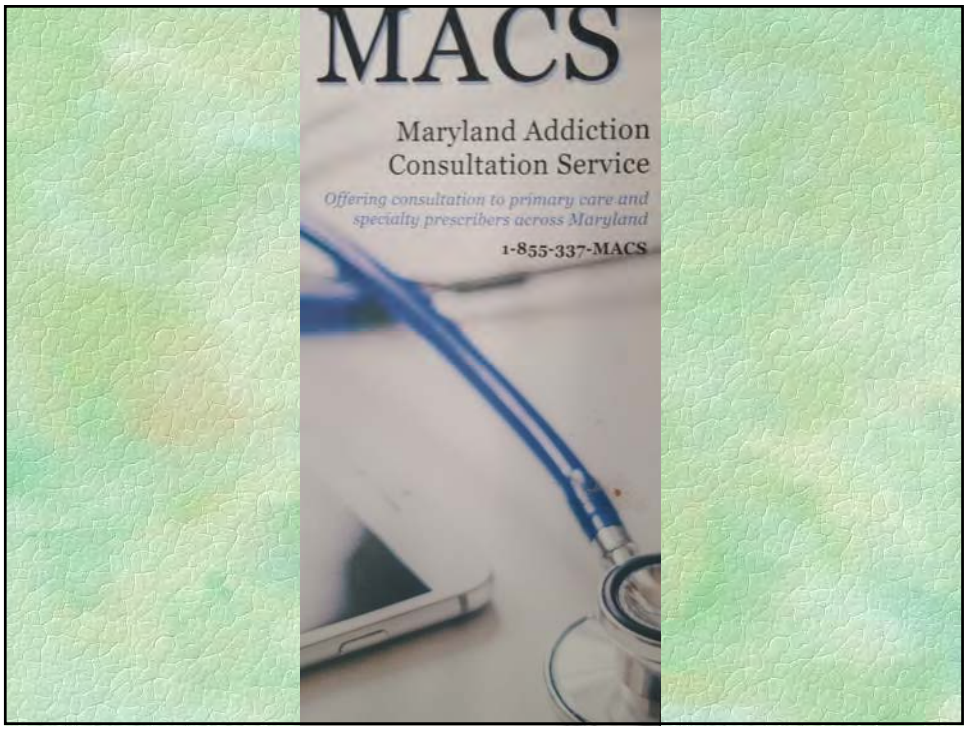
Consumer Affairs
BHA Organization Chart
General Information
Accreditation
Behavioral Health Plans
Consumer Perception of Care Surveys
Data and Data Reports
Data Shorts
Maryland Medicaid eHealth
Overdose Prevention in Maryland
Maryland Certified Treatment Locator
SAMHSA'S Treatment Locator
Learn more about how Maryland is combatting the heroin and opioid crisis
PREVENTION • TREATMENT • RECOVERY
BHA Resources
Community Prevention Services
Need Help
Overdose Response Program
Prescription Drug Monitoring Program (PDMP)
Behavioral Health Advisory Council
Maryland TBI Advisory Board
Suicide Prevention
Beacon Health Options Maryland
Archive
MD MATRS
Maryland Opioid Rapid Response (M.O.R.R.)


MACS
Maryland Addiction Consultation Service
Offering consultation to primary care and specialty prescribers across Maryland
1-855-337-MACS

NOTES

MARYLAND MEDICAID'S Opioid DUR and SUD Initiatives

Lisa A. Burgess, M.D.
Chief Medical Officer, Health Care Financing
October 14, 2017

MARYLAND Department of Health

Disclosures

NONE

MARYLAND Department of Health

Overview

1. Introduction
2. Maryland's Opioid Legislative Update
3. Maryland Medicaid's Initiatives
4. Resources

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Objectives

1. To learn about Maryland's Opioid Legislation
2. To learn about Maryland Medicaid's Opioid Drug Utilization Review (DUR) Policies and Preliminary Outcomes
3. To learn about Maryland Medicaid's Substance Use Disorder (SUD) Initiatives and Outcomes

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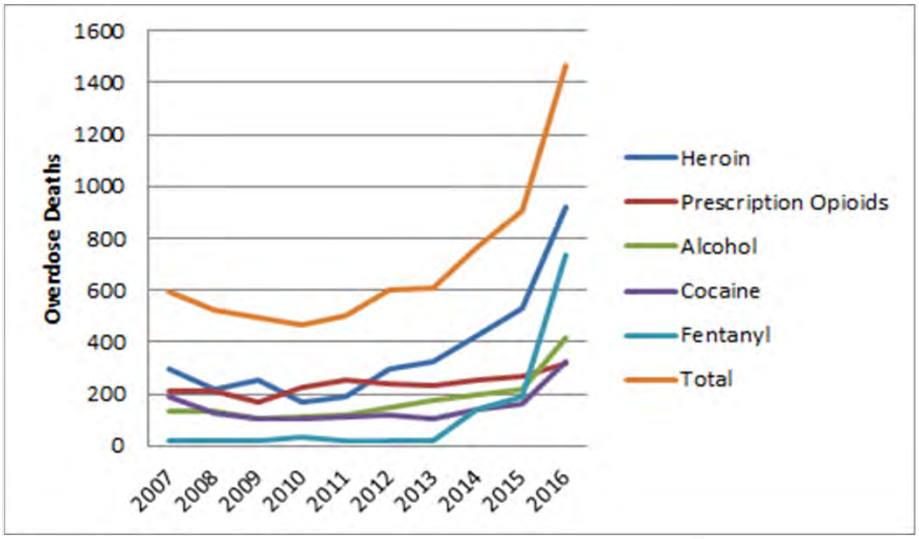
Maryland Medicaid
DUR Initiatives


Opioid Overdose
Epidemic Overview
(MARYLAND'S EXPERIENCE)

Maryland Overdose Deaths by Drug Class 2007-2016*



Opioid Legislative Update

- Heroin and Opioid Education and Community Action Act of 2017 *(HB 1082/SB 1060 Start Talking Maryland Act)*
- Heroin & Opioid Prevention Effort (HOPE) & Treatment Act of 2017 *(SB 967/HB 1329)*
- Health Insurance – Prior Authorization for Drug Products to Treat an Opioid Use Disorder – Prohibition *(HB 887)*
- Health Care Providers – Prescription Opioids – Limits on Prescribing (*HB 1432 The Prescriber Limits Act of 2017*

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Why Target Medicaid?

- Over 20% of Marylanders enrolled in Medicaid
- Statewide reach
- 6 of 8 MCOs are integrated provider and payer networks
- **816 (65%)** of opioid overdose deaths in 2015 were enrolled in Medicaid at any point after January 1, 2011. Of that amount **691 were enrolled in Medicaid at some point during CY 2015.**
  - 67.5% of participants were male
  - The majority of participants were **white (61.9%) or African American (29.2%).**
  - **Most participants lived in suburban Baltimore (35%), Baltimore City (33.1%), and Western Maryland (10.5%)**

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DUR Opioid Workgroup

- DUR Opioid Workgroup consisted of MDH's policy and clinical teams and all 8 Medicaid MCOs.
- The Workgroup met throughout last year (2016) to build consensus around a set of prescribing policies to be implemented July 1, 2017.
- Policies take into consideration the 12 recommendations in the CDC Guidelines for Prescribing Opioids for Chronic Pain.
- MDH prescribing policies (for Medicaid recipients) aim to :
  - Prevent non-medical opioid use, opioid abuse and dependence, over prescribing of opioids;
  - Identify and treat opioid dependence early in the course of the disease;
  - Prevent medical situations that arise from dependence and overdose;
  - Identify and outreach to providers who have patients on high risk opioid prescriptions

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Maryland Medicaid Prescribing Policies

- **Policy 1:** Improve coverage for first line treatment like non-pharmacologic and non-opioid medication treatment
- **Policy 2:** Obtain Prior Authorization for Opioids every 6 months
  - Above 90 MME/day
  - All Long Acting Opioids, Fentanyl, and Methadone for Pain
  - High Quantity (anything above the 30-day quantity limit) - Even if <90 MME/day
- **Policy 3:** Screen for SUD before prescribing opioids and controlled substances
  - (i.e.) SBIRT = Screening, Brief Intervention and Referral to Treatment
- **Policy 4:** Refer patients with SUD to treatment
  - Maryland Medicaid offers BH services via Beacon Health Options
- **Policy 5:** Prescribe naloxone to high risk patients
- **Policy 6:** Check PDMP prior to prescribing (HB437 / Chapter 147, 2016)
  - Highly recommended for Medicaid providers. Required for all Maryland CDS prescribers on July 1, 2018.

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DUR Outreach Activities

- **Prescriber notification**
  - 5,000 prescribers were notified of our upcoming policy changes (January/February 2017)
  - Additional round of high-risk prescriber notification occurring at the MCO and FFS level (April through June 2017)
- **Recipient notification**
  - Recipient letters sent out informing them of changes in opioid prescribing (April through June 2017)
- **Webinars**
  - Over 600 providers trained to date
  - Additional webinars for the hospitals are being held in June 2017

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Outreach to Prescribing Boards and Associations

- **Prescribing Boards:** Dental, Nursing, Pharmacy, Physicians & Podiatry
- **Prescriber Associations:** American College of Emergency Physicians; American Academy of Family Physicians; Maryland Association of Osteopathic Physicians; Maryland Academy of Pediatric Dentistry; Maryland Academy of Pediatrics; Maryland State Dental Association; American Academy of Dermatology (Maryland Chapter); American College of Physicians (Maryland Chapter); Maryland Society of Addiction Medicine; Nurse Practitioner Association of Maryland; American College of Obstetricians and Gynecologists; Maryland Society of Eye Physicians and Surgeons; and Mid-Atlantic Society of Oral and Maxillofacial Surgeons

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Outreach to Local Entities and Other Organizations

- Local Addiction Authorities and Core Service Agencies
- Local Health Departments
- Federally Qualified Health Centers
- Pain Connection
- Hospitals - including - Baltimore City and County, Eastern Shore, Southern MD and Western MD

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DUR Opioid Presentations

- Maryland Coalition of Families
- Maryland Hospital Association Quality Council
- Hospitals - MedStar, Johns Hopkins, University of Maryland
- Three pain clinics
- Board of Physicians (Panel A)
- Maryland Drug Utilization Review Committee and Corrective Managed Care Committee
- University of Maryland Pain Management Team
- PDMP Leadership
- Xerox
- Medicaid Advisory Committee
- Maryland Addiction Directors Council
- MedChi
- Opioid Operational Command Center

MARYLAND Department of Health

Overdose Response Program - Naloxone

- Overdose Response Program
  - *State Statute: Health-General §§13-3101-3111, effective Oct. 1, 2013*
  - *State Regulations: COMAR 10.47.08.01-.12, effective March 3, 2014*
- Expands access to naloxone
  - All MD-certified pharmacists may dispense naloxone without a prescription to any certified individual
  - MDH BHA oversees the certification of any individual to recognize and respond to opioid-related overdoses and safely administer naloxone
  - 55 entities authorized to conduct trainings
  - Over 39,000 people trained

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Medicaid Telehealth Program

- Model: “Hub-and-Spoke” Model
- 2015: Streamlined telemedicine and telemental health programs into one “telehealth program”
- 2016: Incorporated methadone clinics and community-based substance use providers into the program
- 54 behavioral health and 6 somatic originating sites

Telehealth Participation

MARYLAND Department of Health

Reimbursement Changes for OTPs

- Maryland Medicaid is rebundling weekly rates for methadone maintenance services to allow Opioid Treatment Programs (OTP) to bill for methadone and outpatient counseling separately.
- Research indicates that methadone and counseling together result in better patient outcomes than treating patients with methadone alone.
- Reimbursement rates were changed to align with clinical best practices.
- New policy also allows for guest dosing in the instance an individual needs medication assisted treatment from an OTP other than the one they normally attend.
- Rates were finalized after about a year of stakeholder feedback and engagement.
- Effective May 15, 2017.

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Residential SUD Treatment

- December 2016, CMS approved Maryland Medicaid 1115 waiver renewal, which included its request to provide IMD services for substance use disorder treatment
  - Waives Medicaid IMD exclusion and allows Maryland Medicaid to offer SUD services in IMDs with more than 16 beds
- With this addition, the program covers ASAM's full continuum of care for SUD treatment
- Effective July 1, 2017, Maryland Medicaid provides reimbursement for up to two nonconsecutive 30-day stays in a rolling year for ASAM levels 3.7 WM, 3.7, 3.5, and 3.3.
- Special populations will be phased in January 2018.
- Coverage will be expanded to ASAM level 3.1 beginning on January 1, 2019.

MARYLAND Department of Health

Resources

MDH Opioid Website
https://mmcp.health.maryland.gov/healthchoice/opioid-dur-workgroup/Pages/medicaid-opioid-response.aspx

MDH Opioid Email
dhmh.opioiddur@maryland.gov

Beacon Health Options Provider Alerts
http://maryland.beaconhealthoptions.com/provider/prv_alerts.html

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NOTES

NOTES

MARYLAND

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Maryland Medicaid Pharmacy Program

201 W. Preston Street
Baltimore, Maryland 21201

http://mmcp.health.maryland.gov

1-800-932-3918