Tapering and Microdosing

Buprenorphine

Your Speaker Today

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Disclosures

- I have no financial interests in any methods or medications mentioned today. Any references to name brand medications are only to increase recognition.

Objectives

1. Participants will be able to state at least 2 strategic approaches to tapering buprenorphine.

2. Participants will state improved confidence with standard inductions, home inductions, and micro-dosing inductions.

Question Time!!!

Buprenorphine

Exhibit 1. Buprenorphine Products for Treatment of Opioid Use Disorder

Product Name/Active Ingredient(s)	Route of Administration/ Form	Available Strengths	Recommended Once-Daily Maintenance Dose
Bunavail®[17,20] • Buprenorphine hydrochloride • Naloxone hydrochloride	Buccal film	2.1 mg/0.3 mg 4.2 mg/0.7 mg 6.3 mg/1 mg	Target: 8.4 mg/1.4 mg Range: 2.1 mg/0.3 mg to 12.6 mg/2.1 mg
Generic combination product[20,21] • Buprenorphine hydrochloride • Naloxone hydrochloride	Sublingual tablet	2 mg/0.5 mg 8 mg/2 mg	Target: 16 mg/4 mg Range: 4 mg/1 mg to 24 mg/6 mg*
Generic mono-product[20,22] • Buprenorphine hydrochloride	Sublingual tablet	2 mg 8 mg	Target: 16 mg Range: 4 mg to 24 mg*
Suboxone®[20,23] • Buprenorphine hydrochloride • Naloxone hydrochloride	Sublingual film	2 mg/0.5 mg 4 mg/1 mg 8 mg/2 mg 12 mg/3 mg	Target: 16 mg/4 mg Range: 4 mg/1 mg to 24 mg/6 mg*
Zubsolv®[18,20] • Buprenorphine hydrochloride • Naloxone hydrochloride	Sublingual tablet	1.4 mg/0.36 mg 2.9 mg/0.71 mg 5.7 mg/1.4 mg 8.6 mg/2.1 mg 11.4 mg/2.9 mg	Target: 11.4 mg/2.9 mg Range: 2.9 mg/0.71 mg to 17.2 mg/4.2 mg

* Dosages higher than 24 mg buprenorphine per day and 24 mg/6 mg buprenorphine/naloxone per day have not been demonstrated to provide a clinical advantage.[22,23]

SAMHSA (2016). Subligual and transmucosal buprenorphine for opioid use disorder review and update. *SAMHSA Advisory, 15*(1).

Buprenorphine Treatment

- Methadone historically has had slightly better retention than buprenorphine treatment, but only slightly
- Long-term treatment with buprenorphine is more effective than short-term buprenorphine with a taper
- Buprenorphine has a slightly lower risk of adverse reactions and death than methadone due to a ceiling effect on respiratory depression
- However, there is still higher risk of accidental poisoning when taken along side other drugs, especially benzodiazepines and alcohol

SAMHSA (2016). Subligual and transmucosal buprenorphine for opioid use disorder review and update. *SAMHSA Advisory, 15*(1).

Question for you

Tapering Buprenorphine

- There is a greater than 90% relapse rate in patients who taper from buprenorphine, even after long term care (SAMHSA, 2016)
- It is important for patient and provider to discuss risks and benefits of tapering prior to initiating a taper
- There was hope years ago that buprenorphine could be used as a “detox” agent and be quickly initiated and taper. This turned out to be wrong
- There is no optimal length of buprenorphine treatment
- Patients should take buprenorphine as long as they benefit from it and as long as they wish to continue

Tapering Buprenorphine

- There are many reasons why a patient may wish to discontinue buprenorphine
- Retention rates vary wildly (20-82.5%)
- The most frequent reason for patients coming off buprenorphine is either disagreement with treatment staff or some kind of compliance issue with treatment
- Only about 4% of patients discontinuing treatment did so due to feeling they had been successful in treatment
- Less than half of those coming off buprenorphine do so with medical management

Weinstein, Z.M. et al. (2018). Tapering off and returning to buprenorphine maintenance in a primary care Office Based Addiction Treatment program. *Drug and Alcohol Dependence (189),* (166-171).

Tapering Buprenorphine

- ✓Take it slow
- ✓Increase monitoring of the patient
- ✓Expect times of over use
- ✓Keep doors and communication open

Tapering Buprenorphine

- Decreases should be 10% or less of the initial dose
- For example, a patient who is taking 8 mg buprenorphine a day, should be decreased by 0.8 mg (1/2 – 1 mg decrease is reasonable)
- I, personally, would not go any faster than decreases once every 4 weeks unless there is an important safety issue
- Due to the long half-life of buprenorphine, staggered tapering may be better for the patient
- Example: A patient can reduce their dose every 3 days

Staggered Tapering Example From 8 mg/day – 6 mg/day

Week #	Sun	Mon	Tue	Wed	Thurs	Fri	Sat
1	8.0	8.0	6.0	8.0	8.0	6.0	8.0
2	8.0	6.0	8.0	8.0	6.0	8.0	8.0
3	6.0	8.0	8.0	6.0	8.0	8.0	6.0
4	8.0	8.0	6.0	8.0	8.0	6.0	8.0
5	8.0	6.0	6.0	8.0	6.0	6.0	8.0
6	6.0	6.0	8.0	6.0	6.0	8.0	6.0
7	6.0	8.0	6.0	6.0	8.0	6.0	6.0
8	8.0	6.0	6.0	8.0	6.0	6.0	8.0
9-12	6.0	6.0	6.0	6.0	6.0	6.0	6.0

At the end of week 12, be sure to reassess for readiness to start to transition from 6-4 mg

Staggered Tapering

- The design can be whatever is agreed between the patient and provider
- Decreases can be less, and less frequent
- I usually frame this with the patient as “sneaking up on the reduction” or “convincing your brain that you feel well on lower doses”
- Sometimes I will tell the patient to “practice” or to “go in training” taking a little less every few days before an official medication reduction is made
- Many patients are under the impression that they will be “in trouble” for reducing their dose on their own

Tapering tips

- The approach is to support the patient in THEIR goals
- Not YOUR goals, not their spouse's goal, not the pope's goal
- Encourage your patient to be open to changes, pauses, delays
- Pitfalls:
  - Specific discontinuation dates
  - Strict rules of dose reductions
  - No backup plan
  - No plan for follow up
  - Anticipatory withdrawal
  - No other supports

Let's talk withdrawal

- As you would expect, buprenorphine withdrawal is very similar to withdrawal from any other opioid
- Withdrawal can last for a month or longer compared to heroin withdrawal which lasts for about 7 days
- First 72 hours, physical symptoms include nausea, vomiting, diarrhea, diaphoresis, irritability, and anxiety
- In about 1 week these symptoms resolve, body aches will continue as well as insomnia and mood issues
- After 2 weeks, depression may increase
- After about a month, the psychological symptoms may continue and makes relapse highly probable

Aids to success

- Leave the door open to return to treatment without shame or judgement
- Post-taper naltrexone (helps with cravings)
- Follow up after the taper is over
- Encourage healthy lifestyle of eating well, engaging in things that bring great joy and connection, regular EXERCISE
- Assess for increasing alcohol use
- Helpful pharmacology: clonidine, lofexidine; dicyclomine, loperamine, promethazine, ondansetron; trazadone, hydroxyzine; SSRI/SNRI
- Avoid other controlled medications – do not invite a new substance use disorder

Case #1

John is a male patient in his early 40's

- First discussion of tapering 3 years ago
- Encouraged engagement in counseling
- Began a staggered taper 2 years ago
- Progress slowed by divorce, fall with injury (from a roof), and the death of his mother
- We have begun the discussion again about his approach to taper and he will let me know when he wishes to begin this again

Case #2

Jamie is a 35 year old female patient

- This is her fourth time coming back to your practice
- She has typically stayed in your program for 2-6 months and then does not come back
- She has gone through withdrawal on her own and abstained from drugs from 1-12 months at a time
- She feels best when she is off buprenorphine and when she gets regular exercise
- She has a plan to take a week off from work and withdraw at home. This time she would like comfort medications and will plan to follow up so that we can start naltrexone.

Case #3

Randy is a male patient in his mid 50's

- Has been on buprenorphine for 18 years
- History of overuse
- Over the past 2 years, has been on sublocade monthly injection (topic for another talk)
- Sublocade is VERY long acting
- Tapering via mm, he is at 50% previous dose
- Ongoing experiment for this patient

Microdosing

A WAY IN

Questions

Some Pharmacology

- Buprenorphine is a partial opioid agonist
- It has a very high affinity for the mu receptor
- It displaces other full opioid agonists and results in precipitated withdrawal
- Imagine you are playing “king of the mountain” and a bigger kid comes to play
- The bigger kid has a stronger affinity for the top of the mountain and will displace the smaller kids

Precipitated Withdrawal

- Withdrawal all at once, very fast and very severe
- So, when someone takes buprenorphine when they have full mu agonists on board, they will have precipitated withdrawal
- Agonists include heroin, fentanyl, methadone, oxycodone

Traditional Induction

- Historically, providers have asked patients to abstain from opioids long enough to enter mild to moderate withdrawal
- Then, buprenorphine is typically well tolerated and stops the withdrawal
- This used to work well when the predominant opioid was heroin and oxycodone
- Providers used to have patients take the first dose in the office, could be a lengthy process and we were asking patients to come into the office feeling very sick

- I have noticed over the past few years, patients were coming to me having already making the switch on their own using “street” buprenorphine.

Home Induction

- Often, the patient has already been on suboxone in the past and familiar on when to take their first dose
- Patients often had made their own transition onto suboxone and were able to tell us their preferred dose
- I have not personally done an in-office induction in many years

Well, it's a new day

Compared to Heroin

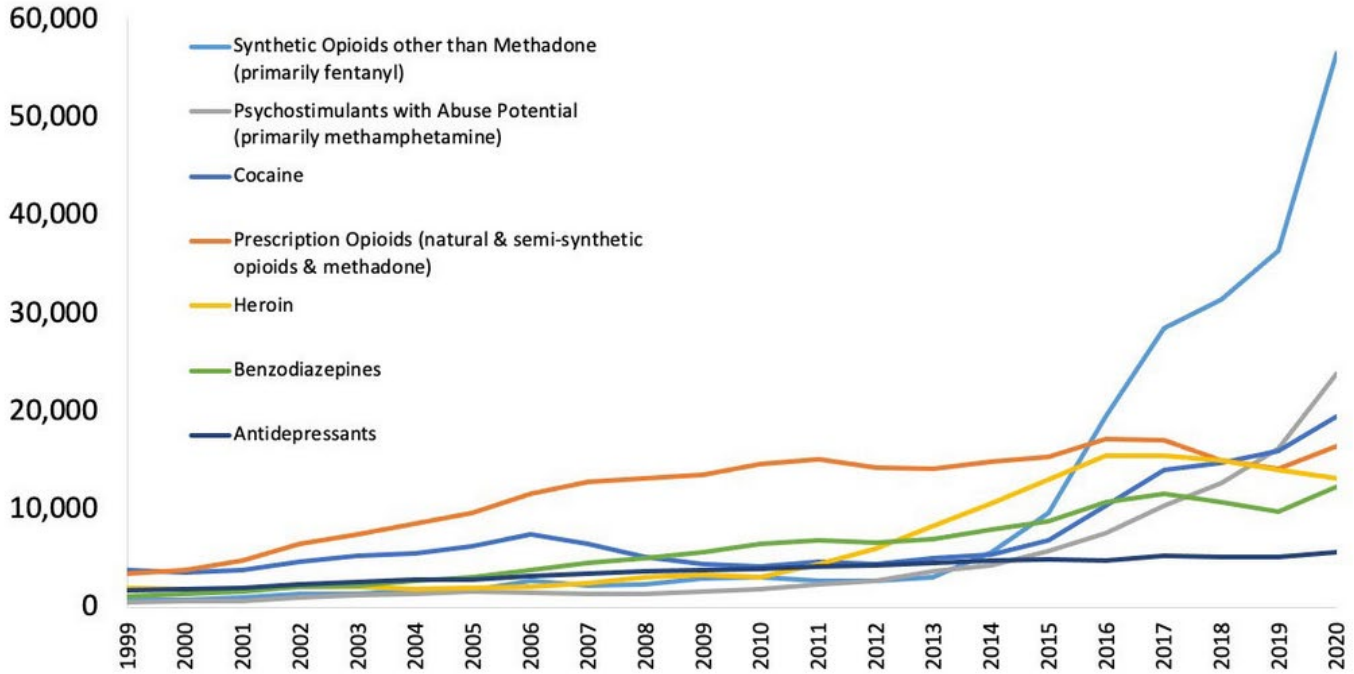
Let's look at Methadone

Parameter	Mean	Range
Bioavailability	70–80%	36–100%
Time to peak concentration	2.5–4 h	1–5 h
Volume of distribution	4.0 L/kg	1.9–8.0 L/kg
Protein binding	87%	81–97%
Half-life	20–35 h	5–130 h

Values are from studies on methadone maintenance populations, healthy volunteers and cancer patients. Reference Lugo article 2002.

Fentanyl predominates

Figure 2. National Drug-Involved Overdose Deaths*, Number Among All Ages, 1999-2020



*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision.
Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2020 on CDC WONDER Online Database, released 12/2021.

Fentanyl

- Easy to obtain (purely synthetic, made in labs)
- Smaller volume for larger doses
- Much ships into Mexico and is carried into this country via cartel activity
- Some of it ships to the US through Chinese labs
- Inexpensive
- There is virtually no heroin available in the US today
- Heroin is made from poppy plants and involve farming, harvesting, processing

A Problem for Recovery

- Due to the long acting properties of illicit drugs (fentanyl), it poses big problems for buprenorphine induction
- It takes longer for the fentanyl to clear the system, but people who use fentanyl are still dosing 1-2 times a day
- To be proper, the fentanyl should be stopped for at least 3 days prior to induction and still might be a difficult induction
- This is a similar situation for patients on methadone therapy who wish to transition to suboxone
- People who are using drugs are struggling to get themselves onto suboxone due to precipitation of withdrawal and continued dosing with fentanyl

The Bernese Method

Micro-induction

- First described in English in 2016, but in German in 2010
- The researchers observed that a tiny dose of buprenorphine was tolerated in patients who were on methadone
- They also observed that in patients who were on mu agonists, they could be given naloxone and would withdraw, but that withdrawal would eventually stop in spite of repeated doses of naloxone
- The hypothesis was that tiny doses could be given of buprenorphine in spite of other opioids and the buprenorphine would gradually build up on receptors and not cause out and out withdrawal

Hammig, R., Kemter, A., Strasser, J., von Bardeleben, U., Gugger, B., Walter, B., et al. (2016). Use of microdoses for induction of buprenorphine treatment with overlapping full opioid agonist use: The “Bernese method.” *Substance Abuse and Rehabilitation 7* (99-105).

Micro-induction

- There are many published accounts of case studies of micro-dosing and micro-induction
- There is no standard methods
- We are lacking randomized controlled studies
- **HOWEVER, this process mimics what our patients have been doing for years!**

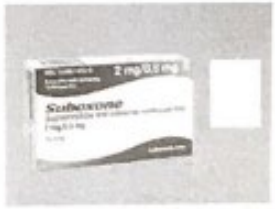
What I am Doing

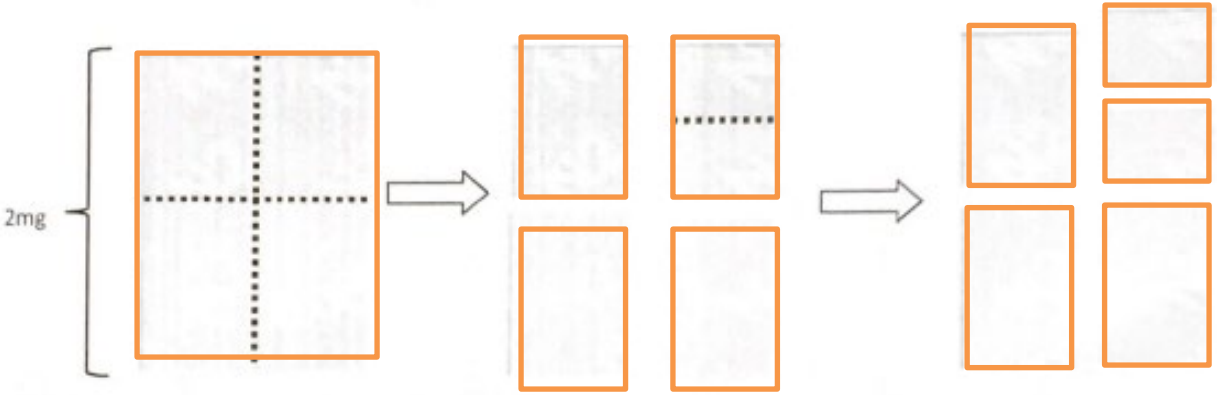
- The patient is asked to come to their first appointment NOT in withdrawal. Although I do not want someone impaired, I do want them at their normal function
- Sign paperwork and collect urine screen
- Discussion about suboxone treatment and plan to transition to suboxone
- The **patient** selects the day to start microinduction
- I write the prescription with appropriate quantity and appropriate fill date depending on patient's choice for induction

Induction instructions

DAY 1

1. Taper down your opioid as much as tolerated.
2. On the morning of day 1, cut your **2-0.5mg buprenorphine-naloxone film** **(do not do this with higher dose films)** into 4 equal pieces. Then take one of the 4 pieces, and cut it in half.





Induction Day 1

3. You should now have 5 total pieces (2 small pieces, and 3 larger pieces). Line the pieces up from smallest to largest and take one piece, place it under your tongue, and let it dissolve. Do this every 2 hours similar to the schedule below.

The patient may continue taking opioids as needed through day 1

Induction Day 2

- Switch to 8 mg strips
- Start the day with ¼ strip (2 mg)
- Dose 2 mg every 2 hours to a max of 8 mg

- STOP other opioids

Induction Day 3

- Start day with entire 8 mg strip
- Dose 2 mg every 2 hours to a max of 16 mg for the day

- NO other opioids

Induction Day 4

- Max of 16 mg suboxone
- Be sure your patient has comfort medications including clonidine, loperimide, promethazine, flexeril, others for symptom management

Patient Monitoring & Safety

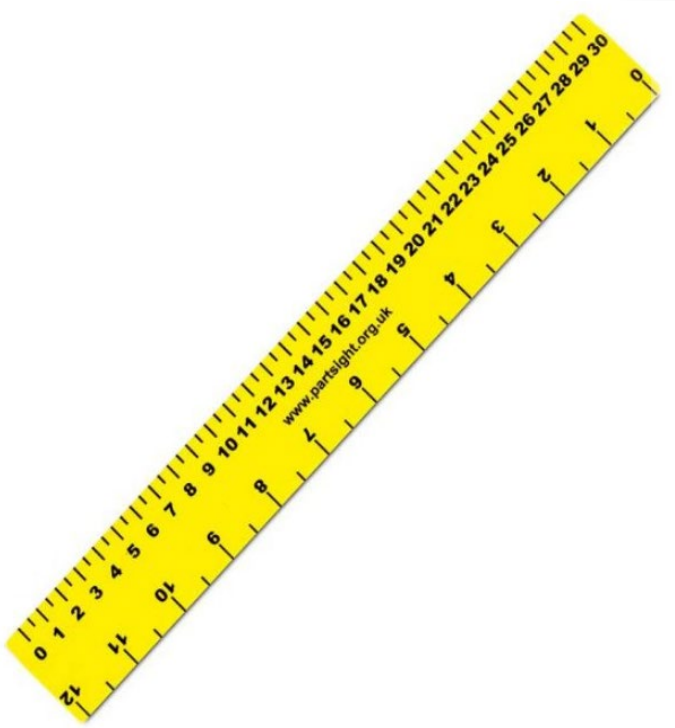
- Be sure that your patient has Narcan on hand
- It is BEST but not required that the patient have someone at home who is aware of what they are doing
- Patient should be invited to call with any difficulties
  - Slow down the process
  - Provide more comfort medications
  - Counsel and encourage
- In office visit within 1-2 weeks

Eva's Anecdotal Experience

- I have now managed about 10 micro-inductions
- Surprisingly, most of these have been for patients on daily dose methadone who desired more freedom
- Patients report to me the most difficulty on days 3 and 4
- Patients report to me that the slight discomfort is far better than having straight-out withdrawal
- "If I had known how easy it would be, I would have done this a long time ago."
- The majority have had to be "out sick" for only 1 day, some not at all
- I did have one lady say that she spent 4 days in bed, but then said that she just wanted to wait until she felt 100%

Length of induction

- I feel shorter duration has better buy in
- The promise of having this done in under a week has been seen as achievable
- I am open to longer transitions
- I also need to consider other prescribers (methadone clinics)



Questions for me

Thank you for your kind attention!