Improving Prescribing

Brian Hurley, M.D., M.B.A., DFASAM
Clinical Director, CCI Addiction Treatment Starts Here
Director of Addiction Medicine, Los Angeles County Department of Health Services
Assistant Professor of Addiction Medicine, UCLA Department of Family Medicine

Brian Hurley, M.D., M.B.A., DFASAM

No disclosures

Before We Jump In

- Introductions
- What are your top questions about integrating medications for opioid use disorder into your behavioral health programs?

Treatment Goals

- Range of treatment goals

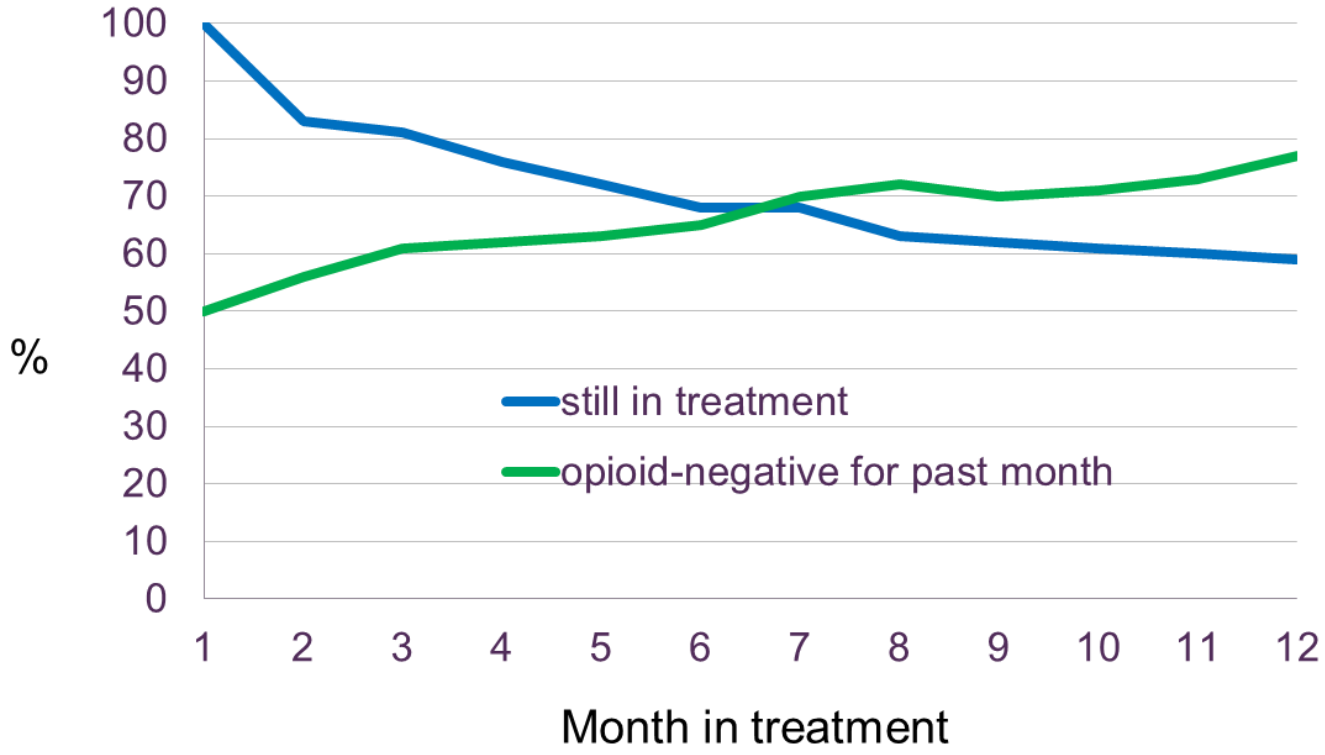
Minimization of harms from ongoing use

Sustained recovery with abstinence from all substances

- Treatment Options; Federations of State Medical Boards 2013
  - Buprenorphine / Methadone / Naltrexone
  - Simple detoxification and no other treatment
  - Counseling and/or peer support without MAT
  - Referral to short or long term residential treatment

Treatment Retention and Decreased Illicit Opioid Use on MAT

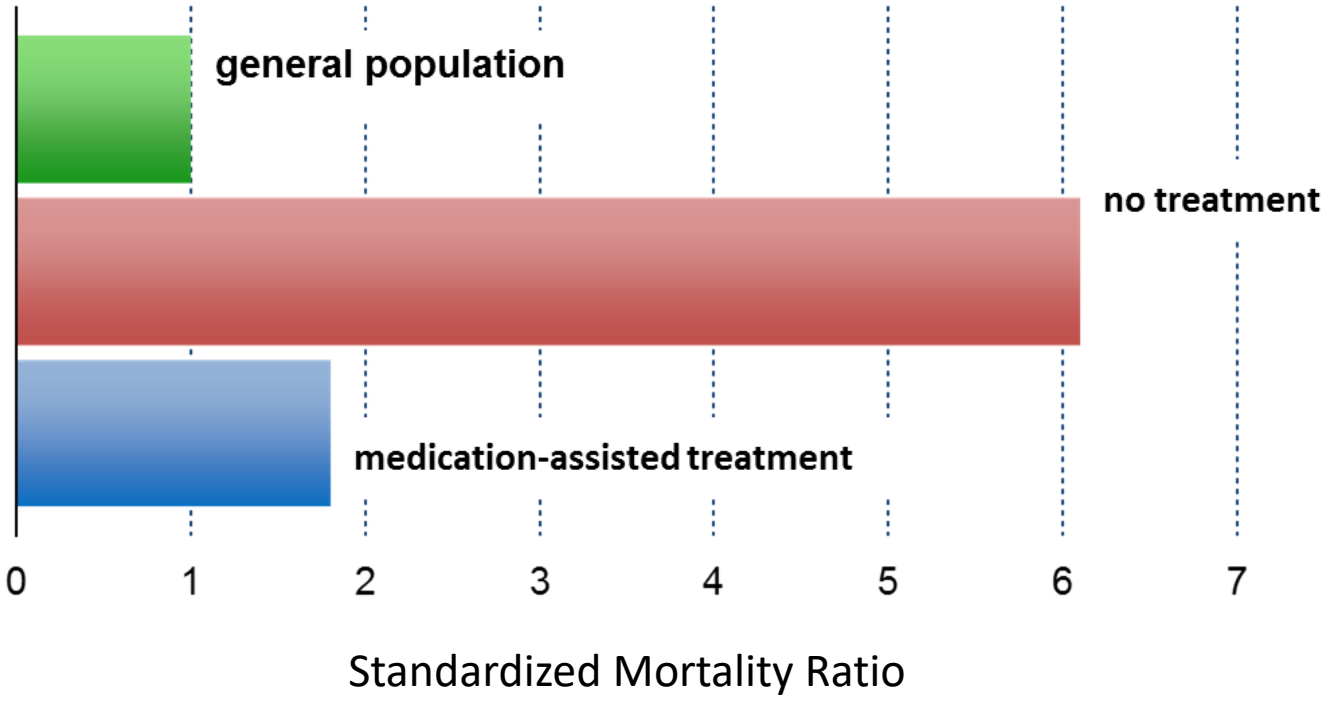
- Buprenorphine promotes retention, and those who remain in treatment become more likely over time to abstain from other opioids



Kakko et al, 2003
Soeffing et al., 2009

Benefits of MAT: Decreased Mortality

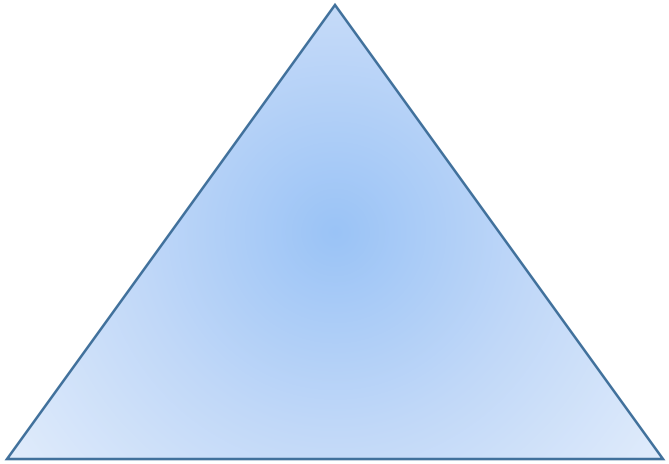
Death rates:



Dupouy et al., 2017
Evans et al., 2015
Sordo et al., 2017

Core Components of Addiction Treatment

*Medications



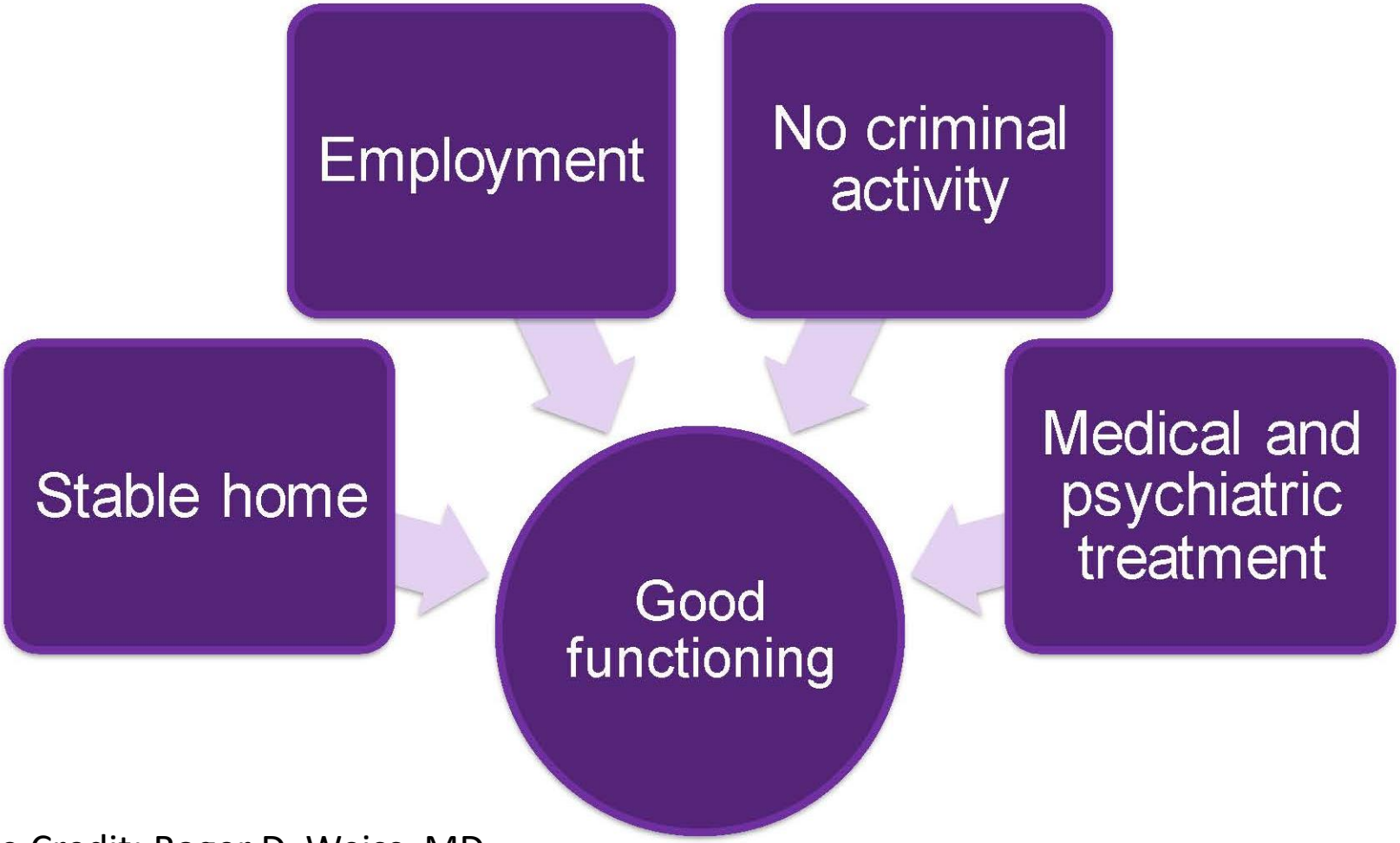
*Counseling

*Support

*When appropriate

Source: https://www.samhsa.gov/treatment

Psychosocial Treatment

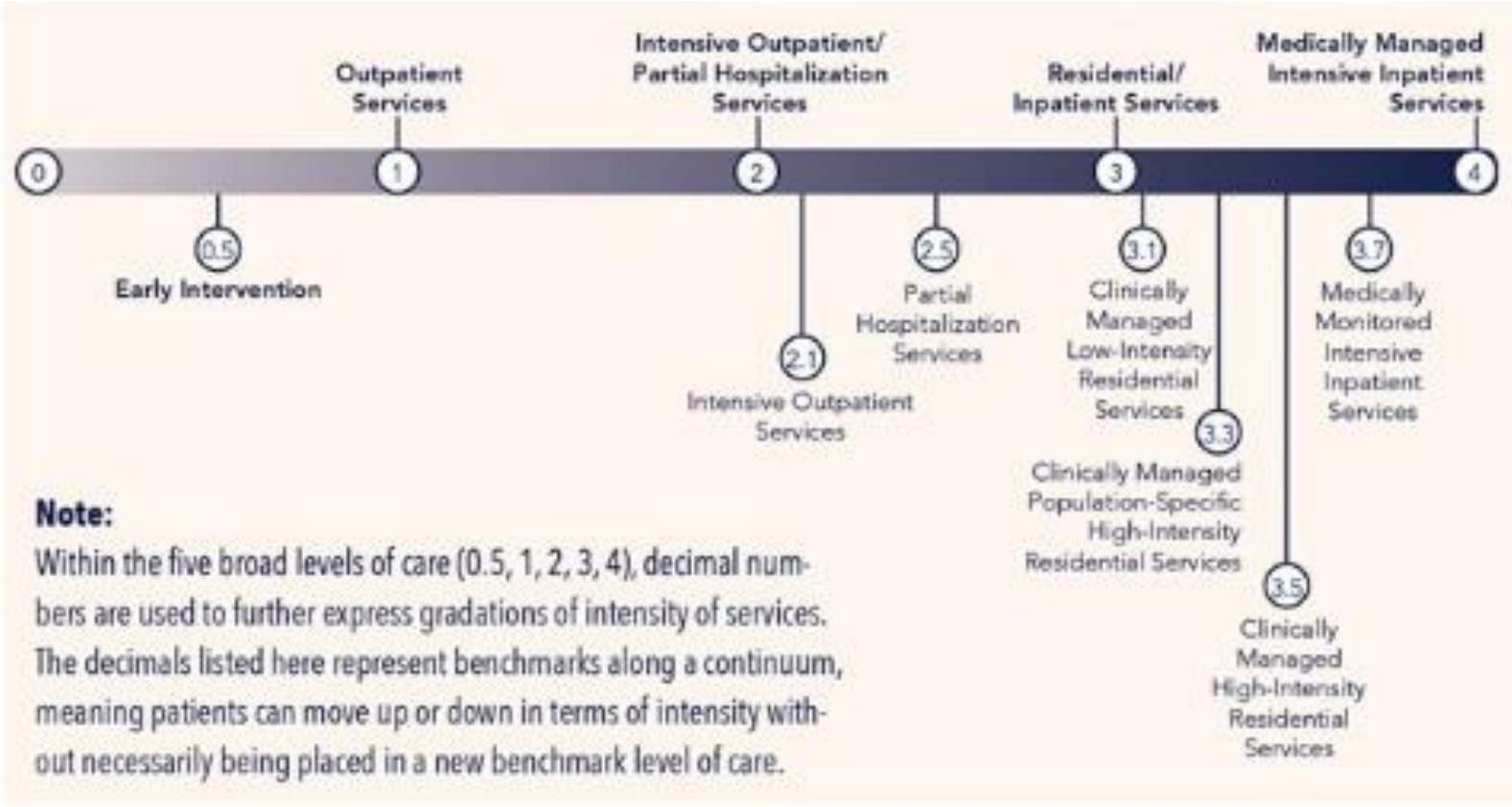


Slide Credit: Roger D. Weiss, MD

Psychosocial Treatment

- 12-step
- Cognitive and/or Behavioral Psychotherapies
- Motivational Enhancement Therapy
- Community Reinforcement
- Contingency Management
- Multisystemic Therapy
- Multidimensional Family Therapy

Addiction Treatment Intenisities



American Society of Addiction Medicine - http://www.asam.org/quality-practice/guidelines-and-consensus-documents/the-asam-criteria/about - accessed 1/15/2016

Psychosocial Treatment

- Many patients do well with medications for opioid use disorder alone, but we're not good at predicting who will and who won't do well
- Limited resources for behavioral treatment
- Some patients don't want counseling
- Understanding the importance of early treatment response may help our decision-making

Carroll, K. M., & Weiss, R. D. (2016). The role of behavioral interventions in buprenorphine maintenance treatment: a review. *American Journal of Psychiatry*, *174*(8), 738-747.

Medication First Model

1. People with OUD receive pharmacotherapy treatment as quickly as possible, prior to lengthy assessments or treatment planning sessions;
2. Maintenance pharmacotherapy is delivered without arbitrary tapering or time limits;
3. Individualized psychosocial services are continually offered but not required as a condition of pharmacotherapy;
4. Pharmacotherapy is discontinued only if it is worsening the person's condition.

- Medication *first* ***does not mean*** Medication *only*

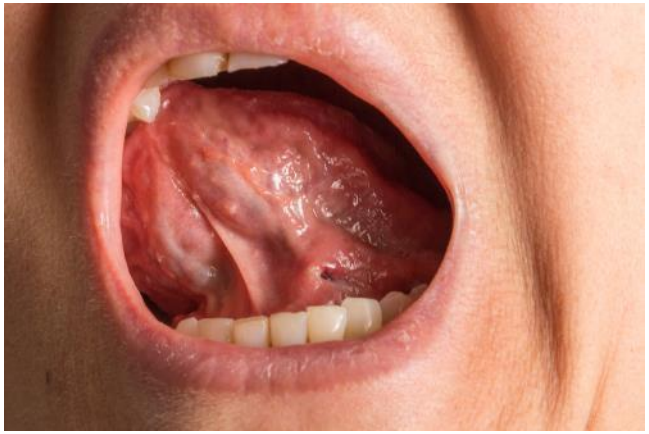
http://MissouriOpioidSTR.org/treatmentFor

In Opioid Use Disorder:
Adding psychosocial support does not change the effectiveness of retention in treatment and opiate use during treatment.

Amato L, Minozzi S, Davoli M, Vecchi S. Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No.: CD004147. DOI: 10.1002/14651858.CD004147.pub4

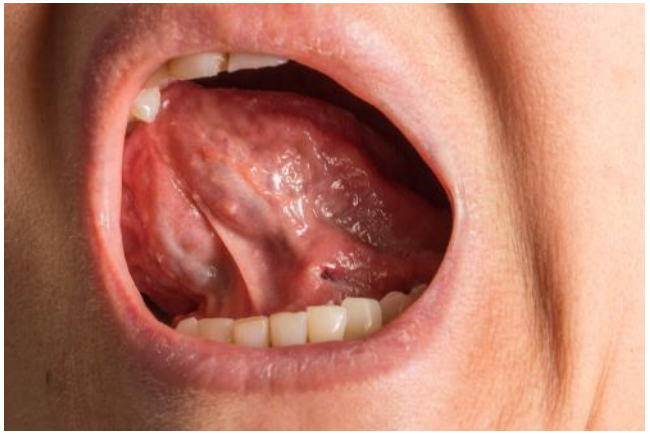
Challenge #1 – How to Start

- How to start buprenorphine?
  - Instruct the patient to stop using opioids, wait until they're in withdrawal, then have them take sublingual buprenorphine and up-titrate until they're not longer in withdrawal.



Challenge #1 – How to Start

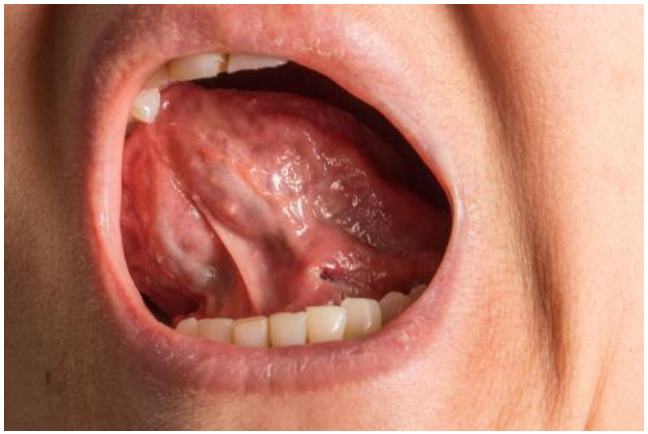
- How to start buprenorphine?
  - Usual dose:
  - 2mg/0.5mg or
  - 4mg/1mg q2H



  - Can go up to a recommended max dose of 8mg-12mg on day 1 and 16mg on day 2; not every patient needs these doses.

Challenge #1 – How to Start

- Patient handouts and education available



Example of a Handout:

How to Start Buprenorphine/naloxone at Home (Suboxone Induction)

Get into some withdrawal before starting buprenorphine

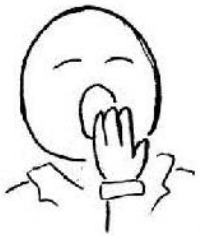
Heroin, oxycodone (Percocet), hydrocodone (Norco), morphine: don't use for 8-18 hours

Extended Release Oxycodone/morphine (Oxycontin, MS-Contin): don't take any for 24-36 hours

Methadone: don't use for at least 72 hours, be down to 20-30mg (maybe longer, ask your provider)

Waiting longer is better. If you take buprenorphine too soon, you can feel worse. You should feel better once starti

You need at least 3 of the following feelings before taking your first buprenorphine dose*:

Yawning	Sweating or chills
Enlarged pupils	Restless/Can't sit still
Joint and bone aches	Anxiety, irritable, fast heart beat
Shaking or twitches	Bumpy skin (Gooseflesh)
Watery eyes/Runny Nose	Lost Appetite, Stomach cramps
Nausea, vomiting or Diarrhea	

Buprenorphine Home Start Instructions (hydrocodone, short-acting oxycodone, heroin, etc)

Prescribe buprenorphine/naloxone 8/2mg tablets or films #14, PRN withdrawal meds are typically not needed but optional

Day One/First Dose: Don't use for 8-18 hours. When you feel bad*, Put 4 mg (1/2 tablet or film) under your tongue and keep it there until it dissolves (about 20 minutes). You should feel better soon. *If you swallow buprenorphine tablets they will not work.*

Second Dose: At 2 hours after your first dose, see how you feel.

If you feel fine, don't take any more. If you still have withdrawal, take another 4 mg dose.

Do not take more than 8 mg (1 tab or film) of buprenorphine on Day One.

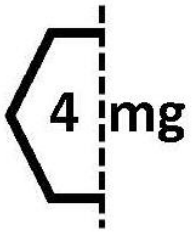
Day Two: Take one full tablet or film under the tongue. Wait 2 hours. If you still feel bad, take another 1/2 (daily dose is 12mg). If feeling ok, don't take more (8mg/day).

Two hours later, You may take a second 1/2 if you still feel bad (daily dose is 16mg).

Day Three and until your next visit

Take Dose from Day two: 1 to 2 tab/film(s) under the tongue as a single dose first thing every morning.

Matt Perez MD 2018



1/2 tab

Buprenorphine Implants and LAI

- Trade Names:
  - Probuphine
  - Sublocade

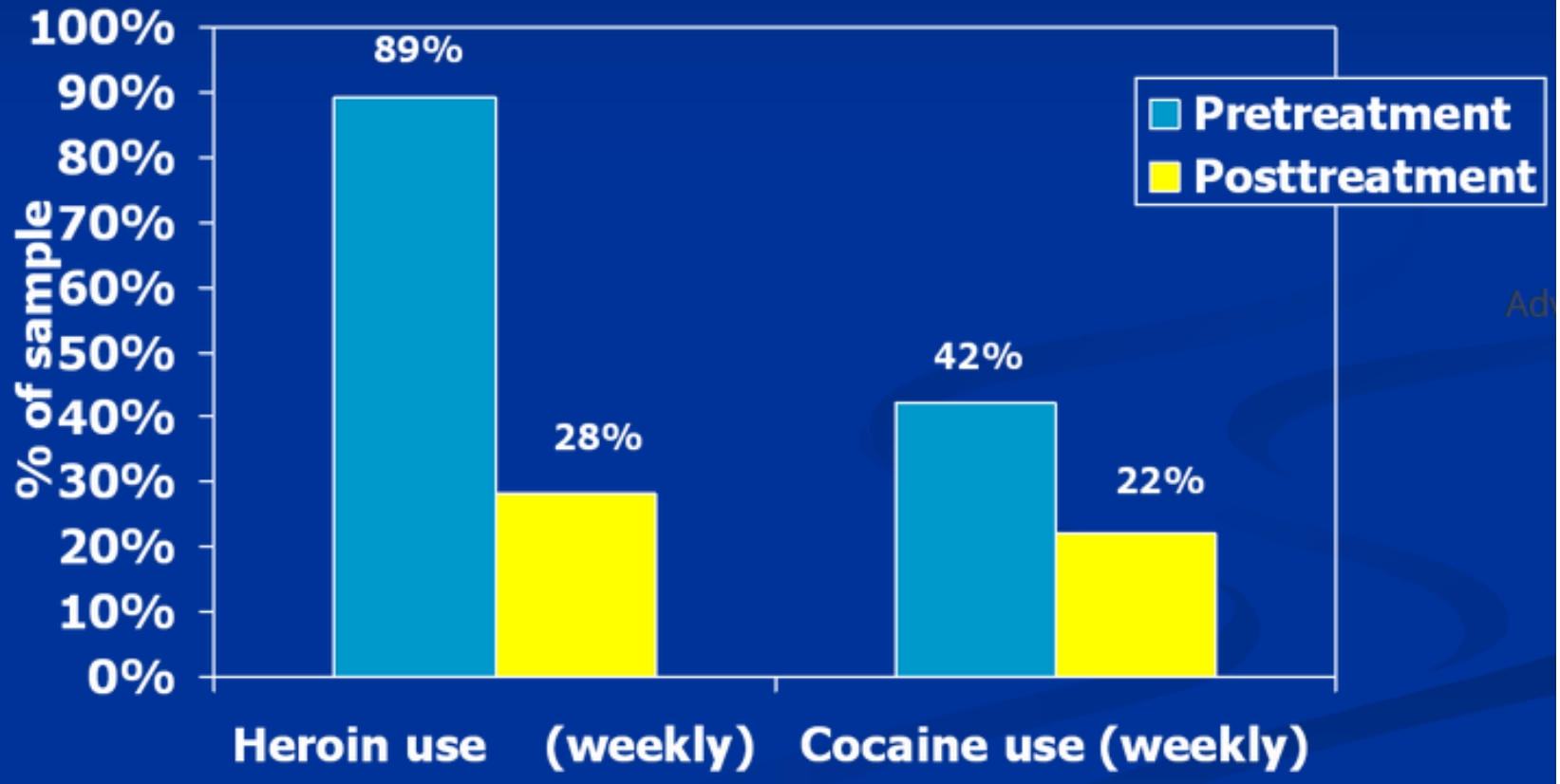
Buprenorphine Implants and LAI

- Requires sublingual buprenorphine lead-in
- Probuphine:
  - Achieved and sustained prolonged clinical stability on transmucosal buprenorphine
  - On 8 mg per day or less of Subutex or Suboxone or its equivalent for three months
- Sublocade:
  - Five day transmucosal lead-in
  - Equivalent of 8 to 24 mg of buprenorphine daily

What About Methadone?

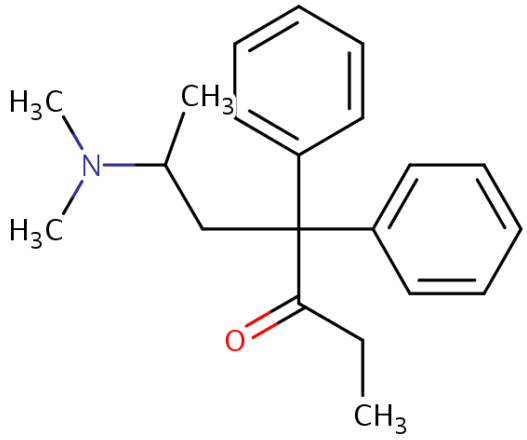
Methadone treatment efficacy

n=727, Hubbard et al. 1997



What About Methadone?

- If a patient is coming off methadone, they need to wait longer before taking buprenorphine



What About Methadone?

Adjunctive medications

Withdrawal Symptoms	Adjunctive Medications
Anxiety/restlessness	▪ a-$_2$ Adrenergic agonists (e.g. clonidine)
Insomnia	▪ Sedating antidepressants (e.g. trazodone)
Musculo-skeletal pain	▪ Acetaminophen, Ibuprofen
GI Distress (nausea, vomiting, diarrhea)	▪ Oral hydration ▪ Antispasmotics (e.g. dicyclomine) ▪ Antiemetics (e.g. ondansetron) ▪ Anti-diarrheals (e.g. loperamide)

What About Pregnant Patients?

- Same process, but use buprenorphine (monotherapy) instead of buprenorphine / naloxone
- Caution the patient about pre-term labor from opioid withdrawal

Home Vs. Office Starts

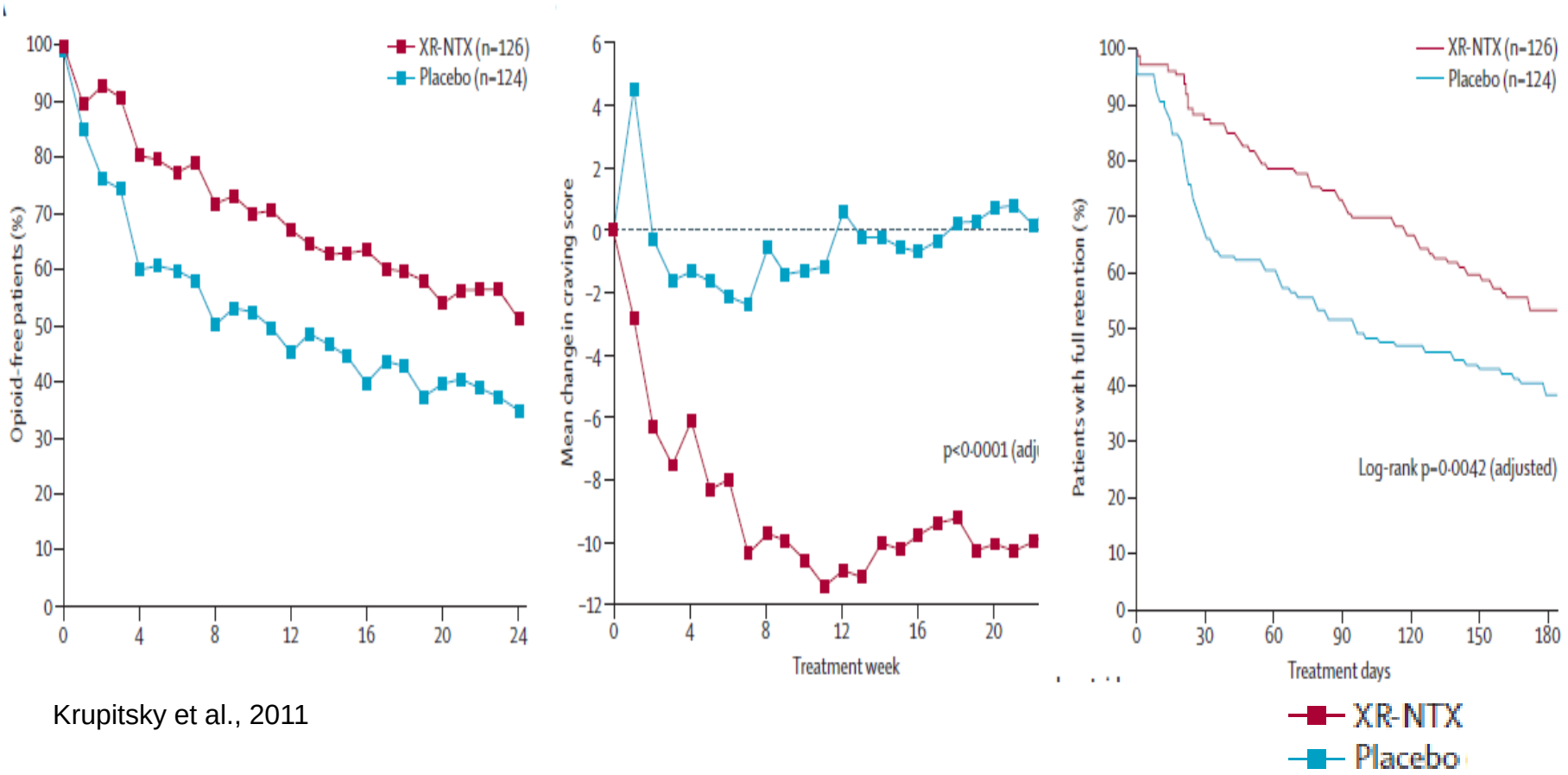
What About Patients In Controlled Settings?

- Start with 2mg/0.5mg daily, then 4mg/1mg daily, then 6mg/2mg daily and up titrate as tolerated

Naltrexone: LAI vs. Oral

- Adherence is key to naltrexone being effective
- Behavioral Naltrexone Therapy (BNT)
  - Voucher Incentives (CM)
  - Motivational and Cognitive Behavioral therapies
  - Involve a significant other (for monitoring medication adherence)

Naltrexone LAI: Efficacy



Krupitsky et al., 2011

There may also be a higher proportion of opioid, cocaine, benzodiazepine, cannabinoids, amphetamine - free patients. Comer et.al.,2011

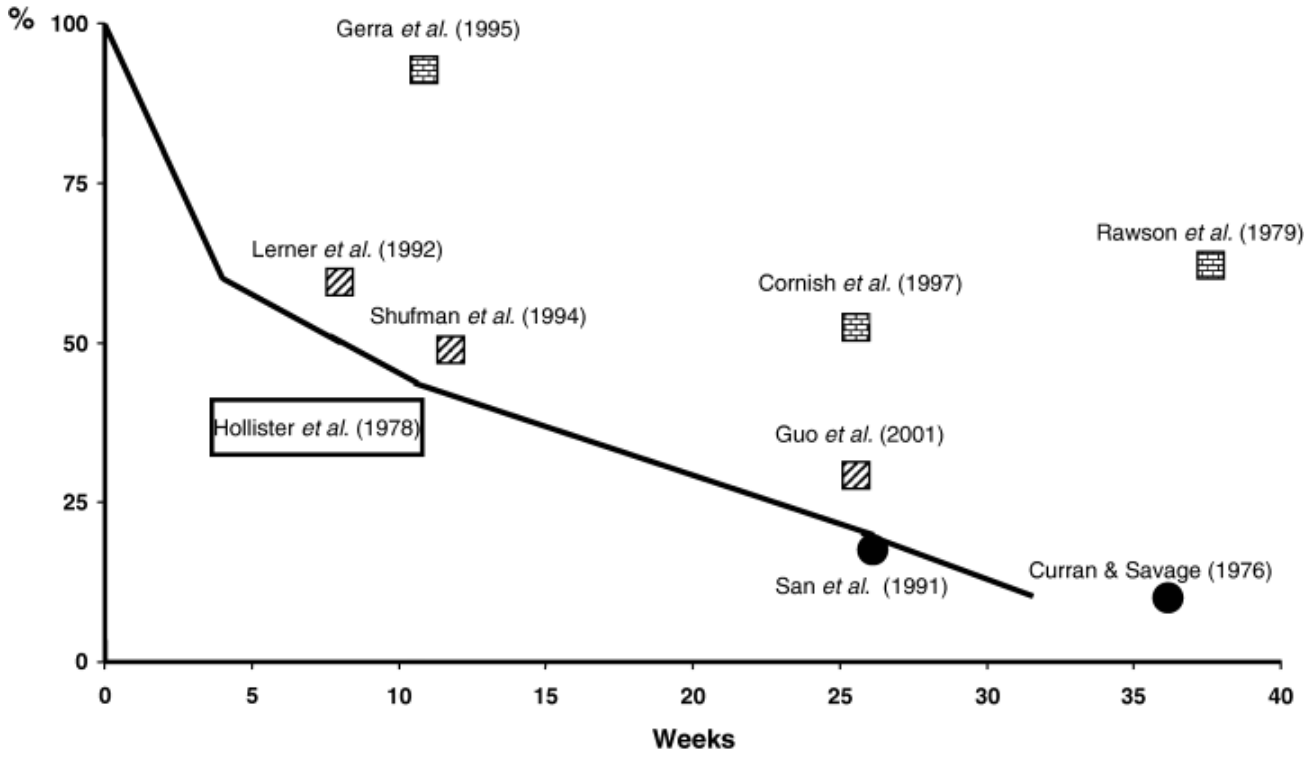
Oral Naltrexone

- Comparing naltrexone versus placebo or no pharmacological treatments, no statistically significant difference were noted.

Minozzi, S., Amato, L., Vecchi, S., Davoli, M., Kirchmayer, U., & Verster, A. (2011). Oral naltrexone maintenance treatment for opioid dependence. *Cochrane Database of Systematic Reviews*, (4).

Oral Naltrexone for OUD

Outcome: Treatment Retention

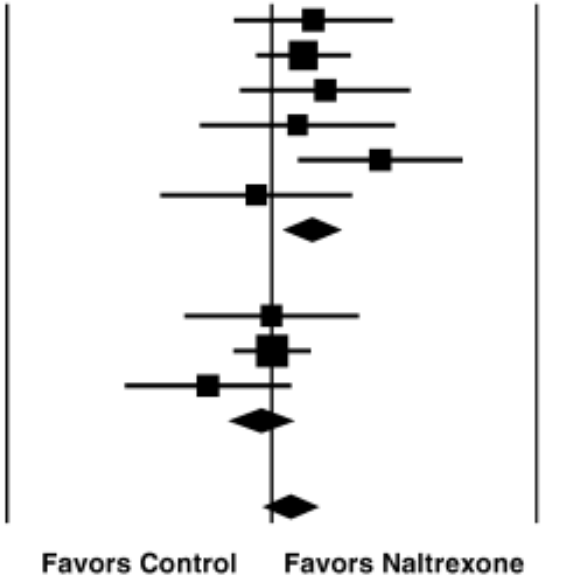


Johansson, B. A., Berglund, M., & Lindgren, A. (2006). Efficacy of maintenance treatment with naltrexone for opioid dependence: a meta-analytical review. *Addiction*, *101*(4), 491-503.

Oral Naltrexone for OUD

Outcome: Treatment Retention

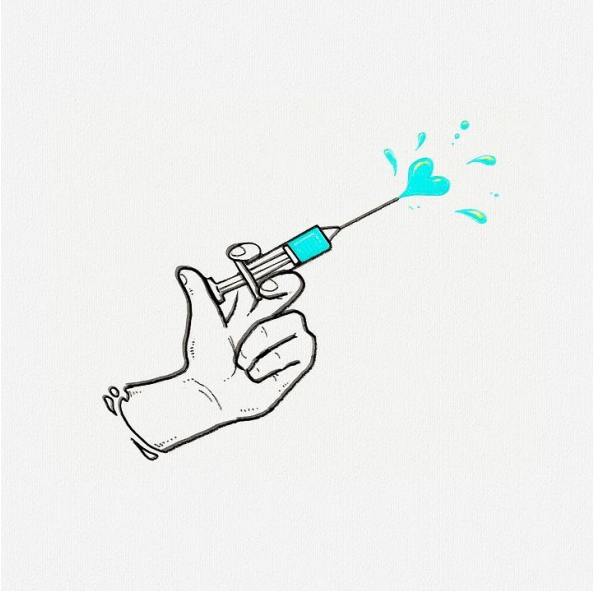
	Retention	Citation	NTotal	Effect	Lower	Upper
	High	Cornish *et al.* 1997	51	.32	-.29	.92
	High	Gerra *et al.* 1995	142	.24	-.12	.60
	High	Guo *et al.* 2001	49	.40	-24	.105
	High	Lerner *et al.* 1992	31	.19	-54	.93
	High	Rawson *et al.* 1979	58	.82	.20	.144
	High	Shufman *et al.* 1994	32	-.12	-.84	.61
Random	**High (6)**		**363**	**.31**	**.08**	**.53**
	Low	Curran & Savage 1976	38	.00	-.66	.66
	Low	Hollister *et al.* 1978	183	.00	-.29	.29
	Low	San *et al.* 1991	43	-.48	-.111	.15
Random	**Low (3)**		**264**	**-.08**	**-.32**	**.17**
Random	**Combined (9)**		**627**	**.15**	**-.07**	**.36**



Johansson, B. A., Berglund, M., & Lindgren, A. (2006). Efficacy of maintenance treatment with naltrexone for opioid dependence: a meta-analytical review. *Addiction*, *101*(4), 491-503.

Naltrexone LAI – How to Start

- How to start naltrexone long acting injection?
  - Window period is biggest factor
  - Doesn't require oral lead-in
  - Doesn't require recent LFTs



Naltrexone Long Acting Injection

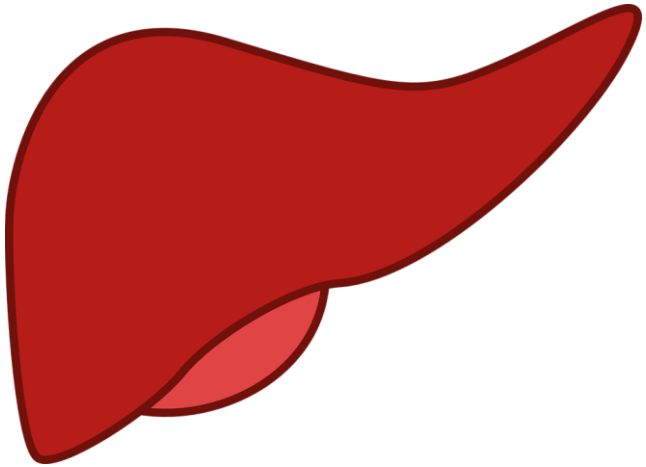
- Window period
  - 7 days from heroin and other short acting opioids (i.e. oxycodone / hydrocodone)
  - 10 days from extended release opioids (oxycodone-CR, or morphine sulfate-CR)
  - 14 days from buprenorphine or methadone

Naltrexone Long Acting Injection

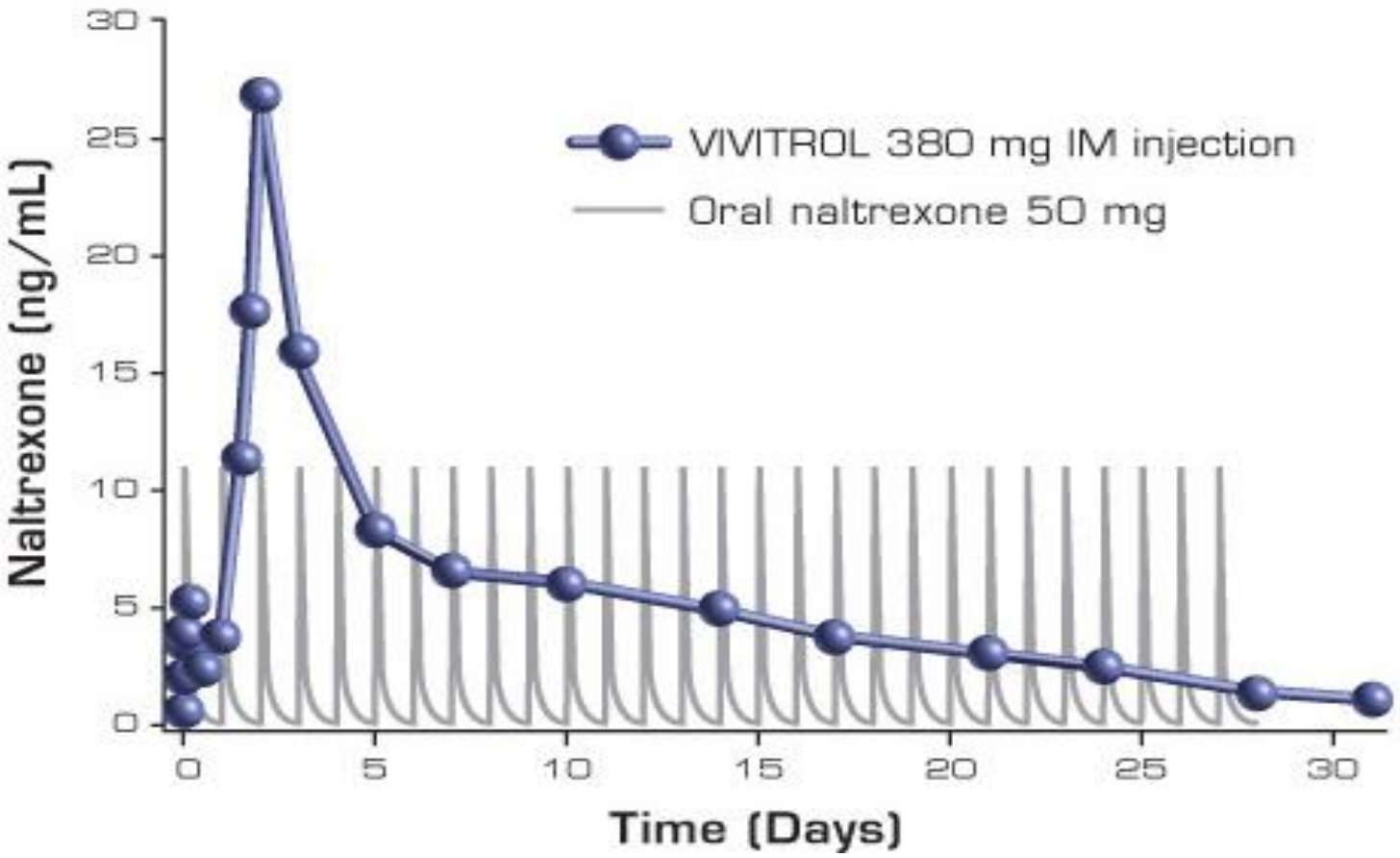
- Window Period - how to be sure?
  - Toxicology information is the usual standard
  - History
  - Collateral
  - CURES
  - *Naloxone challenge administered in the office*

Naltrexone Long Acting Injection

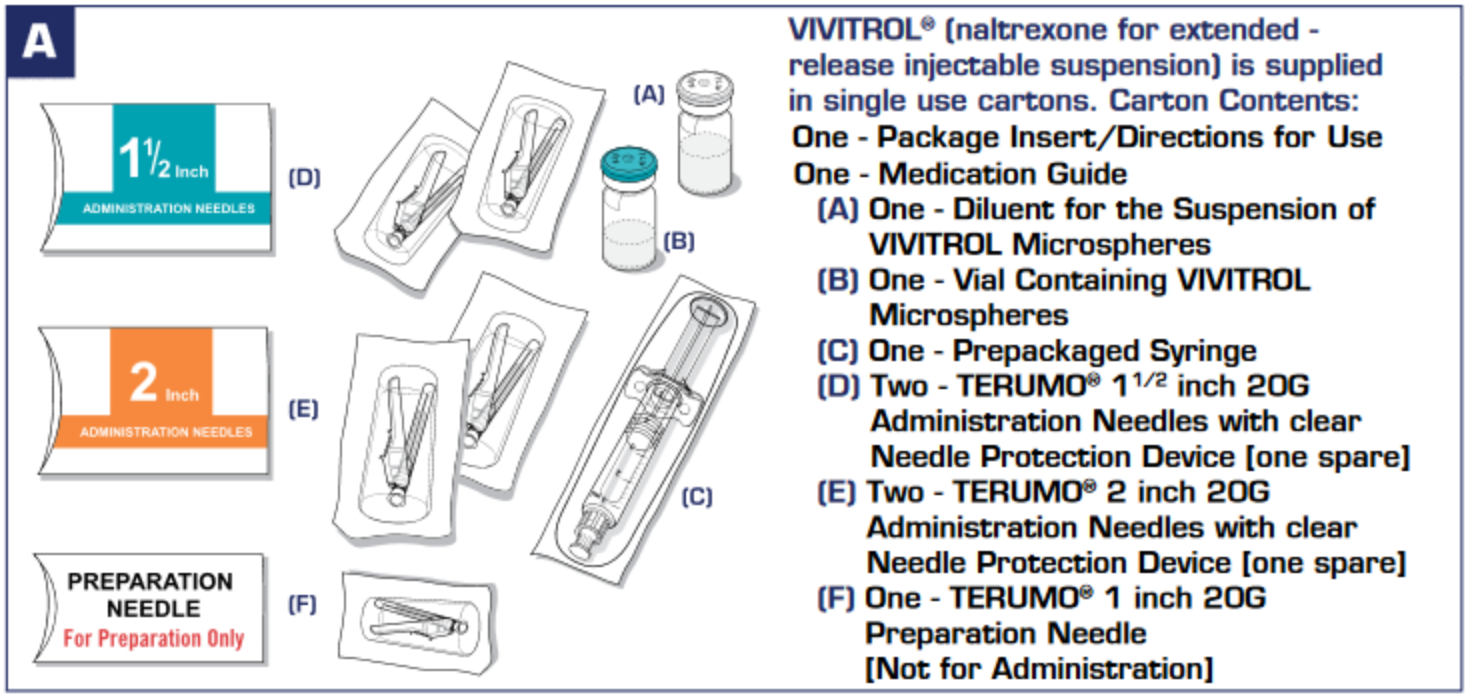
- Monitoring?
  - Liver monitoring only absolutely required if there are signs of liver disease (jaundice, abdominal pain, nausea, vomiting)
  - Generally good practice to obtain quarterly LFTs, but do not withhold naltrexone if liver function testing has not yet been obtained if patient is without signs or symptoms of active liver disease



Naltrexone Long Acting Injection

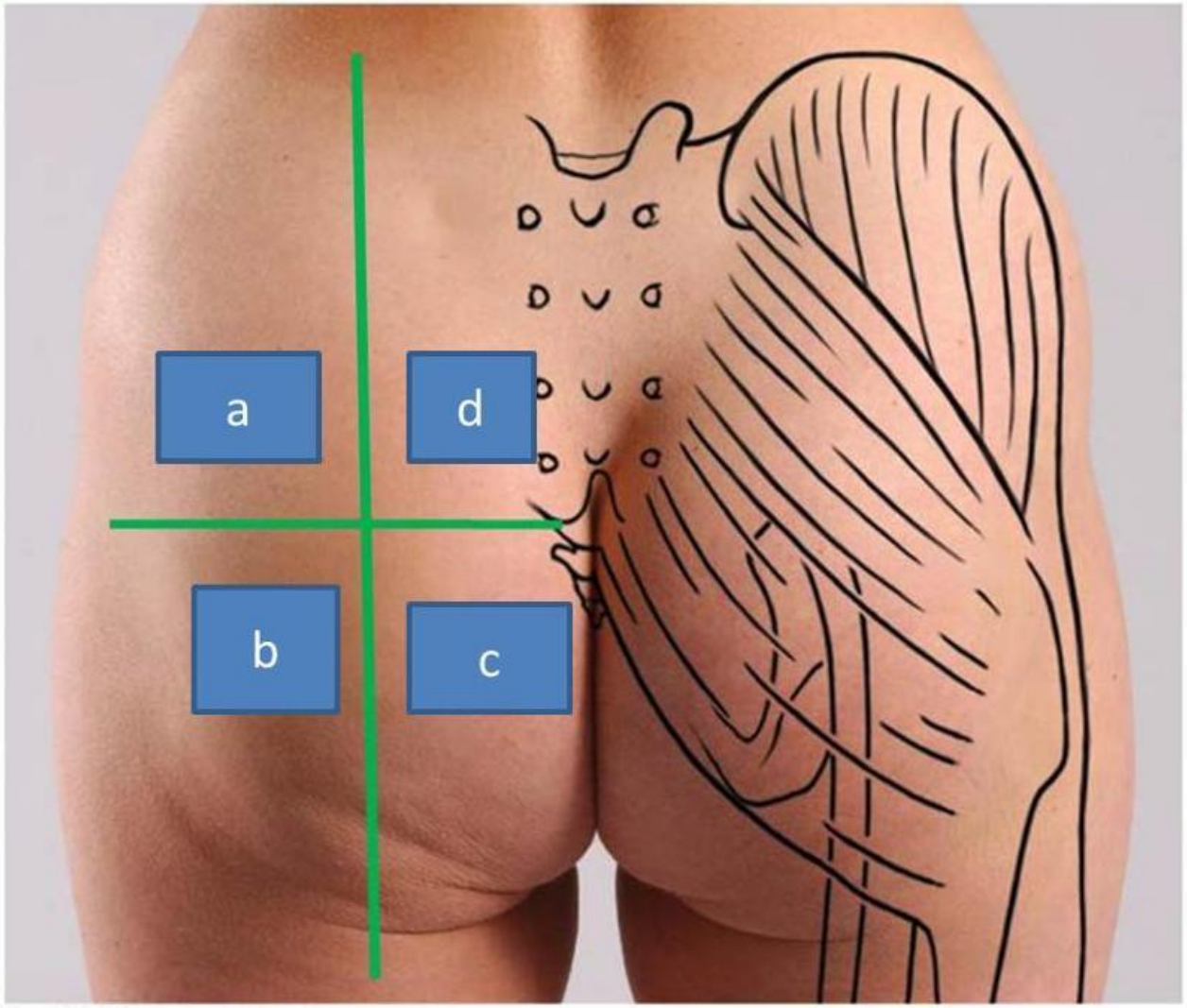


Naltrexone Long Acting Injection

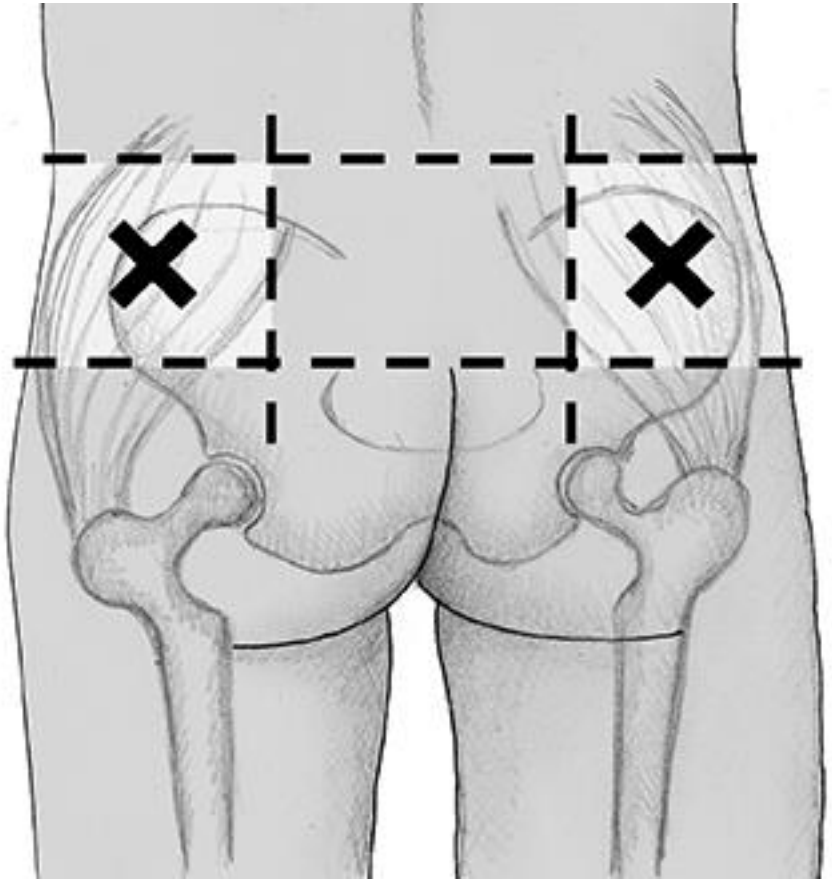


https://www.youtube.com/watch?v=lZBaDCIWSwg

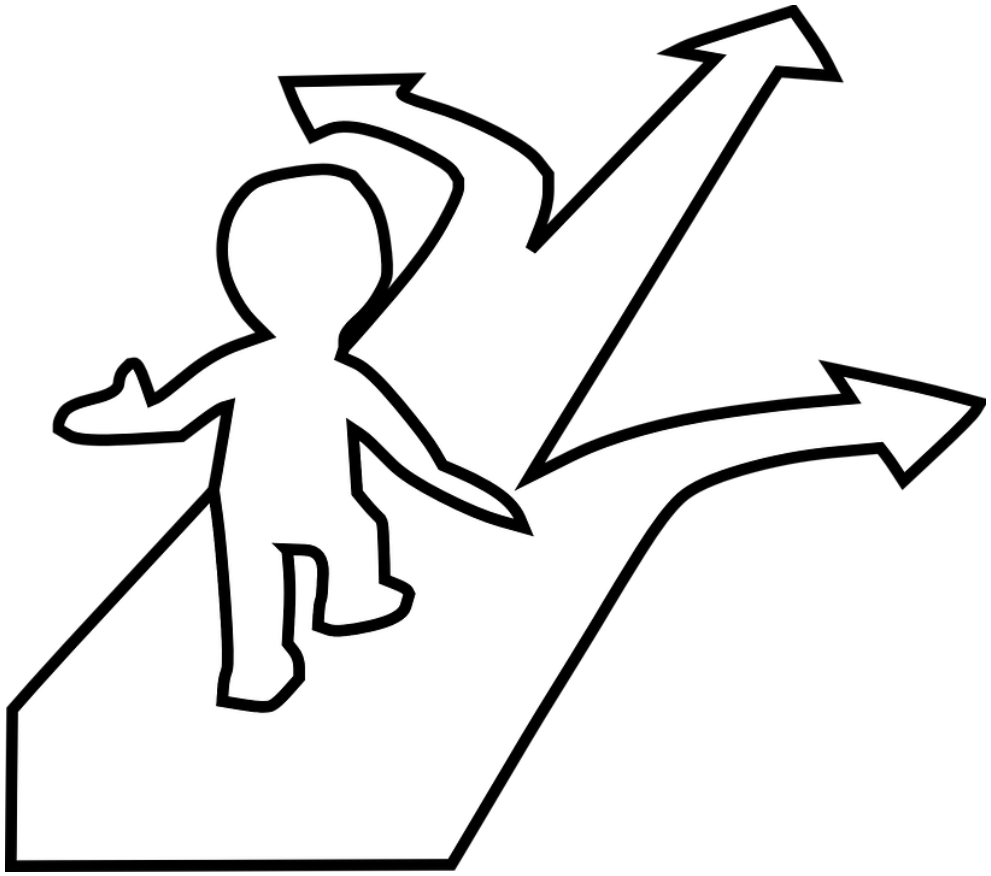
Naltrexone Long Acting Injection



Naltrexone Long Acting Injection



Which Medication to Select?



Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multicentre, open-label, randomised controlled trial

Ease of induction is a limitation of naltrexone and an advantage of buprenorphine.

Once successfully inducted to either naltrexone LAI or buprenorphine / naloxone similar outcomes:

- relapse-free survival
- overall relapse
- retention in treatment
- negative urine samples
- days of opioid abstinence
- self-reported cravings

Lee, J. D., Nunes, E. V., Novo, P., Bachrach, K., Bailey, G. L., Bhatt, S., ... & King, J. (2017). Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X: BOT): a multicentre, open-label, randomised controlled trial. *The Lancet*.

How To Guide Patient Medication Selection

Payer Questions

- Medi-Cal covers with no TAR / PA:
  - Buprenorphine/Naloxone tablets (generic)
  - Buprenorphine/Naloxone film (Suboxone®)
  - Buprenorphine/Naloxone tablets (Zubsolv®)
  - Buprenorphine tablets (generic)

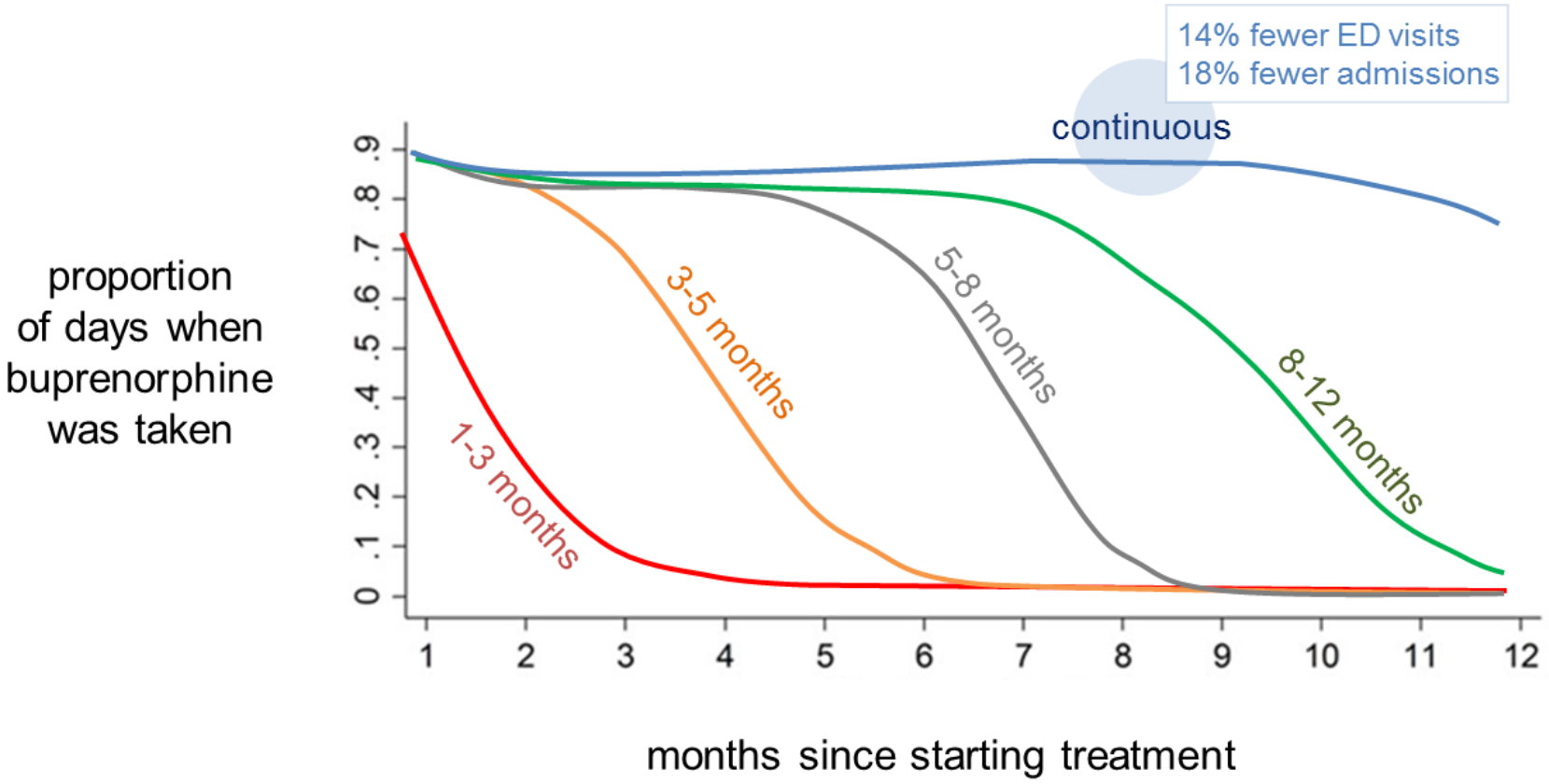
Payer Questions

- Medi-Cal covers with no TAR / PA:
  - Oral Naltrexone
- Medi-Cal covers with a TAR / PA:
  - Naltrexone Long Acting Injection
  - Buprenorphine Implants
  - Buprenorphine Long Acting Injection

Integrating MAT Into Psychosocial Treatment

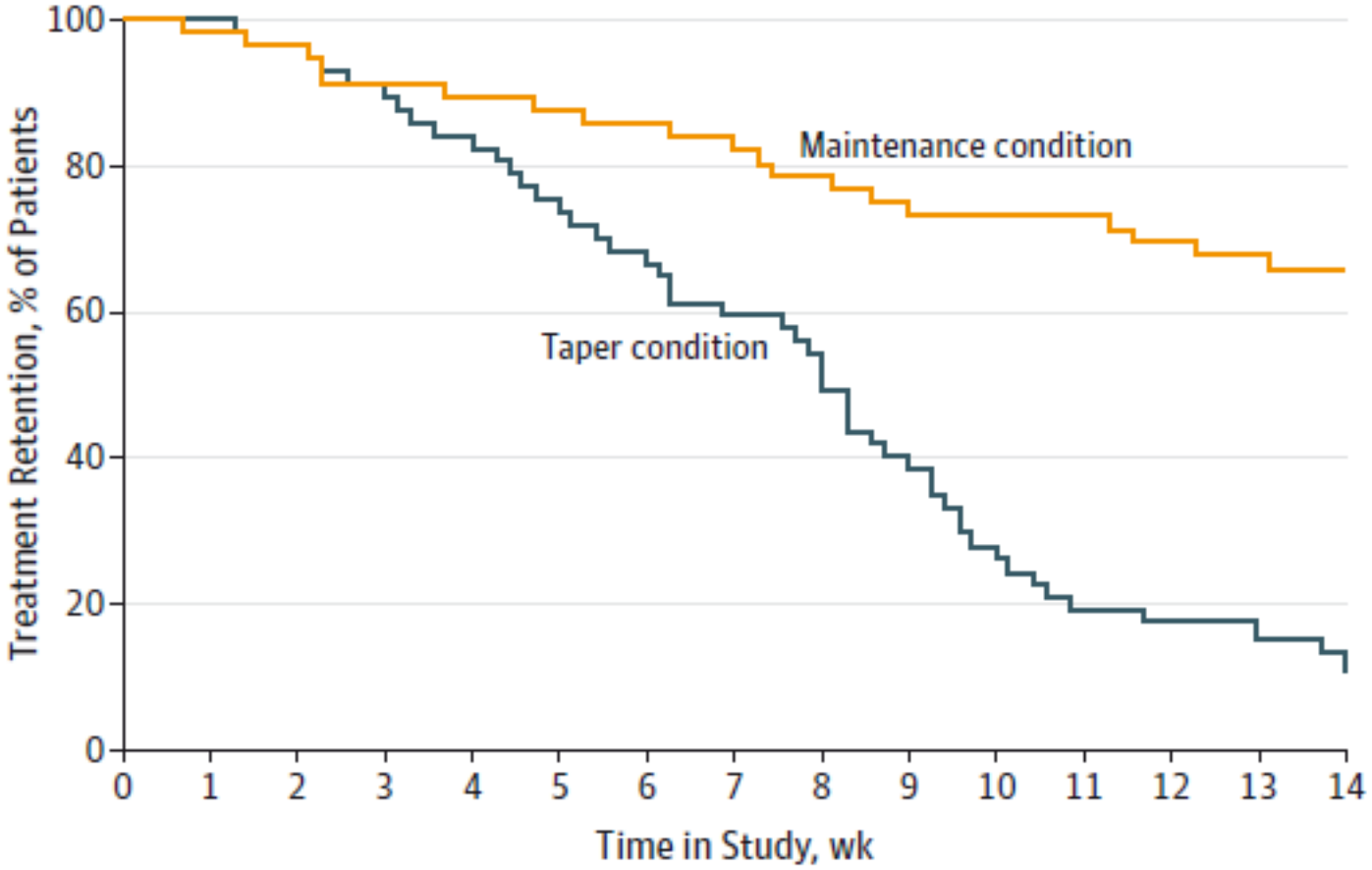
- Behavioral Naltrexone Therapy (BNT)

How Long to Continue Treatment?



Lo-Ciganic et al., 2016

How Long to Continue Treatment?



Fiellin et al., 2014

What Else?

Questions / Feedback

bhurley@ucla.edu

Interested in more? Come to the:

- CA Integrated Care Conference https://dmh.lacounty.gov/event/16th-statewide-integrated-care-conference
- ASAM Annual Meeting: https://www.asam.org
- CSAM Annual Meeting: https://csam-asam.org/page/AnnualConference
- AAAP Annual Meeting: https://www.aaap.org