Office-Based Buprenorphine: Tips and Tricks

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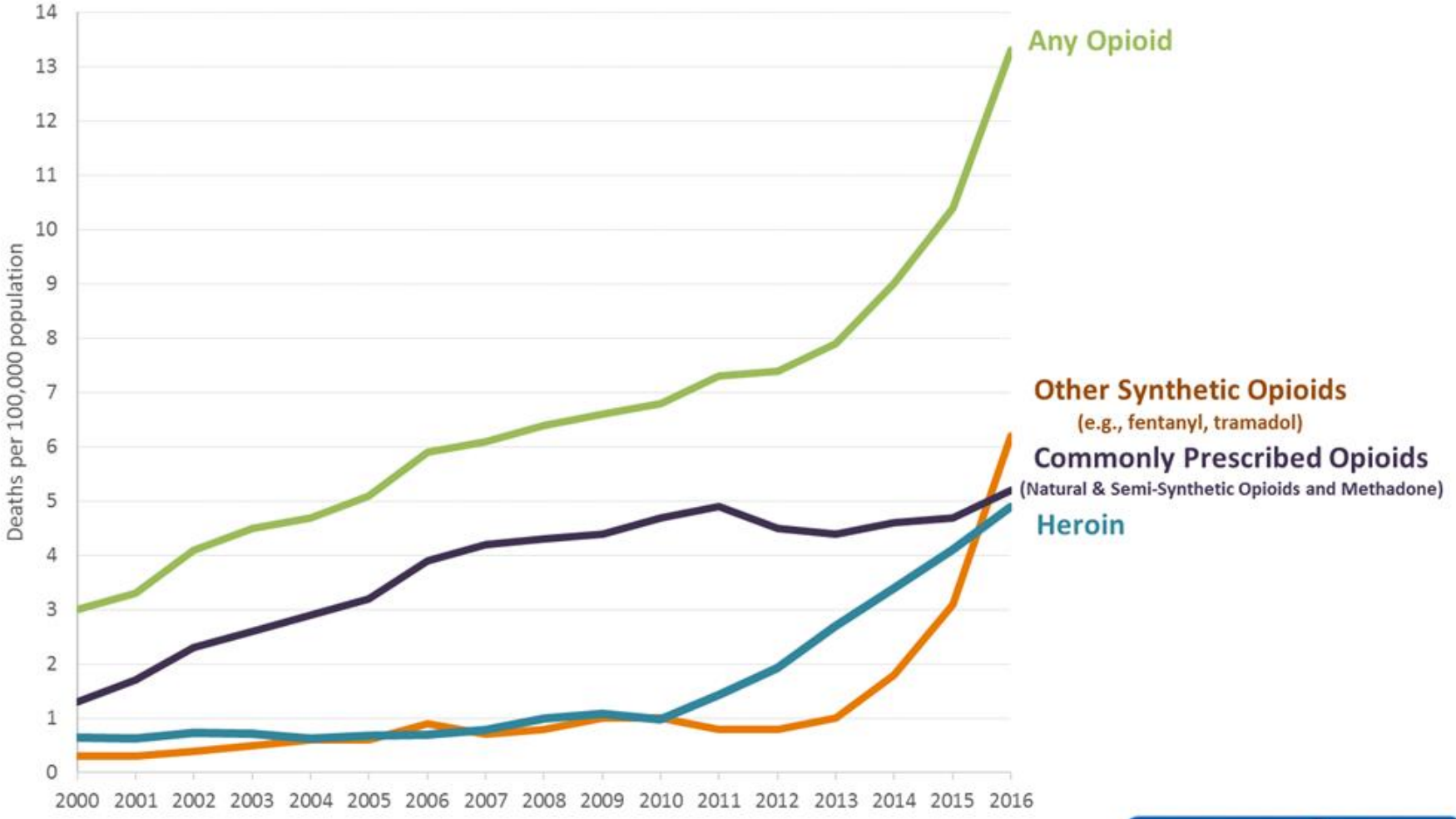
Disclosures

I have no disclosures

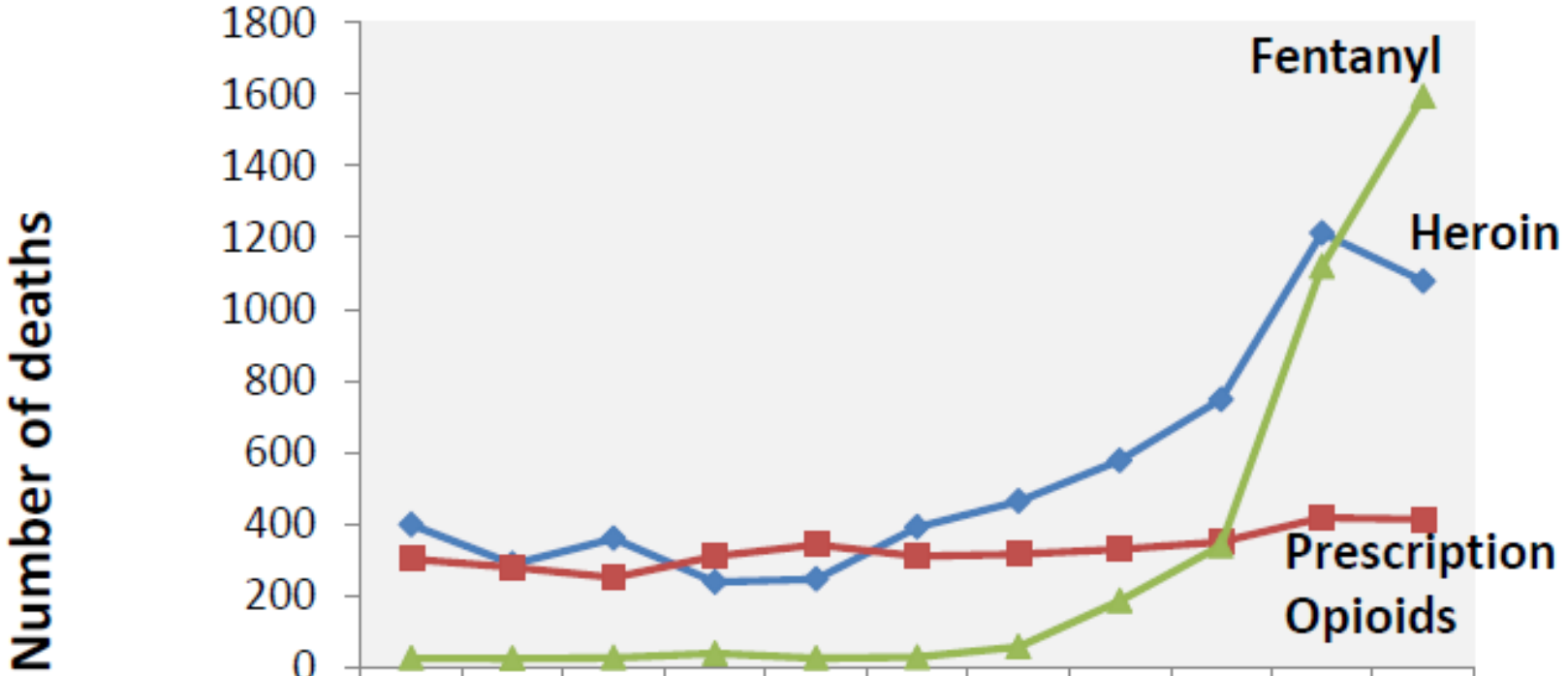
Overdose Death Rates Involving Opioids, by Type, United States, 2000-2016



SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2017. https://wonder.cdc.gov/.

www.cdc.gov
Your Source for Credible Health Information

Figure 7. Number of Opioid-Related Deaths Occurring in Maryland by Substance, 2007-2017.



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Heroin	399	289	360	238	247	392	464	578	748	1212	1078
Prescription opioids	302	280	251	311	342	311	316	330	351	418	413
Fentanyl	26	25	27	39	26	29	58	186	340	1119	1594

Epidemic of our generation

Mortality rates now parallel that of peak of AIDS epidemic in mid-1990s

But there's a highly effective pill that decreases mortality by 50%!

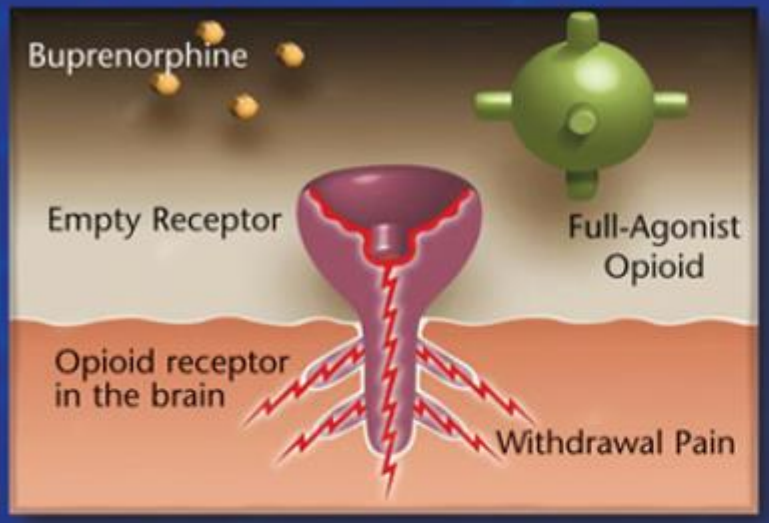
Outline

- Pharmacology and dosing of buprenorphine
- Review of buprenorphine formulations
- How to start buprenorphine via home initiation
- Understand monitoring for buprenorphine maintenance patients in OBOT setting, including appropriate use of urine drug testing
- Identify patients who need to transition to more intensive treatment

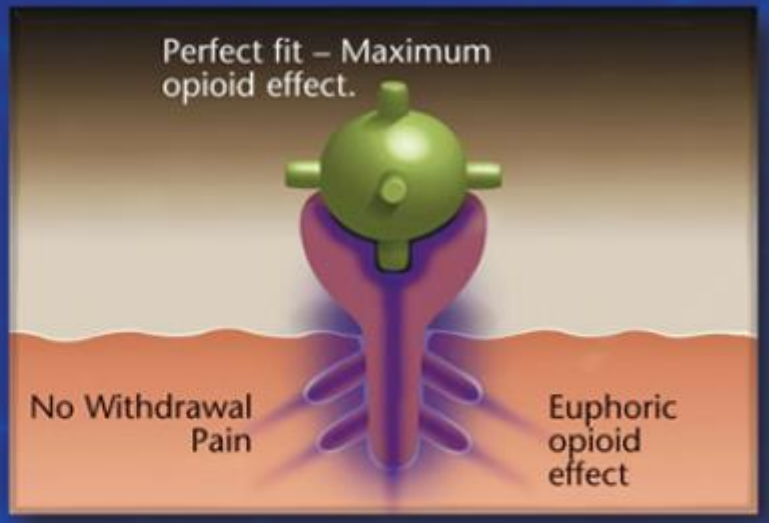
Paradigm Shift in OUD Treatment

Pharmacology of Buprenorphine

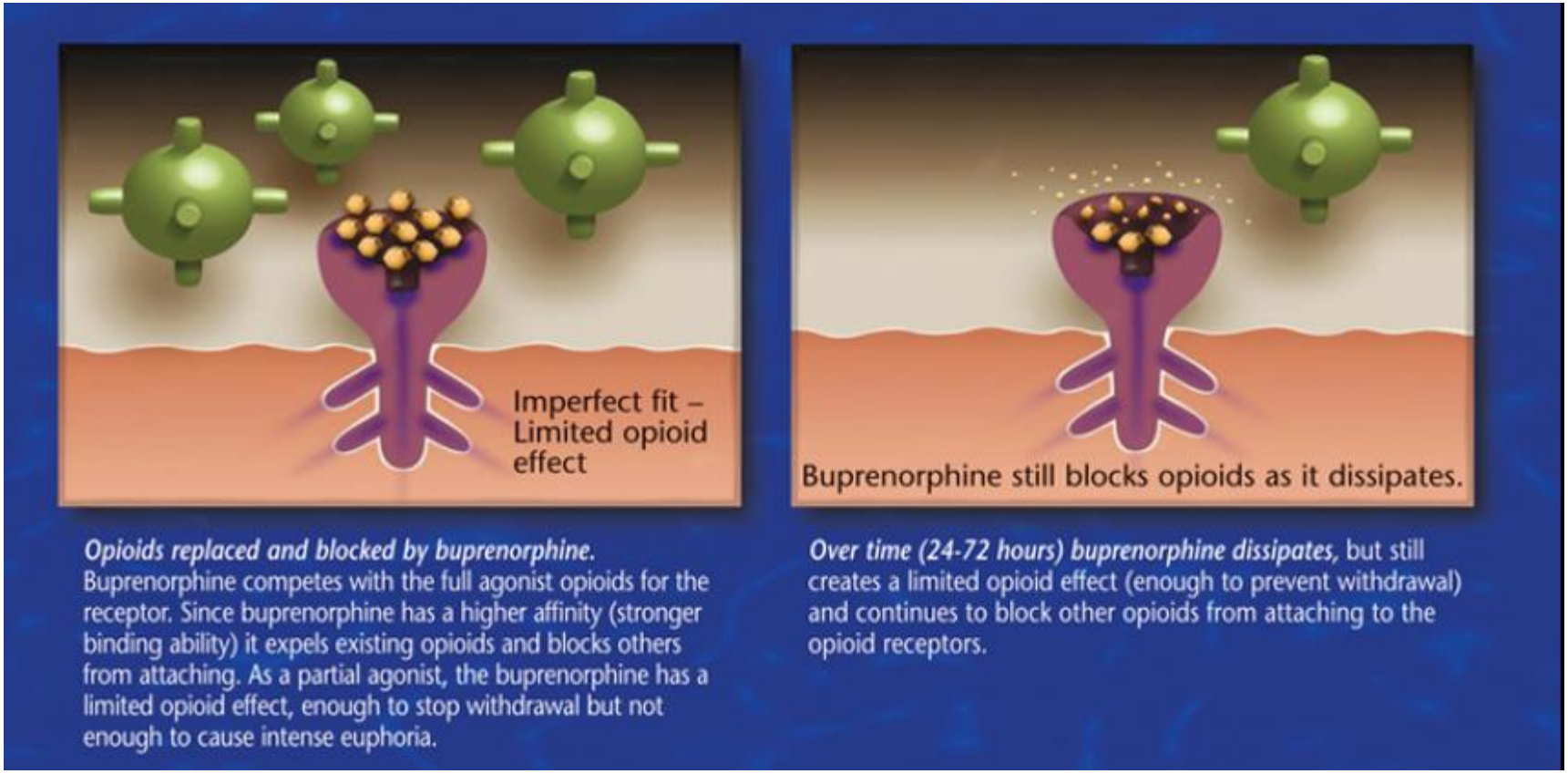
How Buprenorphine Works



Opioid receptor is empty. As someone becomes ***tolerant*** to opioids, they become less sensitive and require more opioids to produce the same effect. Whenever there is an insufficient amount of opioid receptors activated, the patient feels discomfort. This happens in withdrawal.



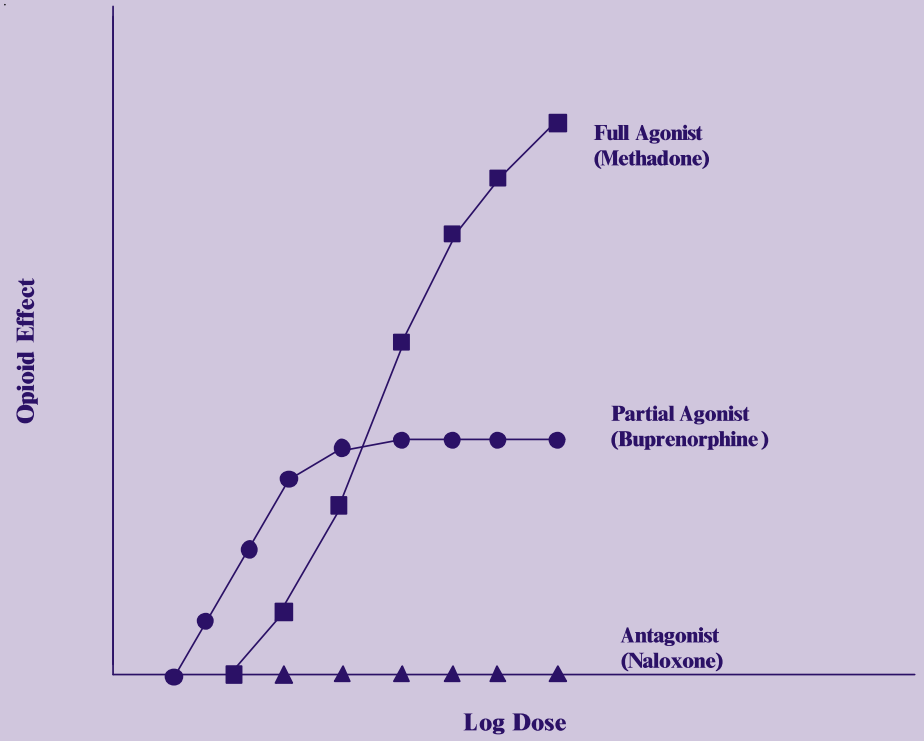
Opioid receptor filled with a full-agonist. The strong opioid effect of heroin and painkillers can cause euphoria and stop the withdrawal for a period of time (4-24 hours). The brain begins to crave opioids, sometimes to the point of an uncontrollable compulsion (addiction), and the cycle repeats and escalates.



Opioids replaced and blocked by buprenorphine. Buprenorphine competes with the full agonist opioids for the receptor. Since buprenorphine has a higher affinity (stronger binding ability) it expels existing opioids and blocks others from attaching. As a partial agonist, the buprenorphine has a limited opioid effect, enough to stop withdrawal but not enough to cause intense euphoria.

Over time (24-72 hours) buprenorphine dissipates, but still creates a limited opioid effect (enough to prevent withdrawal) and continues to block other opioids from attaching to the opioid receptors.

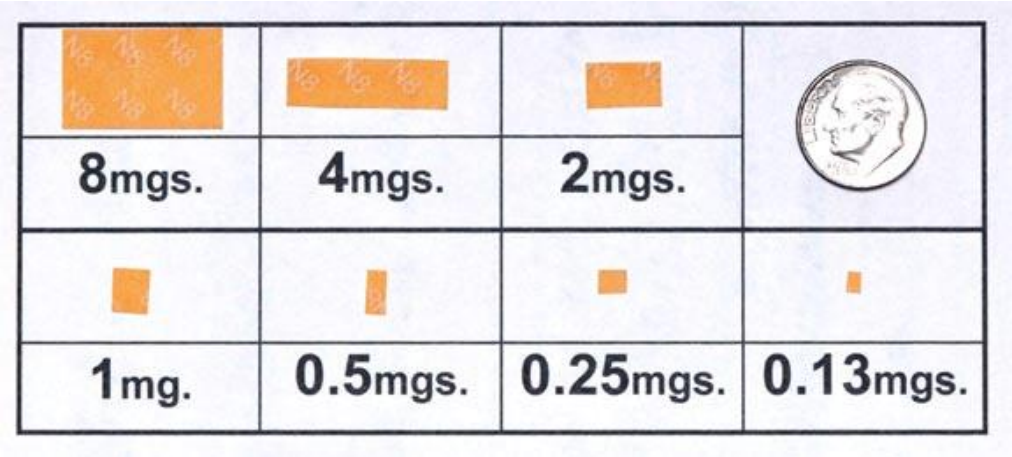
*Conceptual Representation of Opioid Effect Versus Log Dose for Opioid Full Agonists, Partial Agonists, and Antagonists**



Source: TIP-40, SAMHSA.

Formulations of Buprenorphine

- Transdermal
  - Butrans



- Sublingual
  - **Suboxone films (buprenorphine/naloxone)**
  - **Zubsolv (buprenorphine/naloxone)**
  - Subutex (buprenorphine only – for breastfeeding and pregnant patients)
- Probuphine implant
- XR Injection(Sublocade)

Efficacy of Buprenorphine Maintenance

- Meta-analysis showed similar efficacy to methadone for retention in treatment at doses above 16mg (30-75%)
- Decreases mortality by 50% compared to those off treatment
- Decreases criminal activity
- Cost-effective - $35,000/QALY

Cochrane, 2014.
Cornish, 2010.
Schackman, 2012.

Methadone vs. Buprenorphine

- Structured setting with daily visits
- Integrated with groups/behavioral health – better for those with more severe psych/substance use
- Requires slow, monitored dose titration and QTc monitoring
- Full agonist opioid may be better for severe chronic pain

- Can do office based treatment, progress more rapidly to fewer clinic visits (good for employed, less flexible schedule)
- Integrate treatment with primary care
- Engage patients who won't attend methadone program
- Fewer drug-drug interactions
- Safe for home dose titrations
- Less risk of overdose

Integrating Buprenorphine into Outpatient Settings

Buprenorphine in Primary Care

- Effective in office setting across studies
  - 50-60% opiate-negative urines at 1 year
- 55% success at 6 months in urban, primary care practice
- Across multiple office-based studies:
  - High patient satisfaction
  - 38% retention at 2 years with few adverse events
- Home initiations are safe

Fudala, 2003.
Mintzer, 2007.
Fiellin, 2008.

Selection of Patients

- Meets criteria for opioid use disorder
- No medical contraindications to starting buprenorphine
- Patient can attend scheduled clinic visits at your practice
  - Unstable housing, severe OUD and serious mental illness are all considerations for referral to more intensive treatment

At first visit

- Check PDMP
- Complete controlled substance agreement
- Order CMP, toxicology; HCV and HIV testing if exposures
- Give prescription at first visit with instructions on home initiation

Buprenorphine Initiation 101

- Counsel patient to wait until experiencing withdrawal and to let film/tab fully dissolve
- **Day 1**: Give 4mg bup q2-3hours until no more withdrawal (up to 12 mg)
- **Day 2**: 4-8mg in AM and 4-8mg in PM based on prior dose and withdrawal symptoms (most patients will be on 8mg SL BID by day 2)

Precipitated Withdrawal

- Sudden-onset severe withdrawal that occurs from giving buprenorphine when other opioids still in system
- Rule of thumb for starting bup:
  - 8-12 hours after short-acting opioids (heroin, oxycodone)
  - 24 hours after long-acting Rx opioid (MSContin, Oxycontin)
  - 3-7 days after methadone use

Transitioning from Methadone to Buprenorphine

- Methadone is long-acting – high risk of precipitated withdrawal

1) Taper patient to methadone 30-40mg daily (done in conjunction with methadone program)
2) Wait at least 48 hours from last methadone dose and patient experiencing withdrawal
3) Patient takes 4mg buprenorphine, patient to wait 1-2 hours – if still having withdrawal, then can take another 4mg buprenorphine -> max 4-12 mg on first day
4) From day 2, can increase up to 8mg BID

Maintenance Dosing

- 8 - 24mg per day, divided per patient preference (usually BID – TID)
  - Increase by 2-4mg if experiencing withdrawal
  - Decrease by 2-4mg if over-sedated
- Most effective at doses >/ 16mg/day

Buprenorphine for Chronic Pain

- Good option for patients with chronic pain on opioid therapy who show signs of medical misuse of opioids
- Divide buprenorphine dose Q6-Q8hrs (more frequent than for dependence) and can increase daily bup dose up to 24mg (ex. 4-6mg SL QID)

Roux, 2013

Practical Tips on Bup Prescriptions and Prior-Auths

- Default prescription “buprenorphine-naloxone 8-2mg films SL BID”
- Include X-number on prescription
- Write “ok to substitute tab or film”
- Any quantity over 60 tabs/films per 30 days will require PA from Maryland Medicaid
- Most Medicare plans require prior-auth

Monitoring

- Frequency of visits based on patient stability (usually range from weekly to q3months)
- Can alternate MD visits with nurse/MA visits
- Check PDMP and obtain toxicology test at every visit where you write new prescription

Toxicology

- Standard immunoassay (urine or saliva)
  - Test for opiates, methadone, oxycodone and fentanyl PLUS buprenorphine (may require add-on)
- If concern for urine tampering, do quantitative buprenorphine → absence of norbuprenorphine metabolite (ratio NORBUP/BUP < 0.02) concerning for urine drug tampering

Quantiative Bup Interpretation

Component	9d ago
Buprenorphine,Qn,Ur	SEE BELOW !

Comment:

TESTS	RESULTS	UNITS	REF. RANGE
BUPRENORPHINE, QN, URINE			
BUPRENORPHINE	110 H	ng/mL	
NORBUPRENORPHINE	150 H	ng/mL	

Very high bup, low norbup concerning for urine spiking.

Component	12d ago
Buprenorphine,Qn,Ur	SEE BELOW !

Comment:

TESTS	RESULTS	UNITS	REF. RANGE
BUPRENORPHINE, QN, URINE			
BUPRENORPHINE	>1000 H	ng/mL	
NORBUPRENORPHINE	4 H	ng/mL	

Actions Based on Tox Results

- Look for patterns and give warning after first aberrant test
- Specific findings:
  - Other opioid use →
    - Opiate or Rx opioid positive → increasing frequency monitoring
    - Methadone positive → counsel on risk of precipitated withdrawal; refer if 2 or more consistent methadone positive tox
  - Benzodiazepine use →
    - If prescribed – coordinate with prescriber, encourage patient to taper
    - Illicit use – depending on severity – refer for detox, increase frequency of monitoring
  - Cocaine → increase frequency of monitoring, engage in other recovery supports
  - THC → no change in bup monitoring

When it isn't going well …

- Start with intensification of OBOT treatment:
  - Increase frequency of visits and shorter length of prescription
  - Wrapper counts
- Refer to higher level of care (inpatient, OTP or IOP)

When to Transfer to Higher Level of Care

- Aberrant toxicology results:
  - Bup-negative
  - Urine tampering (bup pos, norbup neg)
  - Methadone positive
- Opioid cravings uncontrolled on 24mg bup daily → consider methadone
- Inconsistent with appointments
- No evidence of decrease in illicit opioid use

How to get waivered

1) 8 hour free online training
   - **Baltimore Buprenorphine Initiative,** (Kisha.Winston-Watkins@BHSBaltimore.org; 410-735-8576)
   - Webinars through **pcssmat.org**

2) Apply for waiver online via SAMHSA (http://buprenorphine.samhsa.gov/pls/bwns/waiver)

   - Prescribe using X-number – 30 patients in first year, 100 patients per provider second year

Take Home Points

- We all have patients with opioid use disorder
- Buprenorphine is highly effective and lifesaving treatment for opioid use disorder
- Bup can be safely done via home initiations from outpatient settings
- Prescribe Narcan to all patients getting chronic opioids

Questions?