



Low Dose Buprenorphine Initiation

July 2, 2021

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Disclosures

- I receive a stipend for medical advisory work for Path CCM, Inc, a substance use disorder treatment start up company.

Dr. Shawn Cohen

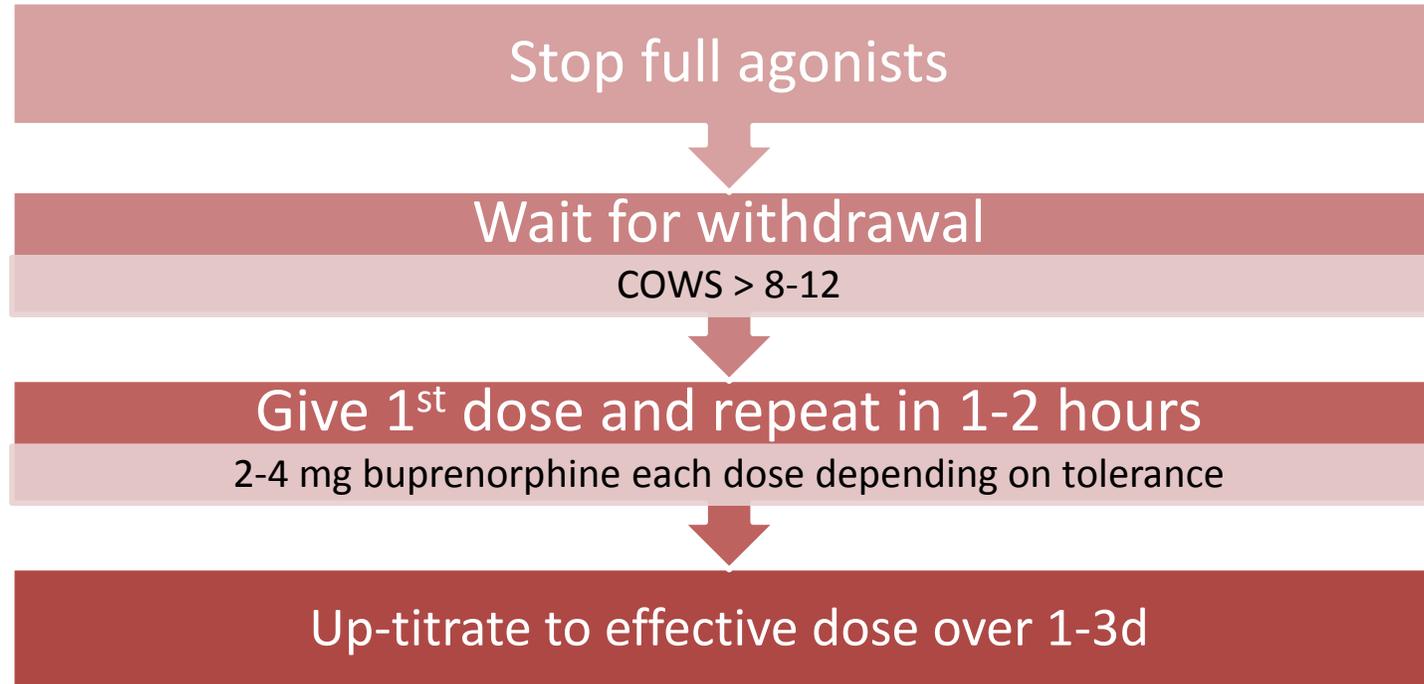
Many slides in this slide set are attributed to Dr. Cohen, recent graduate of the Yale Addiction Medicine Fellowship Program!



A minute on terminology: LOW DOSE INDUCTION vs MICRODOSE

- As we grow as a field well respected in medicine, it is important for us to use the most medical and accurate terms.
- “Microdose”
 - connotation in pharmacology and translational science with “non-medical use” or “non-pharmaceutical use”
 - connotation to use of LSD.
- Can use the term “low dose” or “ultra low dose” or Bernese method
- If you can’t shake “micro” call it “micro-induction”

Classic induction

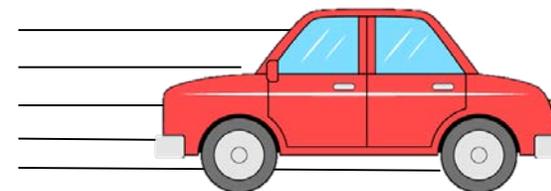
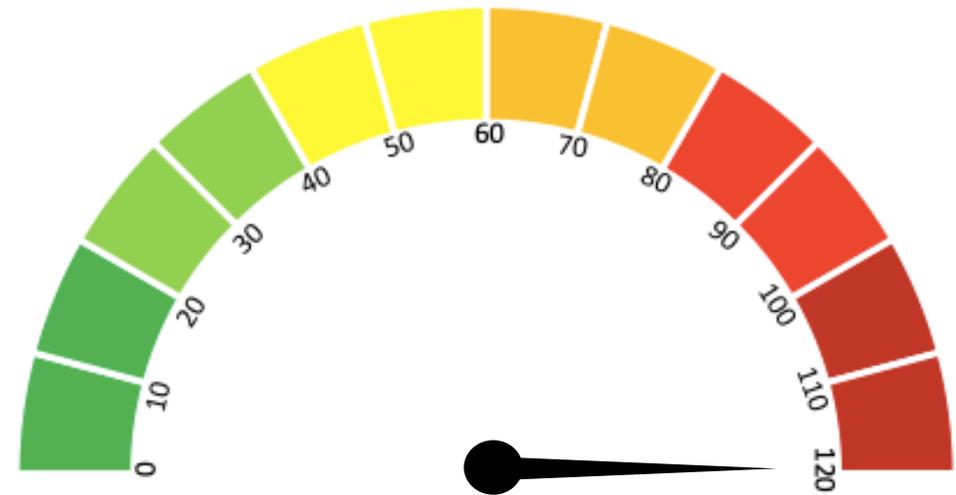




Challenging Clinical Situations

- Transition from methadone to buprenorphine
- Transition from full opioid agonist for pain to buprenorphine
- Initiation of buprenorphine in patient who uses primarily fentanyl
- Patient with history of precipitated opioid withdrawal

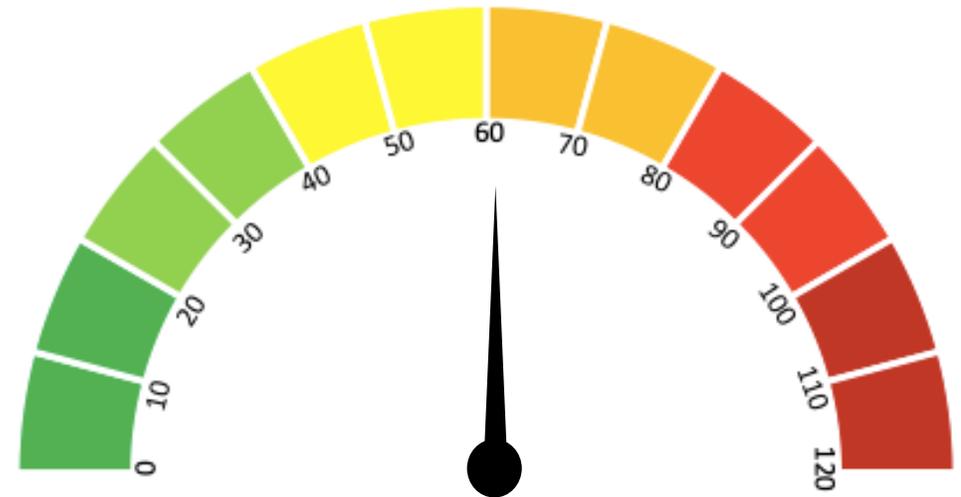
FULL Opioid Agonism



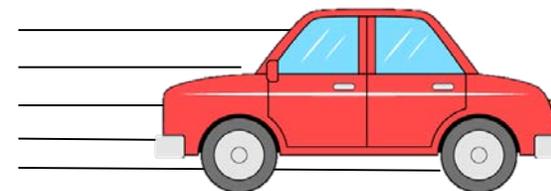
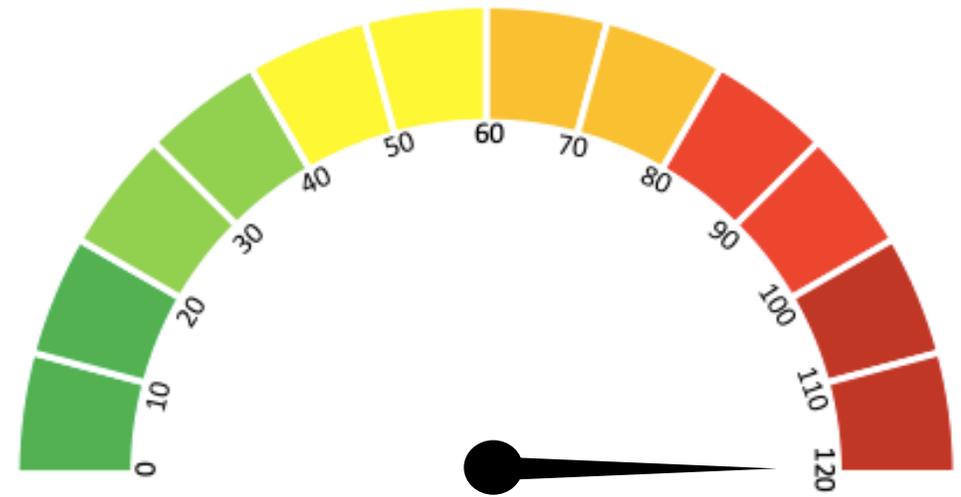
PRECIPITATED WITHDRAWAL



Buprenorphine 4mg



FULL Opioid Agonism



Low dose induction strategy

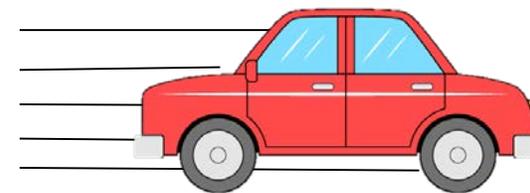
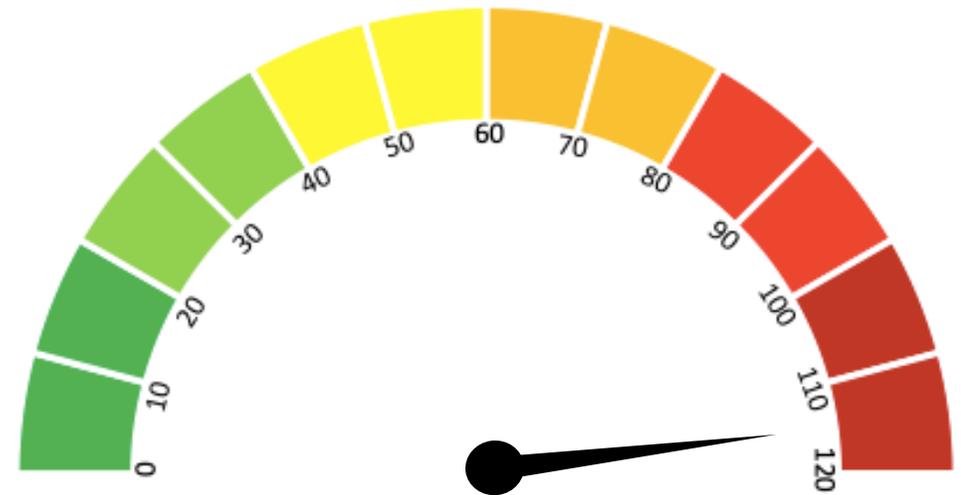


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Buprenorphine SL 0.5mg



Slide attributed to Dr. Shawn Cohen

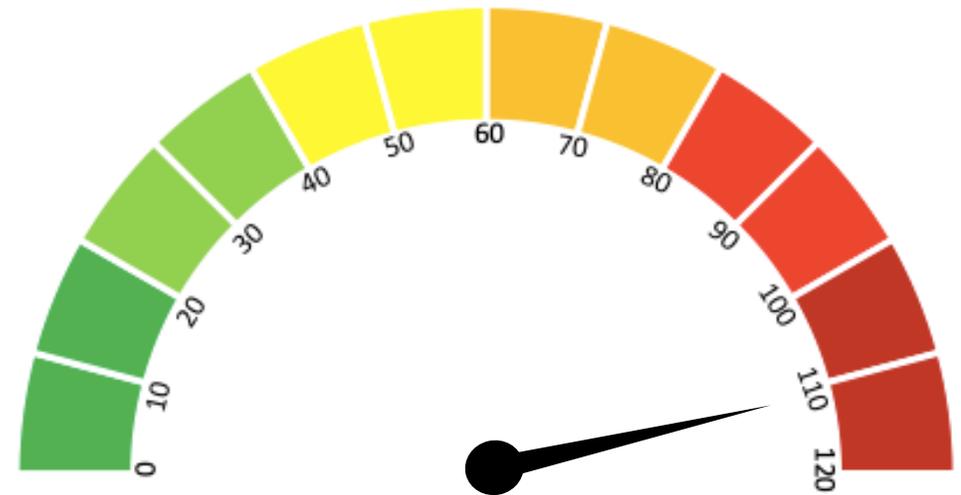


Low dose induction strategy



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Buprenorphine SL 0.5mg BID



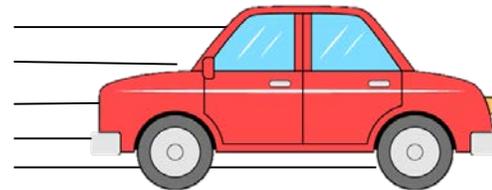
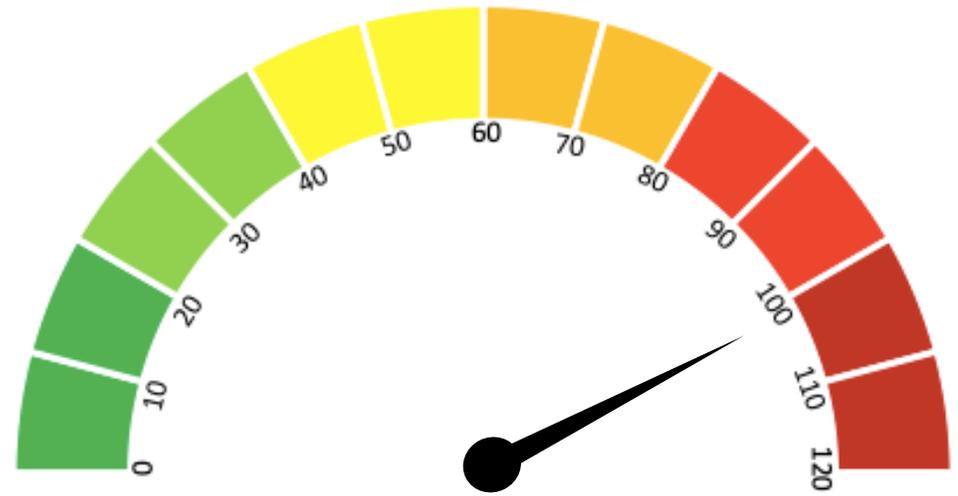
Slide attributed to Dr. Shawn Cohen

Low dose induction strategy



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Buprenorphine SL 1mg BID

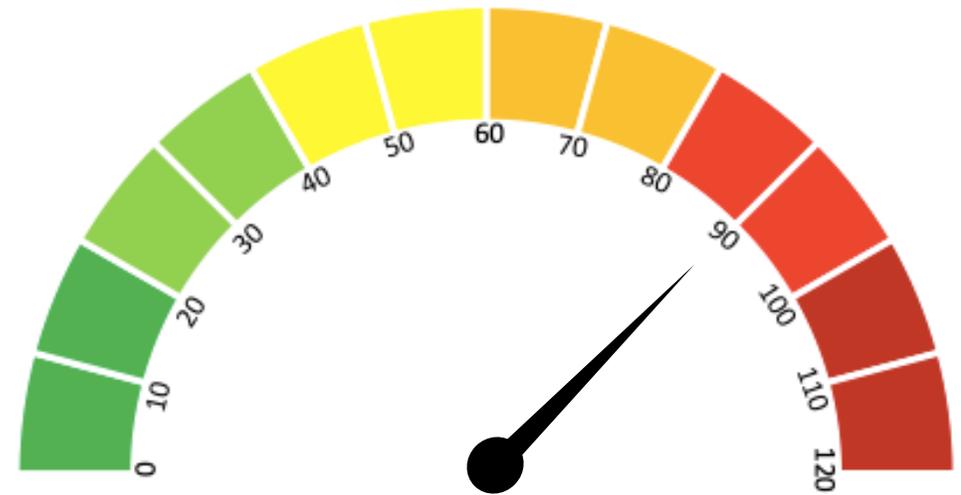


Low dose induction strategy



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Buprenorphine SL 2mg BID



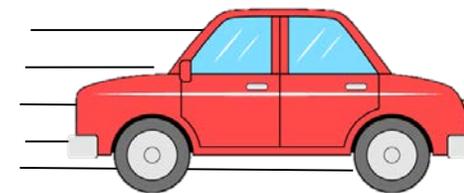
NewHaven
Health

Low dose induction strategy



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Buprenorphine SL 4mg BID



NewHaven
Health

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Low dose induction strategy



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Buprenorphine SL 4mg TID



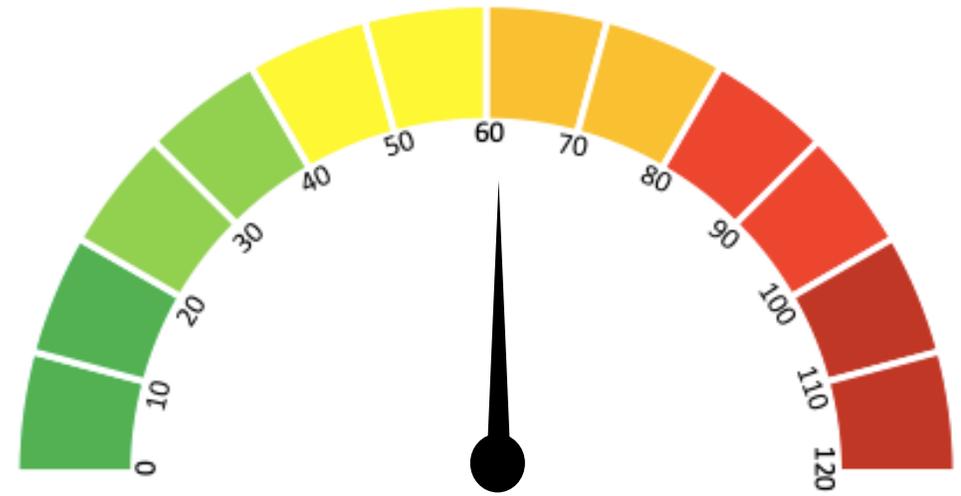
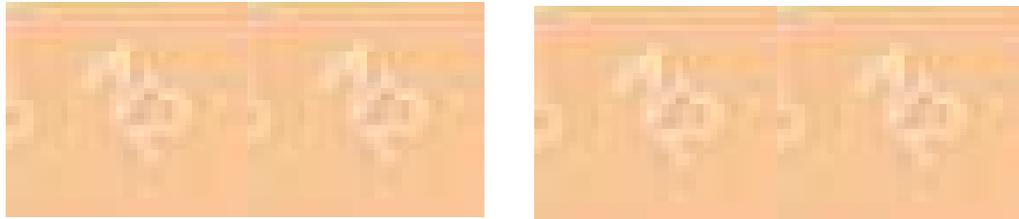
NewHaven
Health

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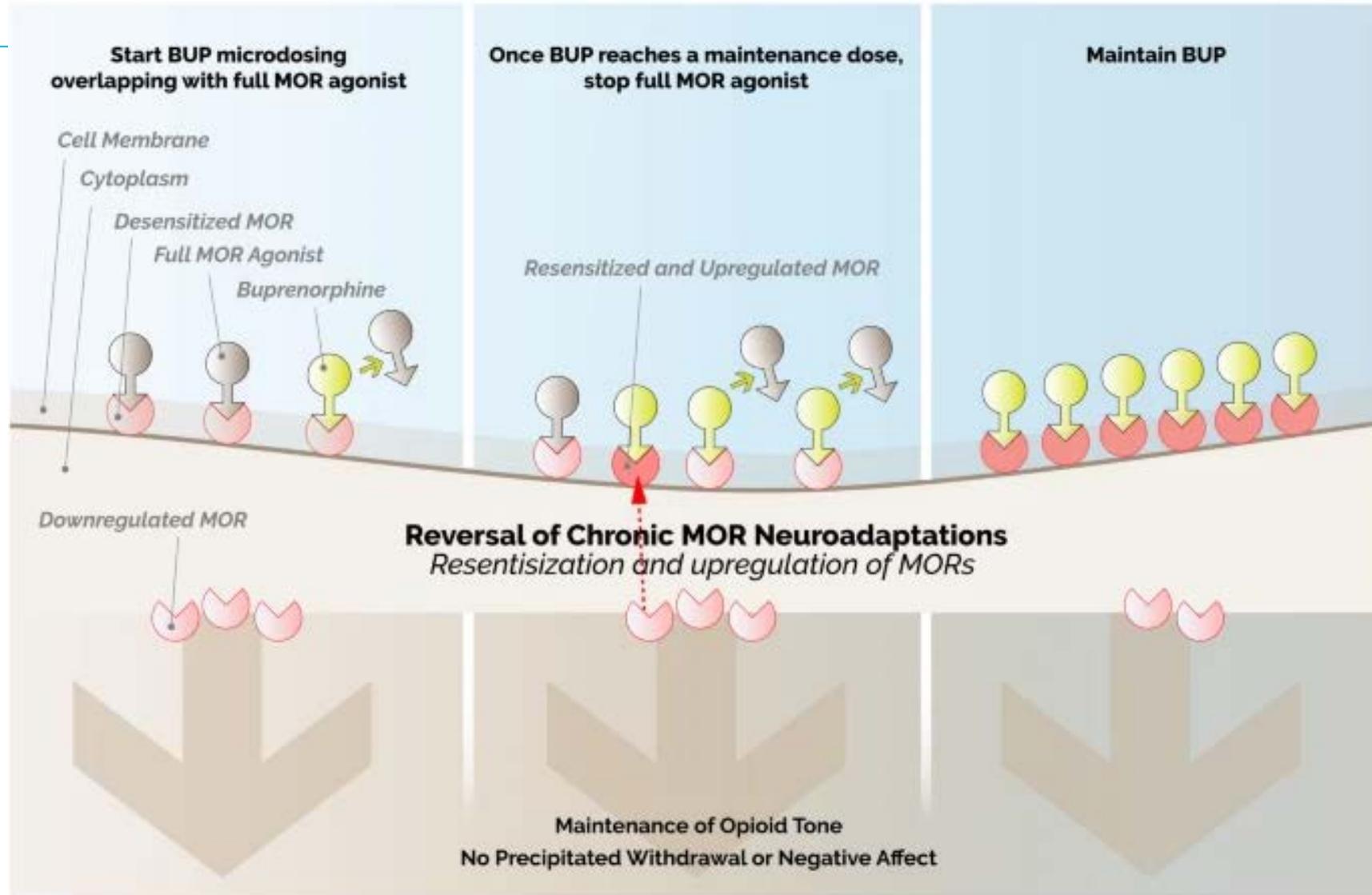
Low dose induction strategy



+
Buprenorphine 8mg BID



Buprenorphine Microinduction in Opioid-dependent Persons



Low dose induction data

- Relatively sparse
 - Case reports
 - Anecdotal
- success



Low Dose Buprenorphine Initiation (*aka Micro-induction*) Techniques

Formulation	Pros	Cons
Buprenorphine injection (Buprenex [®])		-Expensive -Not widely available
Buprenorphine transdermal film (Butrans [®])	Easy to use	-Indicated only for pain -72 hours to reach steady state -Expensive
Buprenorphine/naloxone SL film or tab	Outpatient accessibility	-Concern about stability when quartered (0.5mg) -May not work in hospital setting
Buprenorphine buccal film (Belbuca [®])	4 hours action Less expensive	-Indicated for pain, could be an issue in outpatient setting

Buprenorphine Formulation Equivalencies

Buprenorphine patch dose	Total dose per day	Dose equivalency to Buprenorphine (SUBUTEX) in mg
10mcg patch	240mcg per day	0.125mg
20mcg patch	480mcg per day	0.25mg
40mcg patch	960mcg per day	0.5mg
80mcg patch	1920mcg per day	1mg

Buprenorphine (BELBUCA) tablet dose	Dose equivalency to Buprenorphine (SUBUTEX) in mg
225 mcg	~0.5 mg
450 mcg	~1 mg
900 mcg	~2 mg

Weimer MB, Guerra M, Morrow G, Adams K. Hospital-based Buprenorphine Micro-dose Initiation. J Addict Med. 2021 May-Jun 01;15(3):255-257.

Table 1. Daily Schedule of Buprenorphine Uptitration and Discontinuation of Full Agonist Opioid Therapy for Patient Receiving Controlled-Release Oxycodone, 80 mg 3 Times Daily

Day	Buprenorphine-Naloxone (Only Buprenorphine Dosage Listed)	Controlled-Release Oxycodone Dosage
1	0.5 mg twice daily*	80 mg 3 times daily
2	1 mg twice daily†	80 mg 3 times daily
3	1 mg 3 times daily†	80 mg 3 times daily
4	2 mg 3 times daily	80 mg twice daily
5	4 mg 3 times daily	None
≥6	Adjust dose to symptoms	None

* One-quarter 2-mg tablet.

† One-half 2-mg tablet.

Day of transition	Becker, et al. Bup/nlx dose	Terasaki, et al. Bup/nlx dose	Weimer, et al. Buccal Bup + Bup/nlx Hospital Based
1	Bup/nlx 0.5mg BID (+ OA)	Bup/nlx 0.5mg daily (+ OA)	Buccal Bup 225mcg (+OA)
2	Bup/nlx 1mg BID (+ OA)	Bup/nlx 0.5mg BID (+ OA)	Buccal Bup 225mcg BID (+ OA)
3	Bup/nlx 1mg TID (+ OA)	Bup/nlx 1mg BID (+ OA)	Buccal Bup 450mcg BID (+ OA)
4	Bup/nlx 2mg TID (+ OA)	Bup/nlx 2mg BID (+ OA)	Bup/nlx 2mg BID (+ OA)
5	Bup/nlx 4mg TID (+ OA)	Bup/nlx 4mg BID (+ OA)	Bup/nlx 4mg BID (+ OA)
6	Full transition complete	Bup/nlx 4mg TID (+ OA)	Bup/nlx 4mg TID (+ OA)
7		Full transition complete	Full transition complete

Bup/nlx = Buprenorphine/naloxone
 OA = full opioid agonist

Teraski, et al, Pharmacotherapy 2019.
 Becker, et al, Annals of IM, 2020
 Weimer, et al. Journal Addiction Med, 2021

Outpatient handout for patients and providers

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Buprenorphine dose	0.5mg daily	0.5mg BID	1mg BID	2mg BID	4mg BID	4mg TID	8mg BID
Strip size	2mg	2mg	2mg	2mg	2mg	2mg	8mg
Morning dose							
Afternoon Dose							
Night dose							
Full agonist	Continue	Continue	Continue	Continue	Continue	Continue	STOP



Slide attributed to Dr. Shawn Cohen

Hospital-based Low Dose Buprenorphine Transition Limitations

- CMS conditions for participation
 - Safe delivery of medication
 - Must confirm beyond use dating if meds are manipulated or repackaged
 - Data on buprenorphine integrity when split is mixed
- Cost
 - Transdermal buprenorphine expensive and lasts 7 days, wasteful to use it in varying doses
- Time to steady state
 - TD buprenorphine steady state ~72 hours
 - Buccal buprenorphine steady state ~4 hours, high bioavailability

Table 2: Buccal Buprenorphine Induction Strategy

Day	Buccal buprenorphine film dose	SL buprenorphine/naloxone film dose	Full Opioid Agonist Dose
1	225 mcg PO once (75 mcg film + 150 mcg film)		Full dose
2	225 mcg PO twice daily (75 mcg film + 150 mcg film)		Full dose
3	450 mcg PO twice daily		Full dose
4		2 mg SL BID	Full dose
5		4 mg SL BID	Full dose
6		4mg SL TID	Full dose
7		4mg SL TID – 8mg SL BID	Stop
PO = per oral ; BID = twice daily ; TID = three times daily ; SL = sublingual			

Caveats

- Methadone dose >60-80mg
- Inconsistent use of full opioid agonist
- Inconsistent use of buprenorphine formulation
- High baseline anxiety
- Concomitant benzodiazepine withdrawal
- High anxiety/mistrust about the transition

Questions?

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5-minute version



1 pager

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Upcoming ECHO OUD Session		
Date	Topic	Presenter
07/16/21	Disparities in Treatment of OUDs within the LGBTQ Community	Alex Keuroghlian MD, MPH

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