Buprenorphine Microdosing Induction
An Evolving Practice

Indian Country HCV teleECHO
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Disclosures

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Nothing to disclose

Learning Objectives

At the end of this activity, participants should be able to:

- Explain the need for alternative induction methods
- Describe the reasoning behind buprenorphine microdosing induction
- Utilize a common buprenorphine microdosing strategy
- Discuss the supporting evidence

Precipitated Withdrawal (PW)

- Incidence of Precipitated Withdrawal in a 2020-2022 Multisite ER Trial was low: **0.76%** [1]

  In all cases of PW - the patient had used Fentanyl

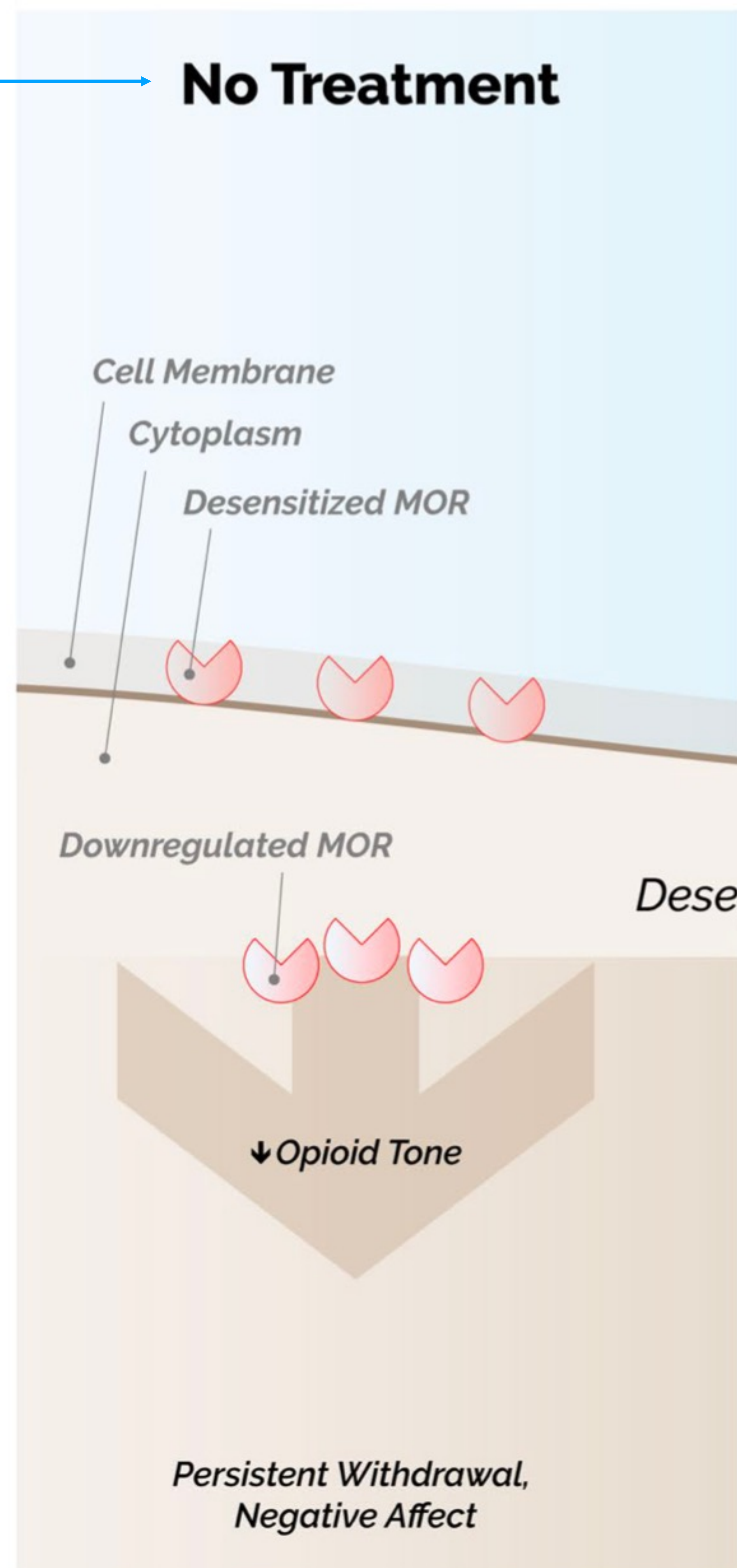
  However, most patients who did NOT have PW, had also used Fentanyl

- Some evidence suggests that experiencing Precipitated Withdrawal decreases subsequent treatment success. [2,3]

1. D'Onofrio, et al. Incidence of Precipitated Withdrawal During a Multisite Emergency Department-Initiated Buprenorphine Clinical Trial in the Era of Fentanyl. *JAMA Netw Open.* 2023;6(3):e236108. doi:10.1001/jamanetworkopen.2023.6108
2. Cunningham CO, Roose RJ, Starrels JL, Giovanniello A, Sohler NL. Prior buprenorphine experience is associated with office-based buprenorphine treatment outcomes. *J Addict Med*. 2013;7(4):287-293.
3. Silverstein SM, Daniulaityte R, Martins SS, Miller SC, Carlson RG. "Everything is not right anymore": buprenorphine experiences in an era of illicit fentanyl. *Int J Drug Policy*. 2019;74:76-83.

Regular Interaction Between Buprenorphine and Full Opioid Agonist in Opioid-dependent Persons

Opioid Dependent Person



Precipitated Withdrawal

Joao P. De Aquino · Suprit Parida · Mehmet Sofuoglu
The Pharmacology of Buprenorphine Microinduction for Opioid Use Disorder
Clinical Drug Investigation (2021) 41:425–436

Buprenorphine Microdosing Strategy (Bernese method)

Day 1: 0.5 mg once a day

Day 2: 0.5 mg twice a day

Day 3: 1 mg twice a day

Day 4: 2 mg twice a day

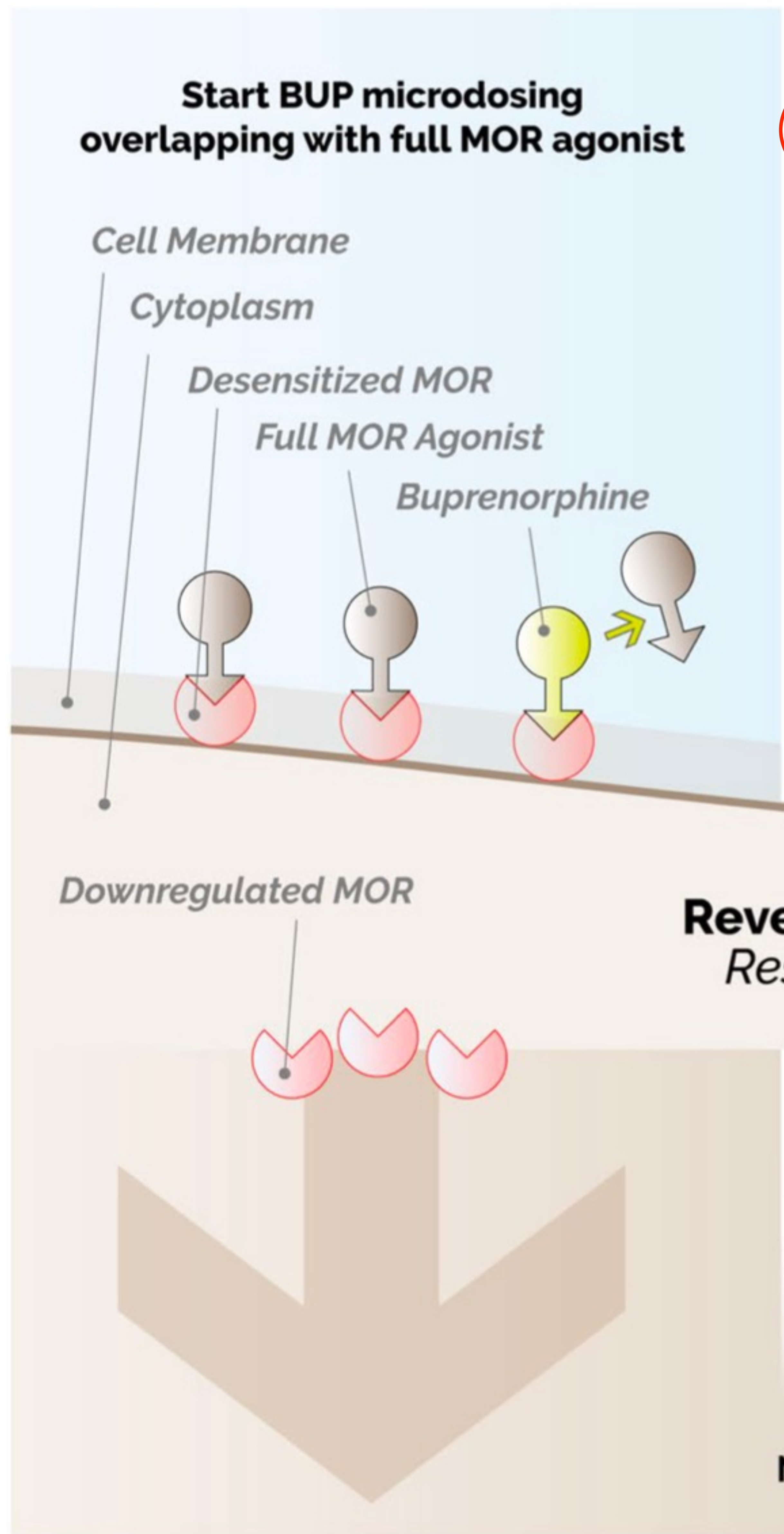
Day 5: 3 mg twice a day

Day 6: 4 mg twice a day

Day 7: 12 mg (stop other opioids)

Randhawa P. Et al. Buprenorphine-naloxone “microdosing”: an alternative induction approach for the treatment of opioid use disorder in the wake of North America’s increasingly potent illicit drug market. *Canadian Medical Association Journal* JANUARY 20, 2020, 192(3)

Buprenorphine Microinduction in Opioid-dependent Persons



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Evidence for Buprenorphine Microdosing

- No randomized, controlled trials!
- Several case reports are published.
- Literature Review of 18 papers: 63 patients were transitioned from other opioids to Bup [1]

  Typical initial Buprenorphine doses were 0.2-0.5mg daily

  Most titration periods were 4-8 days

  Most participants completed titration at Buprenorphine 8-16mg
- A case series of patients using fentanyl, comparing 2 patients experiencing PW during traditional induction, and 2 patients with no PW during bup microinduction [2]

1. Ahmed S, et al. Microinduction of Buprenorphine/Naloxone: A Review of the Literature. *American Journal on Addictions* 2021, 30:305-315
2. Antoine D, et al. Method for Successfully Inducting Individuals Who Use Illicit Fentanyl Onto Buprenorphine/Naloxone. *American Journal on Addictions* 2021, 30:83-87.

Prescribing Pearls

- The dose required to address CRAVINGS is usually higher than the dose required to resolve WITHDRAWAL

- To address co-occurring PAIN, split daily dose to TID or QID [1]

- For STRESS-RELATED cravings, consider CLONIDINE 0.1mg TID (scheduled or PRN) [2]

- For co-occurring ALCOHOL USE DISORDER: don't use Naltrexone, but do consider treatment with ACAMPROSATE (FDA-approved) or TOPIRAMATE (off-label)

- >40% of OUD patients also have PTSD [3], so ask about symptoms and consider use of SSRI/SNRI, MIRTAZAPINE, PRAZOSIN (for nightmares), TRAZODONE (for insomnia), counseling referral

1. Alford D, et al. Acute Pain Management for Patients Receiving Maintenance Methadone or Buprenorphine Therapy. *Annals of Internal Medicine.* Jan 2006; 144(2): 127-134.
2. Kowalczyk W. et al. Clonidine Maintenance Prolongs Opioid Abstinence and Decouples Stress From Craving in Daily Life: A Randomized Controlled Trial With Ecological Momentary Assessment. *American Journal of Psychiatry.* August 2015; 172(8): 761-767.
3. Lopez-Martinez A. Et al. Chronic pain, PTSD and Opioid Intake: a systematic review. *World J Clin Cases* Dec 2019; 7(24): 4254-4269.

Buprenorphine for Pain

Well tolerated, can improve pain scores and affective symptoms

Chong J, et al. Managing long-term high-dose prescription opioids in patients with non-cancer pain: The potential role of sublingual buprenorphine.
Aust J Gen Practice. Jun 2020; 49(6):339-343.

Safe and efficacious pain treatment for patients with SUD or high-risk opioid overuse/misuse; 6-year data set

Kaski S, et al. Sublingual Buprenorphine/Naloxone and Multi-Modal Management for High-Risk Chronic Pain Patients
Journal of Clinical Medicine. March 2021; 10(5)

Significant advantages over other opioids used for chronic pain: better safety profile and tolerability. Less likely to lead to hyperalgesia.

Rudolf G. Buprenorphine in the Treatment of Chronic Pain. *Phys Med Rehabil Clin N Am.* May 2020; 31(2):195-204.

33 studies reviewed; all 33 showed efficacy for buprenorphine in pain relief

Pergolizzi J, Raffa R. Safety and Efficacy of the Unique Opioid Buprenorphine for the Treatment of Chronic Pain. *Journal of Pain Research.*
December 2019;12:3299-3317.

Thank you for what you do!

Questions or Experiences to Share?