# BUPRENORPHINE: How long is enough

Christopher Suelzer, MD.

# Objectives

- Discuss optimal duration of MAT using buprenorphine
- Discuss strategies if one is to discontinue MAT using buprenorphine

# CASE

- 42 yo male on MAT (buprenorphine ) for last 18m.
- Has been stable in all domains (employment, marriage, legal, medical and mental health)
  Is currently on 16mg. Tried to wean 6m after starting, unsuccessful.
  He asks if you feel he should try again?

# No empirical data on the “optimal” duration of treatment using MAT in opioid use disorder

- but we do know some things about duration of treatment

# Defining dosing pattern characteristics of successful tapers following methadone treatment: results from a population –based retrospective cohort study. Nosyk B, et al., Addiction 2012

- British Columbia data base of methadone dispensed looking at those who had a taper
- 4917 tapers
  1305 completed taper to less then 5mg
  659 reentered treatment, died or relapsed
  646 (13% ) successful tapers
- Factor associated with success
  - younger, male, better treatment compliance, lower maximum total dose, longer taper durations (tapers 12-52 weeks were 3.58 more likely to succeed, tapers > 52 weeks were 6.68)

# INITIAL THOUGHTS ON BUPRENORPHINE

- Due to its partial mu agonist pharmacology and extended receptor occupation time should lend itself to a less severe withdrawal syndrome
- The population of opioid users was younger, shorter periods of use, pain pills vs heroin , less IV use, more functional
- Initial hope, maybe enthusiasm, that buprenorphine could be used as a agent for “detoxification” (medically managed withdrawal). This was based on the assumption that most relapse was due to uncontrolled withdrawal symptoms

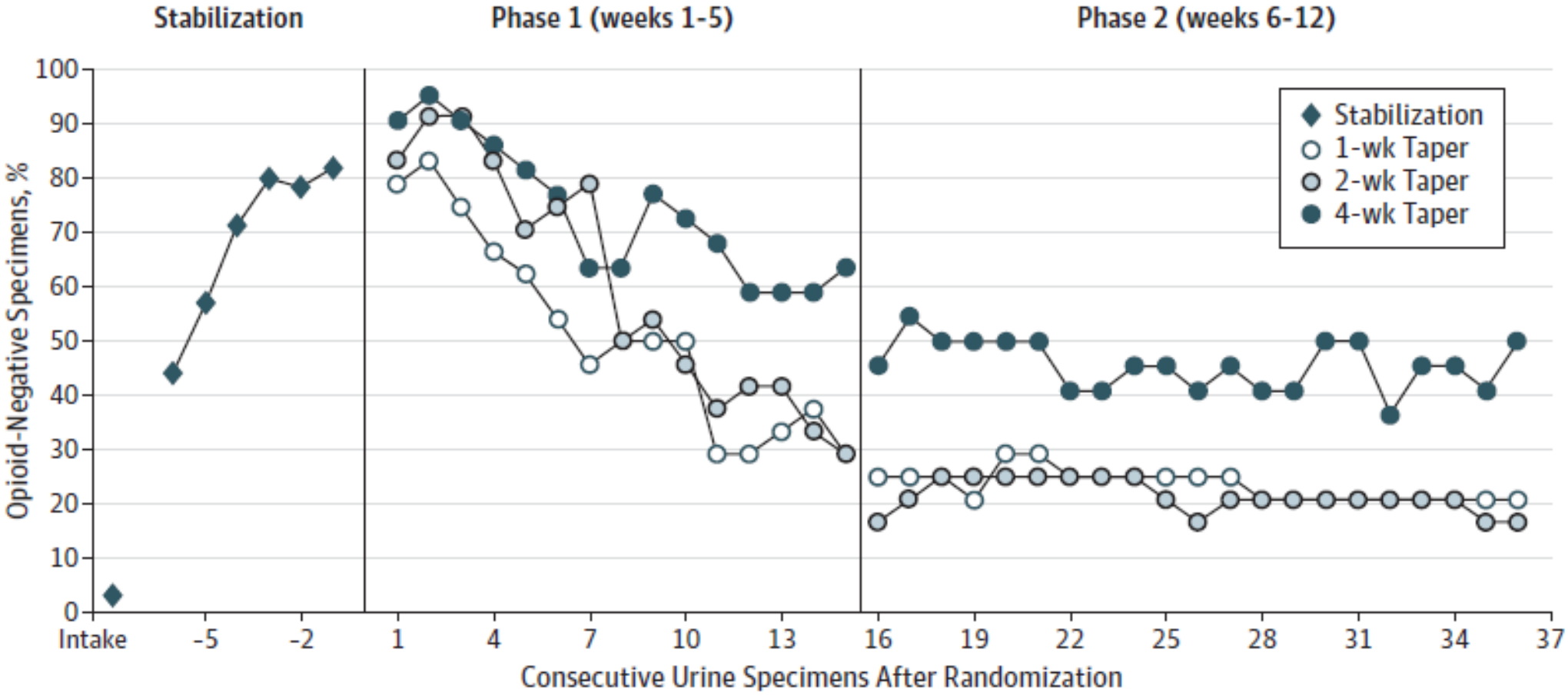

WROOOONG!!!!!

# Buprenorphine tapering schedule and illicit opioid use, Ling W., et al, Addiction 2009:104

- 255 patients in 7 day taper, 261 in 4 week taper
- END OF TAPER
  -44% (113/202) of 7 day taper provided negative urines
  -30% (78/172) of 28 days taper provided negative urines
- 30 Days after taper
  - 18% (45/131) of 7 day taper provided negative urines
  - 18% (46/123) of 28 day taper provided negative uriens
- 90 days after taper
  - 12% (31/92) of 7 day taper provided negative urines
  - 13% (35/114) of 28 day taper provide negative urines

# A randomized, double-blind evaluation of buprenorphine taper duration in primary prescription opioid abusers. Sigmon S.C., et al., JAMA Psychiatry , 2013

**Figure 3. Effects of Buprenorphine Taper Duration on Illicit Opioid Abstinence Achieved**



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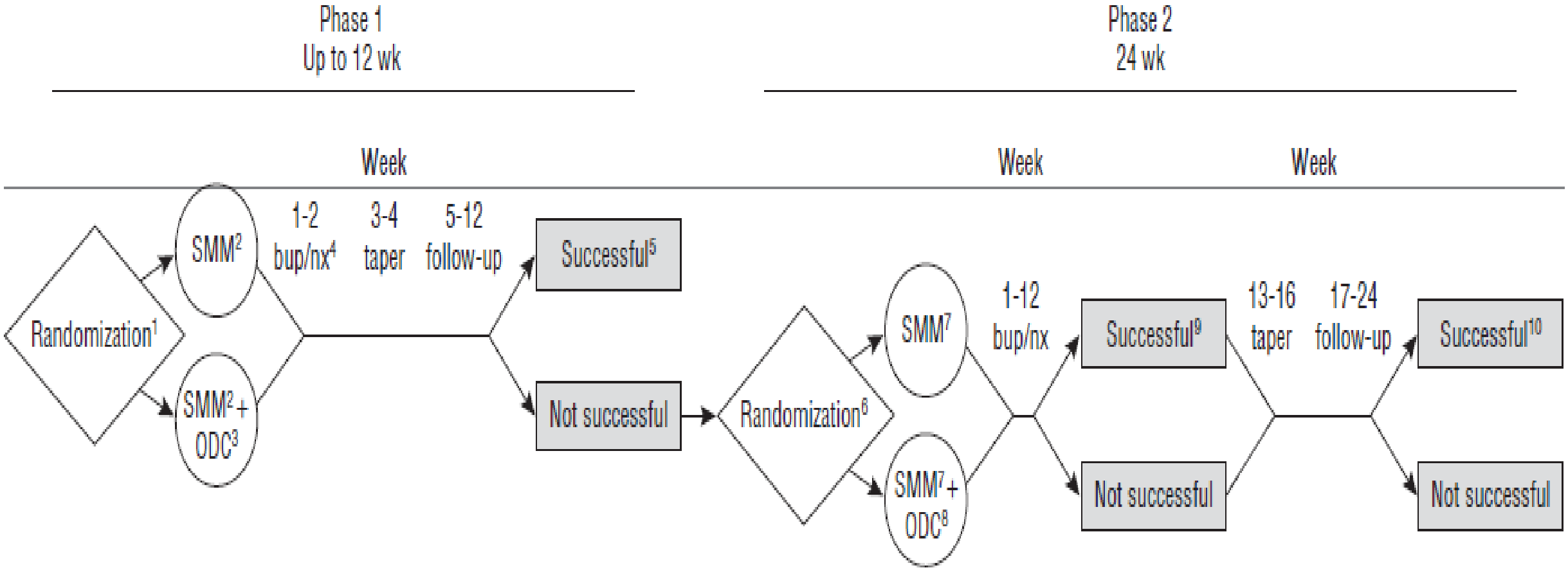
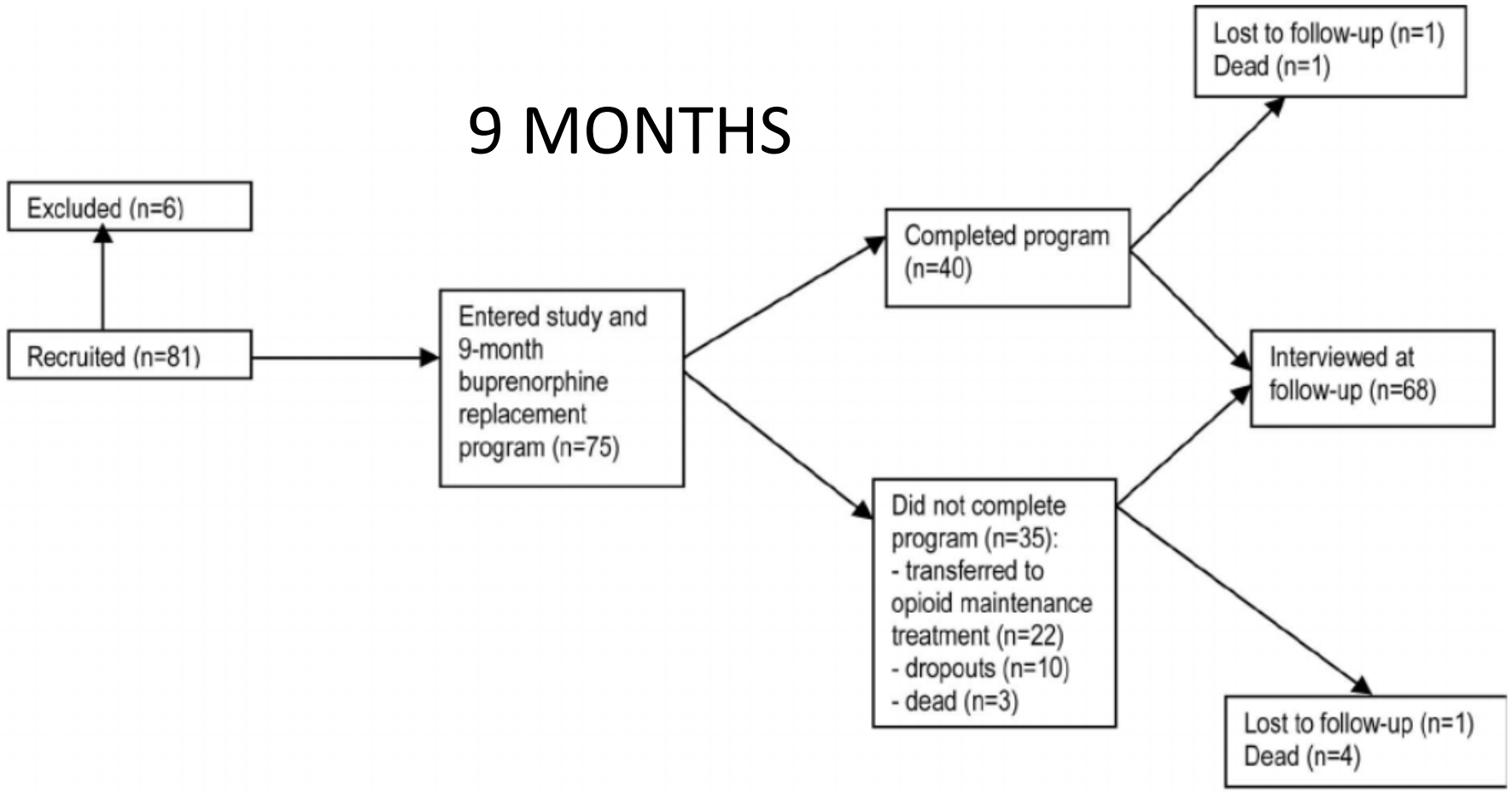


# Adjunctive Counseling During Brief and Extended Buprenorphine-Naloxone Treatment for Prescription Opioid Dependence: A 2-Phase Randomized Controlled Trial. Weiss RD, et al., Arch Gen Psych/vol 68 (12), 2011

- 43/653 (6%) had successful outcomes in phase 1 ( 2 week detox)
- 177/360 (49%) has successful outcomes at week 12 (still on bup)
- 31/360 (8.6%) had successful outcomes at week 24

# Time limited buprenorphine replacement therapy for opioid dependence: 2-year follow up outcomes in relation to programme completion and current agonist therapy status. Kornor H, et al., Drug and Alcohol Review (26), 2007



# Time limited buprenorphine replacement therapy for opioid dependence: 2-year follow up outcomes in relation to programme completion and current agonist therapy status. Kornor H, et al., Drug and Alcohol Review (26), 2007

- 40% did not complete the 9m
- 9 of 75 (12%)  or 9/40 (25%) were abstinent from all opioids at follow up
  - of these 1 spent 30 days in prison, 1 was in a residential treatment program and 5 were on naltrexone)

# The association between outpatient buprenorphine detoxification duration and clinical treatment outcomes: A Review

Kelly, E.D., et al, Drug and Alcohol Dependence 119 (2011)

- Review of 28 studies
- Tapers varied from 0-120 days
- Median 17 days
- Outcomes negative urines

- Median percentage of negative urines  41%
- 65% did not complete the wean
- Median percentage of negative urines at end of wean 30%
- Positive predictors for success
  - Duration of maintenance predictive of final neg, urine
  - Length of taper predicted total negative urines during wean
  - Contingency Management  Median 64%
    No contingency management  Median 23%
  - Post wean with negative urines – 23% (n=5)
- Peak withdrawal varied , between last day of dosing to 14 days after last dose

# OPTIMAL DURATION OF THERAPY

- TIPS 63 “ patients should take buprenorphine as long as they benefit from it and wish to continue it”

- ASAM: No empirical data on the “optimal” duration of treatment using MAT in opioid use disorder

? DOES THIS MAN FOREVER


Forever is a long time but I wouldn't mind spending it with you.
www.RomanceNeverDies.com
@RomanceNvrDie


EXCEPT IF
YOU ARE
BUPRENORPHINE


START

FEAR/ANXIETY

- Leaving something comfortable, life saving
- Pain of withdrawal

ANTICIPATORY WITHDRAWAL

# Why do patients stop buprenorphine

| | Percent endorsing reason |
|---|---|
| Discharged involuntarily due to disagreement with program staff | 24% ( *n* = 33) |
| Discharged involuntarily for missing too many days at the program | 17% ( *n* = 24) |
| Program conflicted too much with life, work, or school obligations | 17% ( *n* = 23) |
| Left to get treatment at another provider | 14% ( *n* = 20) |
| Discharged involuntarily due to too many positive urines | 9% ( *n* = 12) |
| Incarcerated and did not return after release | 7% ( *n* = 9) |
| Did not like the medication | 4% ( *n* = 6) |
| Financial (discharged for not paying fees; insurance ended; too costly) | 4% ( *n* = 6) |
| Left because the provider was too strict | 4% ( *n* = 6) |
| Left because wanted to keep using drugs | 4% ( *n* = 6) |
| Finished treatment successfully | 4% ( *n* = 6) |
| Discharged for breaking program rules | 4% ( *n* = 5) |
| Moved out of town | 3% ( *n* = 4) |
| Did not have transportation to get to the program | 3% ( *n* = 4) |
| Felt addiction recovery was not possible while taking medication | 1% ( *n* = 2) |

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

- 12 year retrospective cohort study of adults on buprenorphine in a primary care practice
- 1308 patients
  48 patients were observed to taper off during the study period
- 13/48 subsequently reengaged
- Return was 2-3 years after taper was completed
- Those who had medically supervised tapers returned less often (3/22)

# Two-year Experience with Buprenorphine-naloxone for Maintenance Treatment of Opioid Dependence Within a Private Practice Setting. Finch,J, et al., Journal of Addiction Medicine , June 2007

- Retrospective chart review of patients enrolled in private practice (OBOT) in North Carolina
- 71 patients over 24 months
- Average age 32, 4 yrs of use, 93% white, 70% employed
- - 24% drop out
  - 43% maintained
  - 21% tapered successfully
  - 7% methadone
  - 4% inpatient treatment

# QUESTIONS THAT NEEDS AN ANSWER

- WE KNOW
  Majority of patients will not taper off
  The majority who attempt taper will fail

- What are the predictors of a successful taper after a period of stabilization?
- What is the most successful strategy to maximize success of tapering off?

# What is the right question

- What do you think about weaning off buprenorphine

or

- Are you comfortable staying with buprenorphine for now and the foreseeable future

# Predicators of successful weaning

- Length in treatment prior to weaning
- Length of abstinence
- Duration of weaning

- Vocational/financial stability
- Socialization with non-drug users
- Strong motivation
- “Lack of detoxification phobia”
- Stable family

**TABLE 1.** The Recovery Capital Checklist (Patients and Counselors Section)

| | | | |
|---|---|---|---|
| 1. | Have you been abstaining from illegal drugs, such as heroin, cocaine, and speed? | Yes | No |
| 2. | Do you think you are able to cope with difficult situations without using drugs? | Yes | No |
| 3. | Are you employed or in school? | Yes | No |
| 4. | Are you staying away from contact with users and illegal activities? | Yes | No |
| 5. | Have you gotten rid of your drug paraphernalia? | Yes | No |
| 6. | Are you living in a neighborhood that doesn't have a lot of drug use? | Yes | No |
| 7. | And are you comfortable there? | Yes | No |
| 8. | Do you have nonuser friends that you spend time with? | Yes | No |
| 9. | Are you living in a stable household or family? | Yes | No |
| 10. | Do you have friends or family who would be helpful to you during a taper? | Yes | No |
| 11. | Do you have a spiritual practice? | Yes | No |
| 12. | Have you been participating in counseling that has been helpful? | Yes | No |
| 13. | Does your counselor think you are ready to taper? | Yes | No |
| 14. | Do you think you would ask for help when you are feeling bad during a taper? | Yes | No |
| 15. | Are you in good mental and physical health? | Yes | No |
| 16. | Do you want to get off methadone or buprenorphine? | Yes | No |

The purpose of this section of the Checklist is to help patients and counselors to decide if the patient is ready to taper or discontinue from MOUD at this time. Each item represents an important part of the process of being ready to discontinue MOUD.

The more questions that can honestly be answered "yes," the greater the likelihood that the patient is ready to taper from opioid medication. Consider that each "no" response represents an area that the patient and counselor probably need to work on to increase the odds of a successful taper and recovery. Circle the appropriate response.

**TABLE 2.** Physician Risk Factor Checklist (Medical Providers Section)

| | |
|---|---|
| 1. | Any unexpected findings on PDMP* |
| 2. | Frequent emergency department visits/minor injuries/MVCs† |
| 3. | Recently appeared intoxicated/impaired |
| 4. | Increased dose without authorization |
| 5. | Needed to take medications belonging to someone else |
| 6. | Patient or others worried about how patient is handling medications |
| 7. | Had to make an emergency phone call or go to the clinic without an appointment |
| 8. | Used pain medication for symptoms other than pain—sleep, mood, stress relief |
| 9. | Changed route of administration |
| 10. | Serious co-morbid mental illness |
| 11. | Recent requests for early refills |
| 12. | Recent reports of lost or stolen prescriptions |
| 13. | Hoarding or stockpiling of medications |
| 14. | Increasingly unkempt |
| 15. | Attempted to obtain prescriptions from other doctors |
| 16. | Concurrent benzodiazepine prescriptions |
| 17. | Concurrent stimulant prescription |
| 18. | Maintenance dose greater than 8 mg or buprenorphine or 80 mg methadone |
| 19. | Current reports of disturbances in sleep |
| 20. | Current reports of problems or lability in mood or energy |

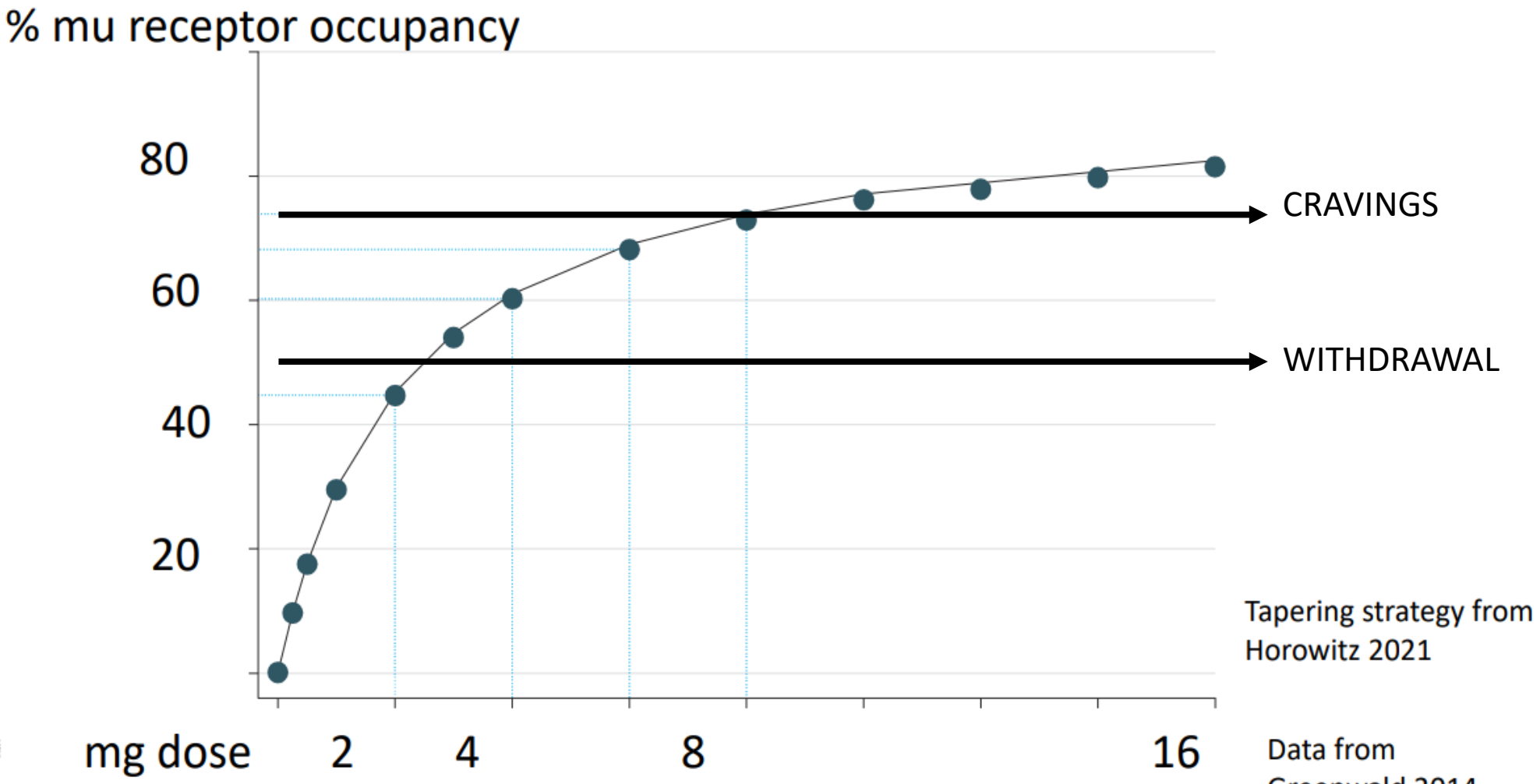
# BUPRENORPHINE WITHDRAWAL

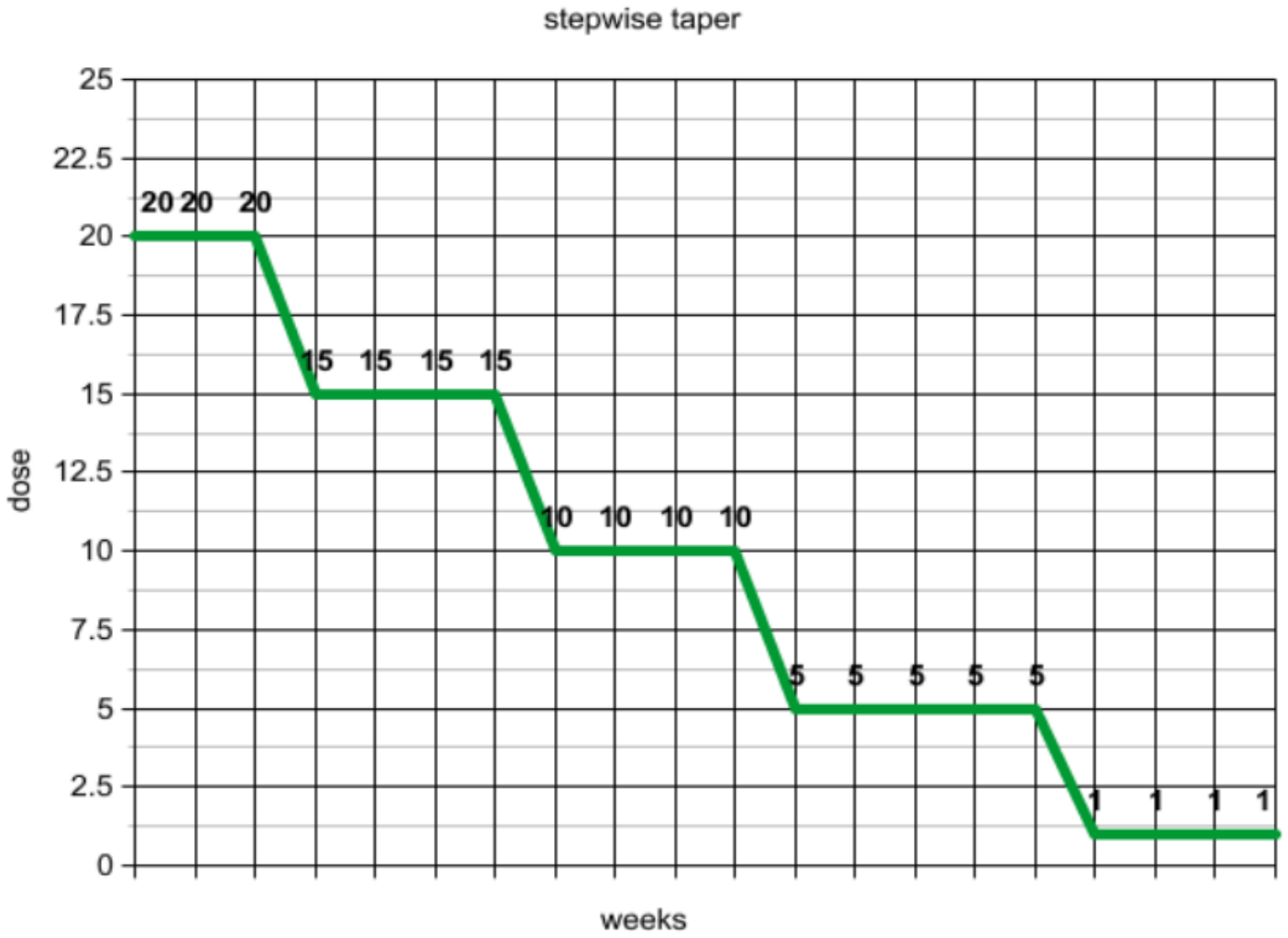
- buprenorphine withdrawal lasts for a month or longer compared to heroin with withdrawals lasting 7 days.
- initial 72 hours physical symptoms predominate including nausea, vomiting, diarrhea, diaphoresis, irritability, anxiety.
- after 1 week the physical symptoms improve and general aches and pains continue with insomnia and mood swings
- after week 2 depression increases
- after one month the psychological symptoms of depressions and cravings continue and relapse likelihood is highest

Effective buprenorphine use and tapering strategies: Endorsements and insights by people in recovery from opioid use disorder on a Reddit forum. Graves, Rl, et al., BioRxiv 2019

- Reviewed 16,146 posts about buprenorphine from 1933 uniques
- Information about tapering was third most common subject (32%)
- More successful recovery with longer tapering schedules, particularly from 2.0 to 0 mg (Mean 95 days) which was viewed as the most challenging part
- Diarrhea, insomnia, restlessness and fatigue most common symptoms
- Physical exercise, clonidine and Imodium were most helpful
- The most frequent/poplar final dose was .063mg

# Mu-receptor occupancy vs daily buprenorphine dose




stepwise taper
25
22.5
20
17.5
15
12.5
10
7.5
5
2.5
0
dose
20 20 20
15 15 15 15
10 10 10 10
5 5 5 5 5
1 1 1 1
weeks

#ASAM2021

# Buprenorphine weaning strategies

- The hardest part may be the 2mg – 0mg
- Pause the taper when a dose decrease causes unacceptable discomfort
- Allow the patient some level of control
- Expect overtaking during a taper
- Adjuvant medications

# Buprenorphine weaning strategies

- Discuss reasons and if patient is at optimal weaning point
- Informed shared decision
- Agree upon strategy
- Start after achieving lowest dose maintenance dose
- Increase support during weaning and post weaning
- Taking buprenorphine once in AM so blood levels are lowest during sleep
- Initial increments can be larger (4mg) but below 8mg reduce increments

# Buprenorphine weaning strategies

- Exercise/mindfulness/community support/family support
- The door remains open to increase or come back (home induction)
- Have a plan for post taper (Naltrexone)

# Adjuvant pharmacology during taper

- Clonidine, lofexidine , tizanidine
- Dicyclomine, loperamine, promethazine, ondansetron
- Trazadone, hydroxyzine, benadryl
- Treatment of anxiety / anhedonia ?
- Avoid benzos and stimulants
-

# FUTURE EXPLORATIONS

- Use of injectable as part of a tapering protocol
- Use of microdosing using patches (5ug) in a tapering protocol
- Ultrarapid detoxifications
- Ketamine

# CASE

- 42 yo male on MAT (buprenorphine ) for last 18m.
- Has been stable in all domains (employment, marriage, legal, medical and mental health)
  Is currently on 16mg. Tried to wean 6m after starting, unsuccessful.
  He asks if you feel he should try again?

# References


- Zweben. J.E., et al., Discontinuing methadone and buprenorphine: a review and clinical challenges. J Addiction Med. 2020 Dec 15, published ahead of print
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- Dunn ED., et al., The association between outpatient buprenorphine detoxification duration and clinical treatment outcome: A Review Drug Alc Dependence 2011, vol 119: 1-9

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