NOW WHAT?
When Opioids Become The Problem

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DISCLOSURE

- I have no relevant financial arrangements with commercial interests to disclose.

OBJECTIVES

PART I: Recognizing A Problem
- Identify patients who will benefit from an opioid taper.
- Contrast opioid addiction vs. dependence.
- Discuss the neurobiology of addiction.

PART II: Tapering
- Review basic guidelines for tapering opioids.
- Discuss communication strategies for managing patients expectations during the tapering process.

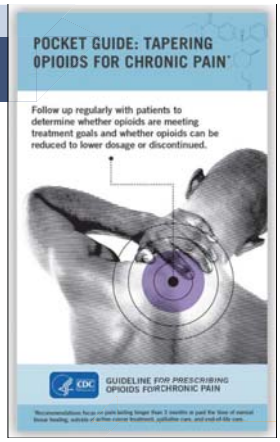
PART III: The Fear of Withdrawal
- Identify the opioid withdrawal syndrome.
- Review management options for opioid withdrawal.

PART III: Buprenorphine As An Adjunct Therapy
- Define complex persistent opioid dependence.
- Review the COWS scale and buprenorphine induction protocols.

1
Recognizing A Problem

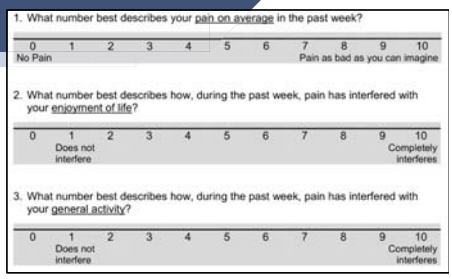
Who?

- Who is included:
  - Pain > 3 months or past the time of normal tissue healing.
  - Exclusions→ active cancer treatment, palliative care, end-of-life care.

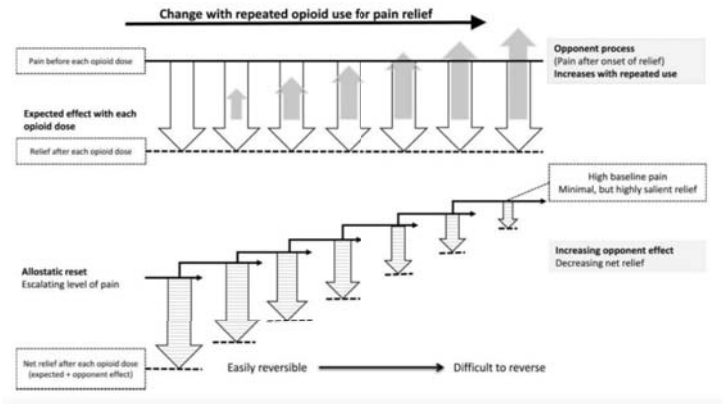


When?

- Requests dosage reduction.
- No clinically meaningful improvement in pain & function.
- Dose ≥ MME/day
- Opioids + Benzodiazepines
- Experiences OD or adverse event.
- Signs of opioid use disorder



PEG Scale
(Pain, Enjoyment, General Activity)



Why?

> *"Addiction is a brain disease. This is not a moral failing. This is not about bad people who are choosing to continue t use drugs because they lack willpo*

Michael Botticelli

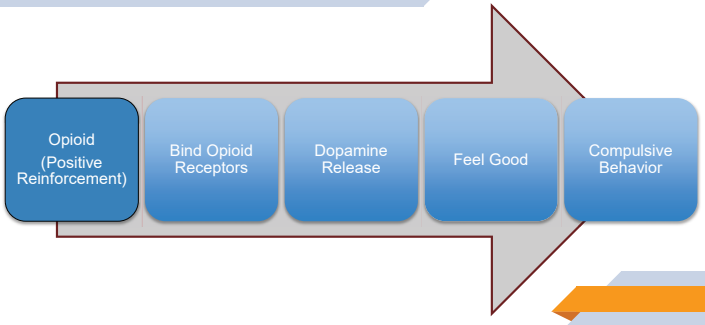
DEPENDENCE

- Frequent & repeated use of opioids leads to structural/physiological changes in the brain.
  - Normal brain function requires the presence of opioids.
- Drug withdrawn → withdrawal syndrome.
- **Physical dependence can occur without addiction!**

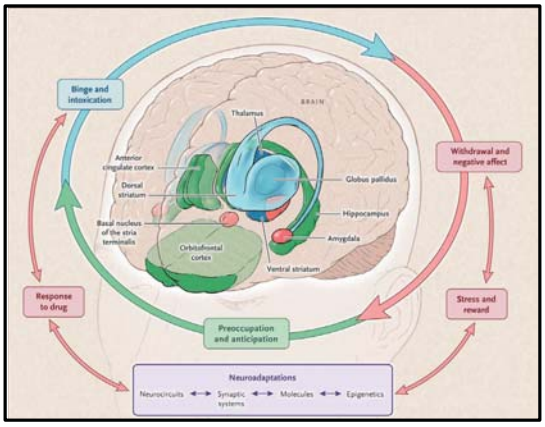
ADDICTION

- A **primary, chronic disease** of brain reward, motivation, memory, and related circuitry.
- Characterized by **compulsive drug seeking & use despite harmful consequences.**
- Involves **cycles of relapse and remission.**

Addiction: The Reward Pathway

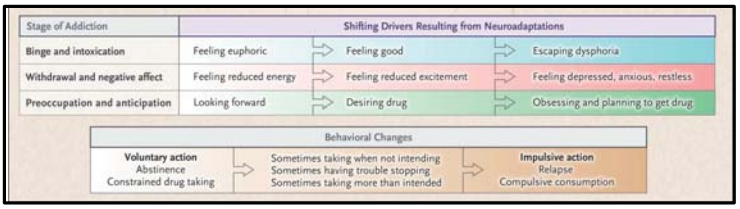


Brain Disease Model of Addiction



Volkow ND, Koob GF, McLellan AT. Neurobiologic Advances from the Brain Disease Model of Addiction. NEJM. 2016;374:363-371.

Neuroadaptation



Stage of Addiction	Shifting Drivers Resulting from Neuroadaptations		
Binge and intoxication	Feeling euphoric	Feeling good	Escaping dysphoria
Withdrawal and negative affect	Feeling reduced energy	Feeling reduced excitement	Feeling depressed, anxious, restless
Preoccupation and anticipation	Looking forward	Desiring drug	Obsessing and planning to get drug

Behavioral Changes		
Voluntary action Abstinence Constrained drug taking	Sometimes taking when not intending Sometimes having trouble stopping Sometimes taking more than intended	Impulsive action Relapse Compulsive consumption

Volkow ND, Koob GF, McLellan AT. Neurobiologic Advances from the Brain Disease Model of Addiction. NEJM. 2016;374:363-371.

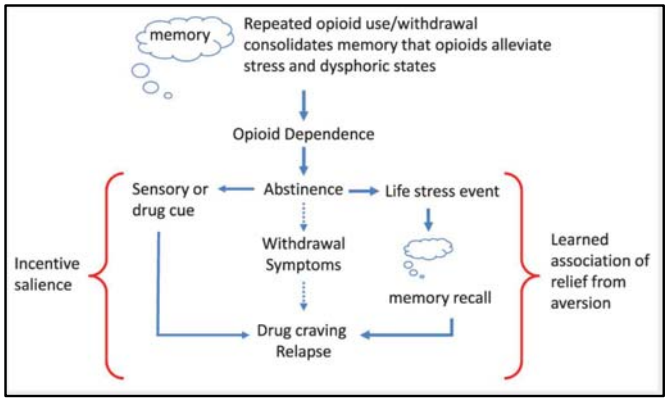


Table 1. Diagnostic Criteria for an Opioid-Use Disorder.*

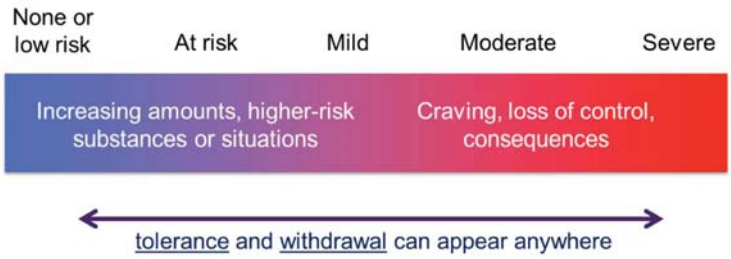
Use of an opioid in increased amounts or longer than intended
Persistent wish or unsuccessful effort to cut down or control opioid use
Excessive time spent to obtain, use, or recover from opioid use
Strong desire or urge to use an opioid
Interference of opioid use with important obligations
Continued opioid use despite resulting interpersonal problems, social problems (e.g., interference with work), or both
Elimination or reduction of important activities because of opioid use
Use of an opioid in physically hazardous situations (e.g., while driving)
Continued opioid use despite resulting physical problems, psychological problems, or both
Need for increased doses of an opioid for effects, diminished effect per dose, or both†
Withdrawal when dose of an opioid is decreased, use of drug to relieve withdrawal, or both†

Schuckit MA. Treatment of opioid use disorders. NEJM. 2016;375:357-368

DSM-V Criteria

Triad:
- Loss of Control
- Physiologic Changes
- Consequences

Severity:
2-3 = Mild
4-5 = Moderate
6+ = Severe



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Tapering

How?

Chou R, Ballantyne J, Lembke A. Rethinking Opioid Dose Tapering, Prescription Opioid Dependence, and Indications for Buprenorphine. Ann Intern Med. [Epub ahead of print 27 August 2019]171:427–429. doi: 10.7326/M19-1488

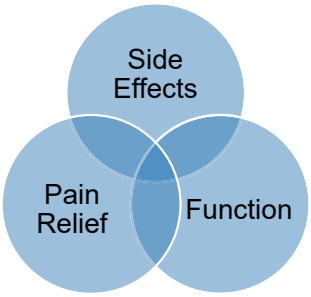
The Bravo Protocol

B = Broaching The Subject
R = Risk-Benefit Calculator
A = Addiction Happens
V = Velocity Matters (And So Does Validation)
O = Other Strategies For Coping With Pain

Broaching The Subject

- Suggesting an opioid taper can trigger anxiety (or terror).
- Identify this feeling for patients, normalize it, and express empathy.
- Make clear that an opioid taper was carefully considered, not impulsive, nor punitive.

Risk-Benefit Calculator



Addiction Happens

Velocity Matters

- ↓ by 5-10% of the starting dose every 1-2 weeks.
- Keep same dosing schedule.
- It's okay to take breaks in the taper, but never go backward!
- Continually validate their experience about opioid withdrawal.

Other Strategies For Coping With Pain

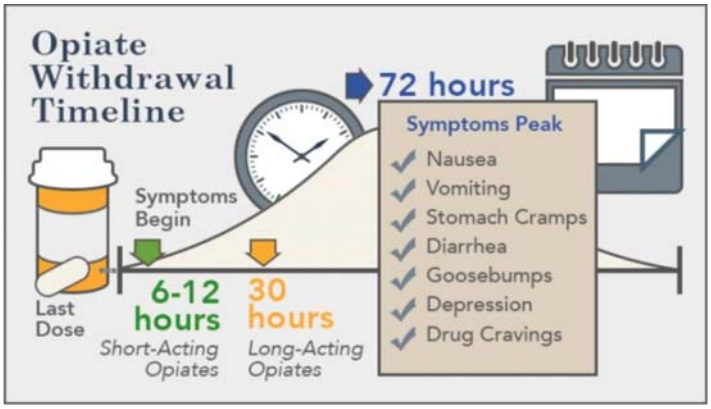
Communication

- Know that the fear of withdrawal can prolong patient's use of opioids.
- Educate on symptoms, how patients may fee and reassurance that it won't last forever.
- Safety is a concern, "We know better, so we need to do better."
- Positive reinforcement & frequent follow up

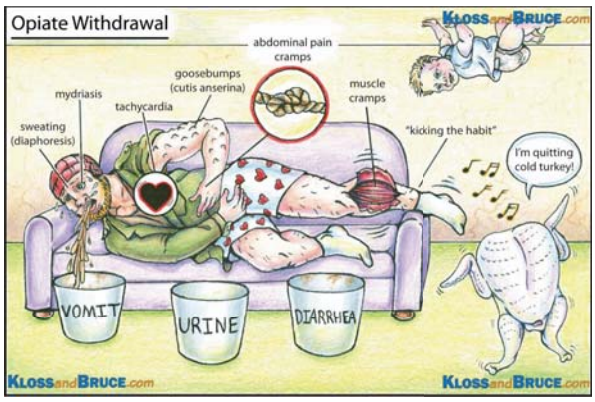
The Fear of Withdrawal

Opioid Withdrawal

- Features of opioid withdrawal reflect sympathetic activity and physiologic changes secondary to dependence *SAMHSA 2018*



Opioids used	Onset of withdrawal	Symptoms peak	Duration of withdrawal
Short-acting opioids (e.g. heroin, oxycodone)	6-12 hours	36-72 hours	about 5 days
Long-acting opioids (e.g. methadone)	36-48 hours	~ 72 hours	up to 3 weeks



COWS:
Clinical Opioid Withdrawal Scale

- Can be added to flowsheets tab in Excellian.
- 11 Item Scale
- Typically don't exceed lowest without objective findings.
- Increase points for symptom severity.
  - Scoring:
    - Mild = 5-12
    - Moderate = 13-24
    - Severe 25-36

J Psychoactive Drugs. 2003 Apr-Jun;35(2):253-9.

The Clinical Opiate Withdrawal Scale (COWS).

Wesson DR[1], Ling W.

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying for one minute* 0 Pulse rate 80 or below 1 Pulse rate 81-100 2 Pulse rate 101-120 4 Pulse rate greater than 120	GI Upset: *over last 1/2 hour* 0 No GI symptoms 1 Stomach cramps 2 Nausea or loose stool 3 Vomiting or diarrhea 5 Multiple episodes of diarrhea or vomiting
Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.* 0 No report of chills or flushing 1 Subjective report of chills or flushing 2 Flushed or observable moistness on face 3 Beads of sweat on brow or face 4 Sweat streaming off face	Tremor *observation of outstretched hands* 0 No tremor 1 Tremor can be felt, but not observed 2 Slight tremor observable 4 Gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 Able to sit still 1 Reports difficulty sitting still, but is able to do so 3 Frequent shifting or extraneous movements of legs/arms 5 Unable to sit still for more than a few seconds	Yawning *Observation during assessment* 0 No yawning 1 Yawning once or twice during assessment 2 Yawning three or more times during assessment 4 Yawning several times/minute
Pupil size 0 Pupils pinned or normal size for room light 1 Pupils possibly larger than normal for room light 2 Pupils moderately dilated 5 Pupils so dilated that only the rim of the iris is visible	Anxiety or irritability 0 None 1 Patient reports increasing irritability or anxiousness 2 Patient obviously irritable anxious 4 Patient is irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 Not present 1 Mild diffuse discomfort 2 Patient reports severe diffuse aching of joints/ muscles 4 Patient is rubbing joints or muscles and is unable to sit still because of discomfort	Gooseflesh skin 0 Skin is smooth 3 Piloerrection of skin can be felt or hairs standing up on arms 5 Prominent piloerrection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 Not present 1 Nasal stuffiness or unusually moist eyes 2 Nose running or tearing 4 Nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing Assessment:_____

Score: 5-12 mild; 13-24 moderate; 25-36 moderately severe; more than 36 = severe withdrawal

Why Treat Withdrawal Symptoms?

- Help patient to have a successful taper/withdrawal experience.
- Due to physical dependence, nearly all patients may experience symptoms of withdrawal.
- Will complicate attempts to taper.

Symptom	Medications	Dose and Route	Notes
Restlessness, sweating or tremors	Clonidine Lofexidine	0.1-0.2 mg orally every 6 hours or transdermal patch 0.1-0.2 mg weekly 0.54 mg QID first day, then taper off over the next 2-4 days	Monitor for significant hypotension
Nausea	Ondansetron Prochlorperazine	4 mg SL Q6H PRN 10 mg PO Q6H PRN	
Diarrhea	Loperamide dicyclomine	2-4 mg each time PRN	Do not exceed 16 mg/QD
GI Distress	aluminum magnesium hydroxide-simethicone	225-200-25 mg/5mL QID PRN	
Muscle pain, myoclonus	Cyclobenzaprine Methocarbamol	10mg TID PRN 750 mg QID PRN	
Pain	NSAIDs Acetaminophen Gabapentin	OTC Dosing OTC Dosing 100-300mg TID	Evaluate kidney (NSAIDS) and liver (APAP) function before using
Agitation, Anxiety	Vistaril	25 mg Q4H PRN	May also treat lacrimation and rhinorrhea
Insomnia	Nortriptyline Trazodone	25 mg at bedtime 50 mg at bedtime	Do not use benzodiazepines or sedative-hypnotics

Pharmacologic Treatment Options: Opioid Withdraw

Symptom	Intervention
Restlessness, sweating or tremors	Cold packs Fan Showering
Nausea, GI Upset	Ginger (lozenge or inhaler) Tea
Diarrhea	Bland diet Increased clear liquids
Muscle pain, myoclonus	Stretching Showering Heating Pad
Pain	Repositioning Aromatherapy (Mandarin, Spearmint)
Agitation, Anxiety	Reduce stimulation Distraction activities
Insomnia	Lavender Avoid screen time before bed White noise

NonPharmacologic Treatments: Opioid Withdrawa

Evidence Based Facts

- Tapering improves function, quality of life, and pain control.
- Multidisciplinary pain programs have strong clinical efficacy and empirical data supporting their cost-efficiency.
- High quality evidence of safety and comparative efficacy is lacking for ultra-rapid detoxification
- Opioid tapers rarely cause significant and long term increases in pain.
- Office-based buprenorphine treatment can be considered for patients with both chronic pain and opioid use disorder

Buprenorphine As An Adjunct Therapy

Milestones In Treatment

Year	Milestone
1970 1973	Methadone is approved by the FDA for *detoxification* Methadone is approved by the FDA for *maintenance*
1974	Opioid Treatment Programs (OTP's) able to dispense Methadone for maintenance treatment
1984	Oral Naltrexone is approved by the FDA
2000	Drug Addiction Treatment Act of 2000 (DATA 2000) allowed qualified physicians to offer Office Based Opioid Treatment (OBOT)
2002	Buprenorphine is approved by the FDA
2010	Extended-release injectable naltrexone is approved by the FDA
2016	Comprehensive Addiction and Recovery Act (CARA) - Allows Nurse Practitioners and Physician Assistants to become eligible to prescribe buprenorphine for treatment of opioid use disorder

Can I Prescribe It For Pain?

Yes.

"limitations and requirements [relating to addiction treatment] in no way impact ability of a practitioner to utilize opioids for the treatment of pain when acting in usual course of medical practice. Consequently, when it is necessary to discon pain patient's opioid therapy by tapering or weaning doses, there are no restrict with respect to the drugs that may be used. This is not considered detoxificatio is applied to addiction treatment."

Heit H, et al. "Dear DEA." *Pain Medicine*. 2004;5(3):303-308.

Can I prescribe it for addiction?

Yes.

- But you need 8 hours of CME training/certification & a DEA "X" waiver.
- Limited to certain formulations – tablets, SL film, implant.
- Open to NP & PA, but require additional training/CME hours (24 vs. 8).

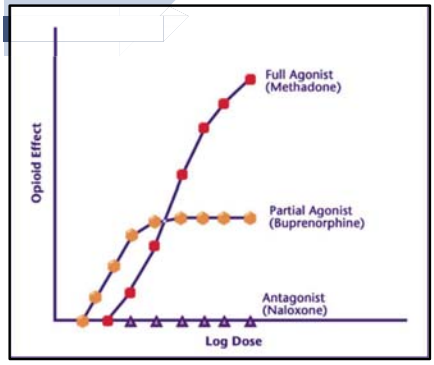
How expensive is it to get the training?

Right now, it's free!

And can be done online!

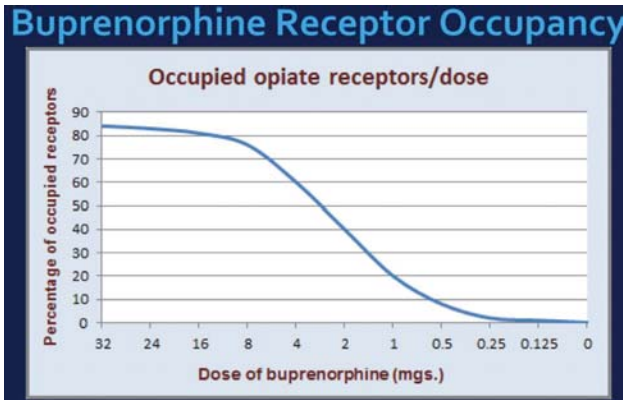
PCSS Providers Clinical Support System

https://pcssnow.org/medication-assisted-treatment/



- Partial Agonist – μ Opioid Receptor
  - Binds with high affinity & dissociates slowly.
  - Blocks other opioids from binding.
  - ↓ respiratory depression
- Weak Antagonist – *k* Opioid Receptor

What is buprenorphine?



Buprenorphine Formulations

Brand Name	Approval Date	Route of Administration	Co-formulated with Naloxone?	FDA Approved Indication(s)
Buprenex	1981	IV, IM	No	Moderate to severe pain
Subutex	**2002**	**SL**	**No**	**Opioid dependence**
Suboxone	**2002**	**SL tablet**	**Yes**	**Opioid dependence**
Suboxone	**2010**	**SL film**	**Yes**	**Opioid dependence**
Butrans	2010	Transdermal	No	Severe pain requiring daily, around-the-clock, long-term opioid treatment for which alternative treatment options are inadequate
Zubsolv	2013	SL	Yes	Opioid dependence
Bunavail	2014	Buccal	Yes	Opioid dependence

Sublocade = Montly SQ Injection

Probuphine = Subdermal Implant

Belbucca = Pain Only

When To Consider Buprenorphine

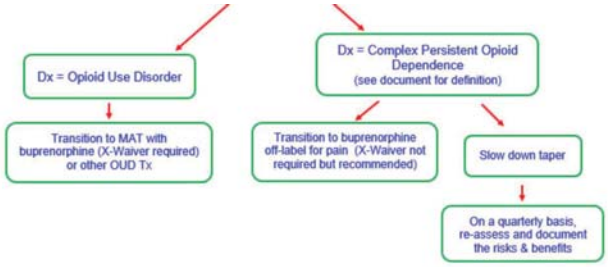
- Meet criteria for opioid use disorder.
- **Complex Persistent Opioid Dependence (CPOD)**
  - Desire to continue taking opioids for treatment of pain.
  - Withdrawal→ anhedonia, sleep disturbance, & hyperalgesia → may not reverse within days.
  - Tapering poorly tolerated.

What Distinguishes CPOD From OUD

- No craving.
- No compulsive use.
- No harmful use that is not medically directed.
  - Patient takes opioid exactly as prescribed.
- Social disruption is attributed to pain and not OUD

BRAVO Protocol Opioid Tapering Flowchart

BRAVO Protocol Opioid Tapering Flowchart



How To Transition

- As a precautionary measure, a factor of 30:1 to 90:1 (morphine milligram equivalents to buprenorphine) is used when converting from other opoiods to buprenorphine.
- Addiction → does not use a conversion factor.
  - Dose is based on need to control cravings and prevent relapse.
- BID dosing for pain may be more effective.

Example Plan

1. 12-48 hours with no opioids to initiate withdrawal.
2. See in clinic; assess for withdrawal (COWS).
3. Discharge with home induction protocol.
   - 2 mg TID PRN daily for the first week (for patients on 150 MEDD or less) .
   - Symptom driven.
   - Withdrawal medications.
4. Nurse check-in during week.

Day #7 FollowUp

1. Assess symptoms, pain control.
   - Dose adjustment?
2. PDMP check.
3. Compliance Drug Screen
4. Refill
5. Weekly/bi-monthly compliance checks & medication refills.

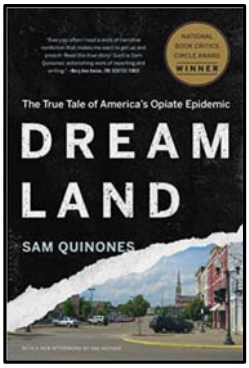
Morphine	Methadone	Buprenorphine
250mg	30	8mg
500mg	40	8-16mg
750mg	60	8-24mg
1000mg MME/Day	80	8-32mg

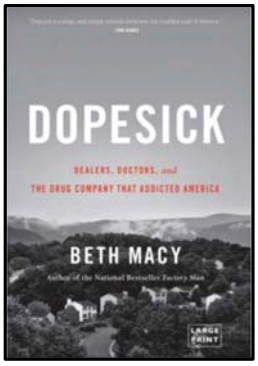
30:1

Example Buprenorphine Calculation: Based On Total Daily M

If this seems too complicated…

Refer to a specialist!





Light Bedtime Reading?