How long and discontinuation strategies for MAT

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Objectives

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

Patient has been on stable dose of buprenorphine for 3 yrs. No relapse, stable in all life domains. Would you have a discussion about trying to wean the buprenorphine

- A. Yes
- B. No

Which are legitimate concerns of patients regarding long term treatment of MAT

- A. Over time I will become more dependent and require higher and higher doses
- B. I have just switched one addiction for another
- Once you are on these medications you will never be able to get off
- Once I am on the medications I will constantly be thinking about them and wanting them
- I will always be tied to the clinic and its policies

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

What is the overall success rate of a short term (1-4 week) “detoxes” using a MAT

A. 10%
B. 25%
C. 50%
D. 65%

METHADONE MAINTENANCE

IT IS THE MOST WELL STUDIED OF ALL MAT

INTIALLY IT OFTEN WAS MANDATORY that PATIENTS WEAN OFF IT AFTER 1-2 YEARS

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


WROOOOONG!!!!!!

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

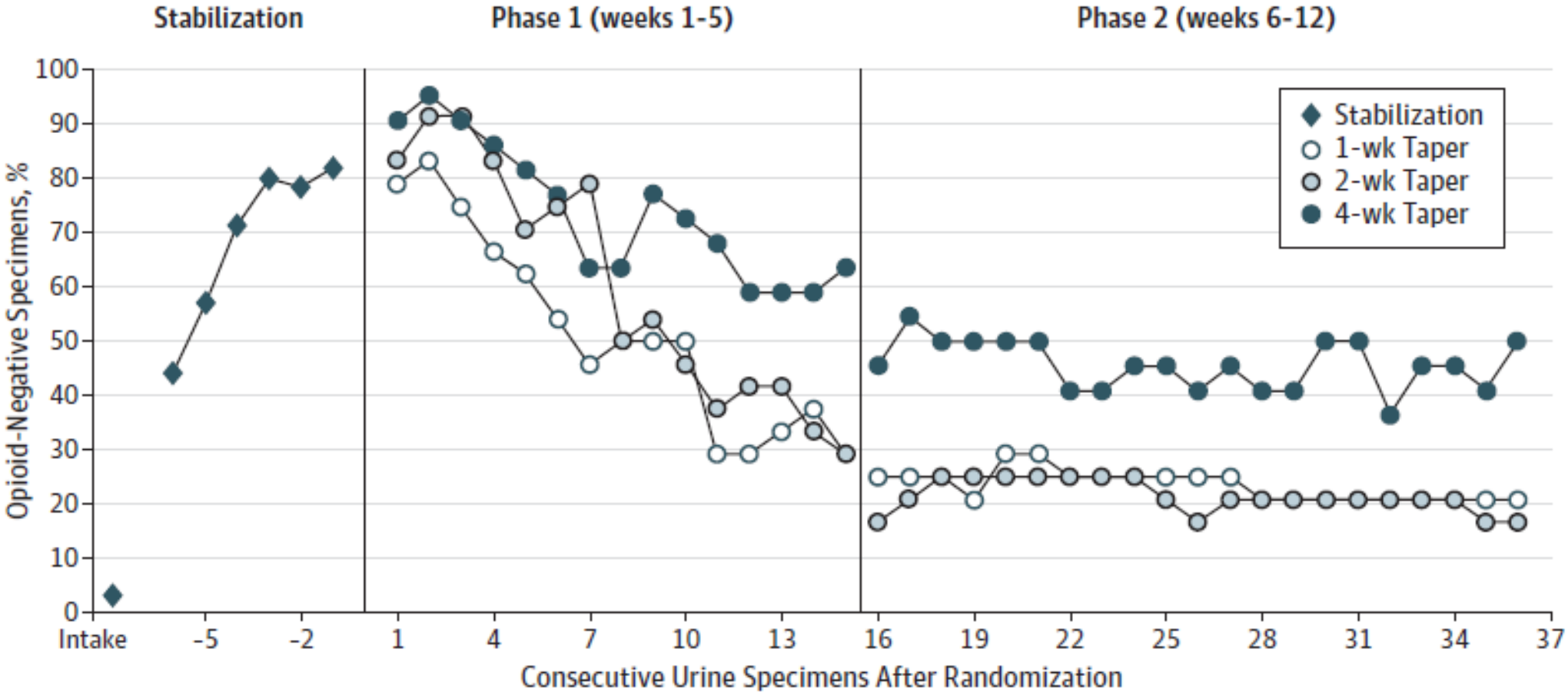
- 255 patients in 7 day taper, 261 in 4 week taper
- END OF TAPER
  -44% (113/202) of 7 day taper provided negative urines
  -30% (78/172) of 28 days taper provided negative urines
- 30 Days after taper
  - 18% (45/131) of 7 day taper provided negative urines
  - 18% (46/123) of 28 day taper provided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

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

	COWS		ARSW		VAS	
	7D	28D	7D	28D	7D	28D
Baseline	8.7	8.3	63	62	71	68
Stabilization	.97	.95	11	11	12	13
End of taper	2.7	2.5	22	18	24	23
1 month	1.6	.98*	15	14	26	22
3 months	.8	1.2	12	13	19	24

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

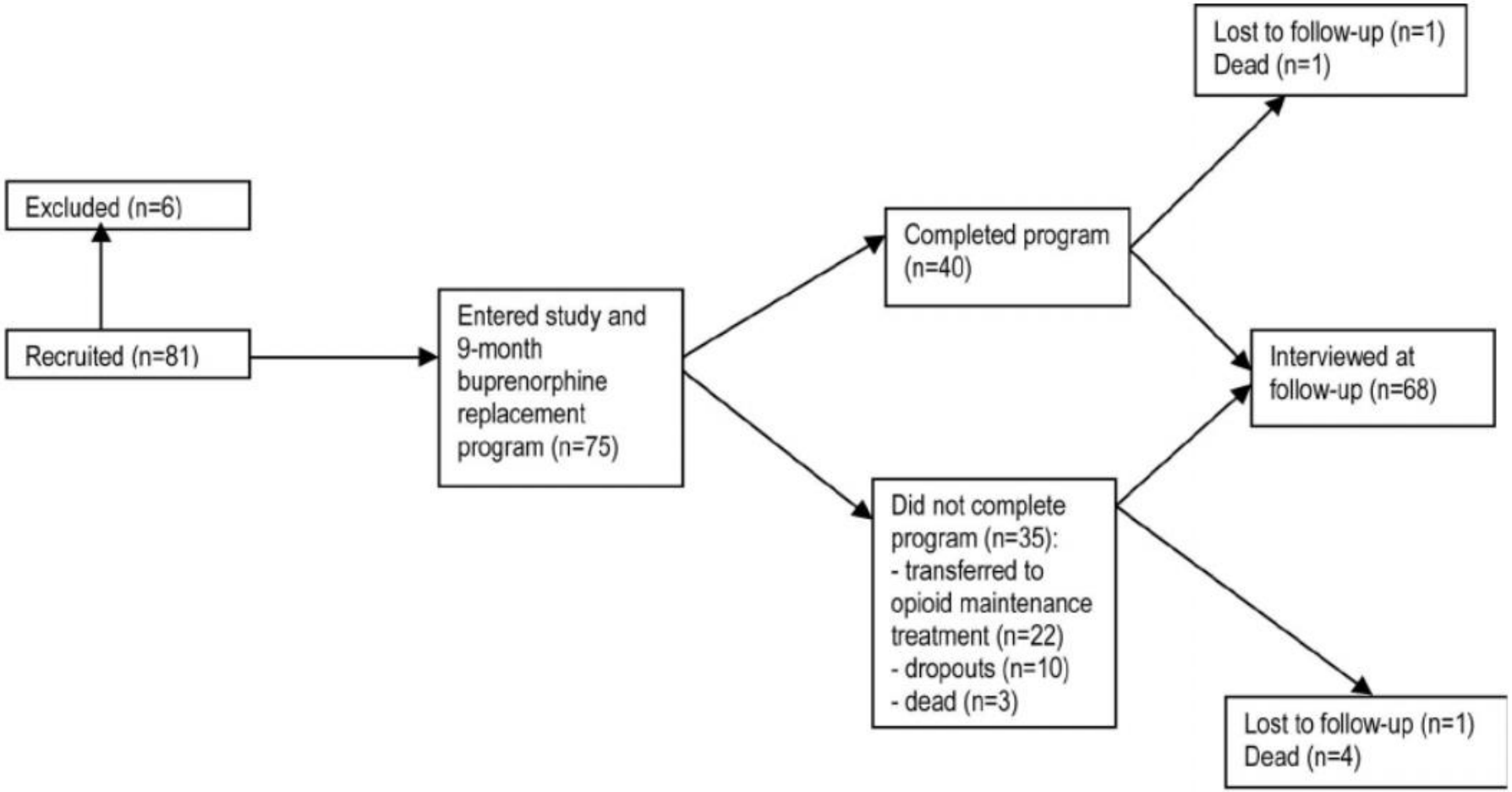
Figure 3. Effects of Buprenorphine Taper Duration on Illicit Opioid Abstinence Achieved



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

- 9 of 75 (12%) 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)

OPTIMAL DURATION OF THERAPY

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


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

EXCEPT IF
YOU ARE
BUPRENORPHINE

Why is an abstinence based approach to opioid use disorder so ineffective?

Long term treatment with MAT can cause the following

- A. Suppression of the pituitary
- B. Chronic depression or anxiety
- C. Loss of bone osteoporosis
- D. Chronic constipation
- E. Increased sensitivity to pain

Why is opioid use disorder different

- Are there more longer term neurochemical changes that result in prolonged cravings
- If there is pain is that a constant trigger for seeking relief with opioids (permanent alteration in pain sensitivity)
- Is the physical dependence just too difficult for most patients to overcome (man in a box) and is that withdrawal more protracted (months)
- Is there a permanent alteration in the endorphin system, reward system, cognition, memory

Evidence for an endorphin dysfunction in methadone addicts: lack of ACTH response to naloxone. Gold MS., et al, Drug Alcohol Dependence, 8(3), 1981

- 7 methadone dependent patients recently “detoxed” -16d
- 7 opioid naïve controls
- Normal response is release of ACTH to injection of naloxone
- All controls had release, none of the methadone patients

Evidence for an endorphin dysfunction in methadone addicts: lack of ACTH response to naloxone. Gold MS., et al, Drug Alcohol Dependence, 8(3), 1981

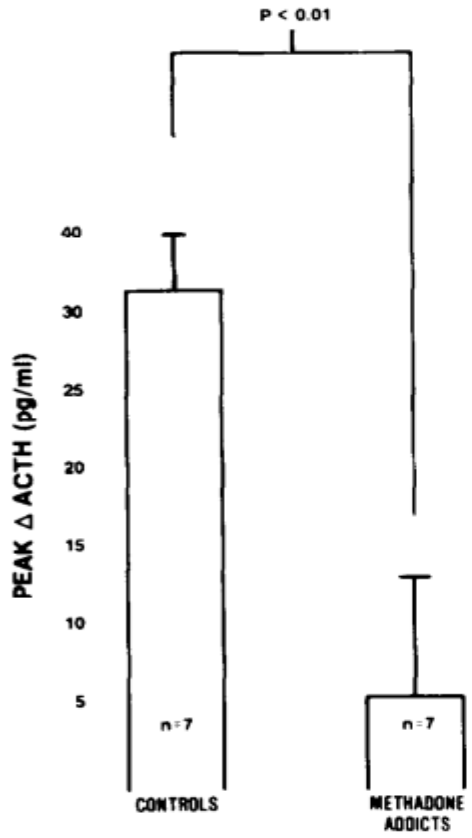
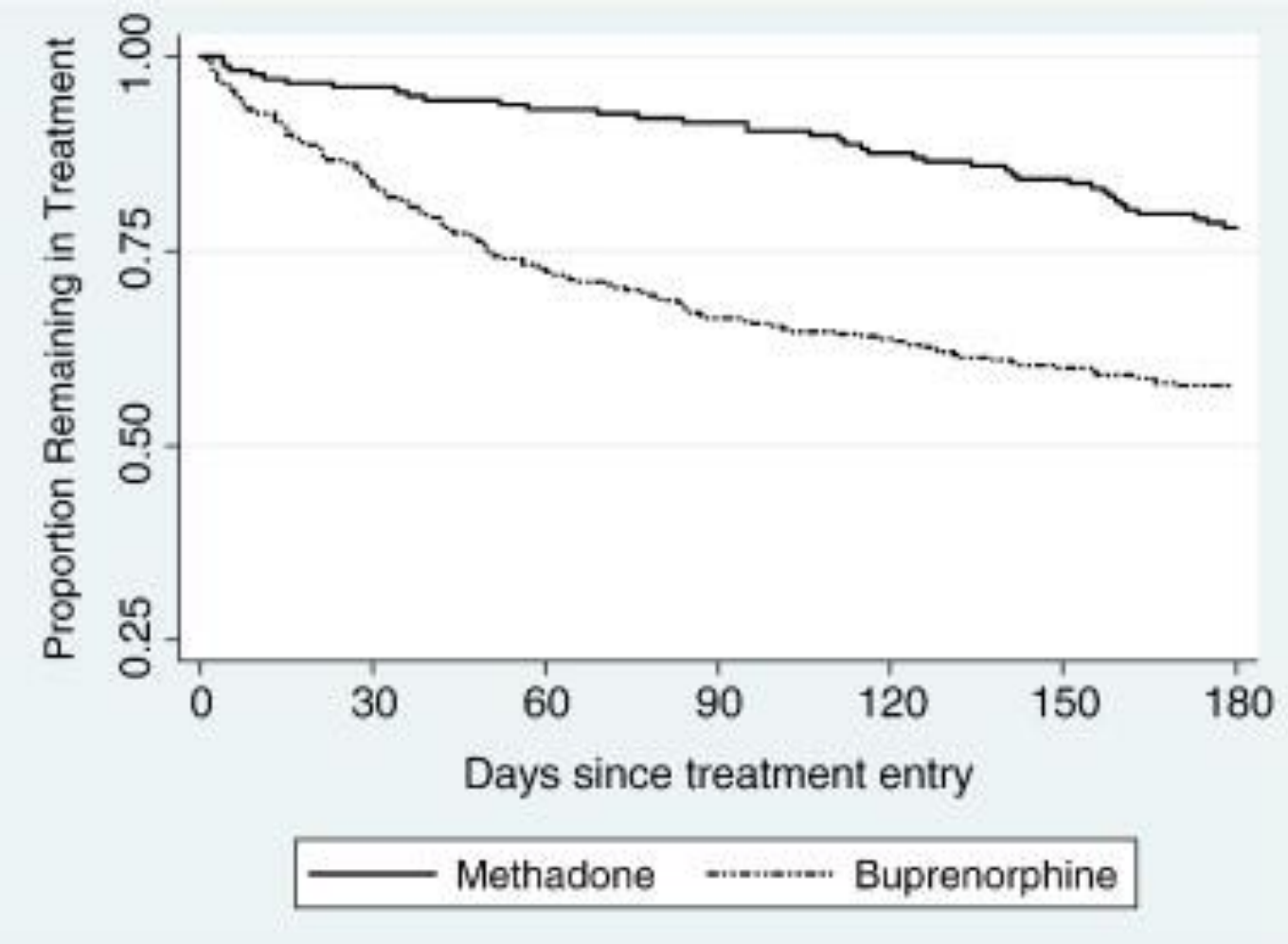


Fig. 2. Significant difference in the endorphin reserve test response in methadone addicts and normal controls after 20 mg intravenous naloxone.

What percentage of patients who start buprenorphine remain in treatment for 6 months?

- A- 10%
- B. 25%
- C. 50%
- D. 75%

Buprenorphine Retention Rates



Retention in methadone and buprenorphine treamtment among African Americans. Gryczynski J, et al., Journal of Substance Abuse Treatment 2013 (45)

Buprenorphine Retention Rates

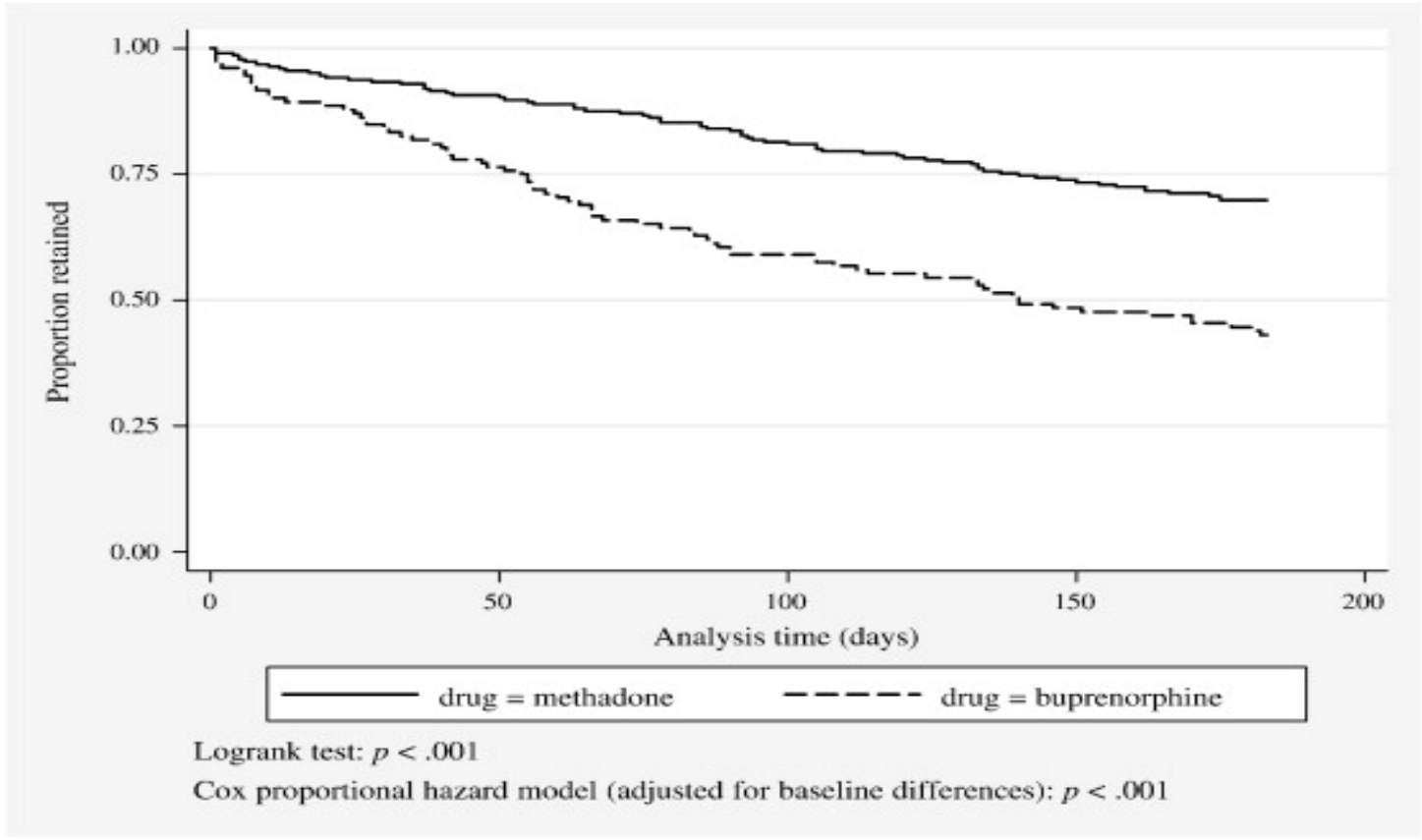


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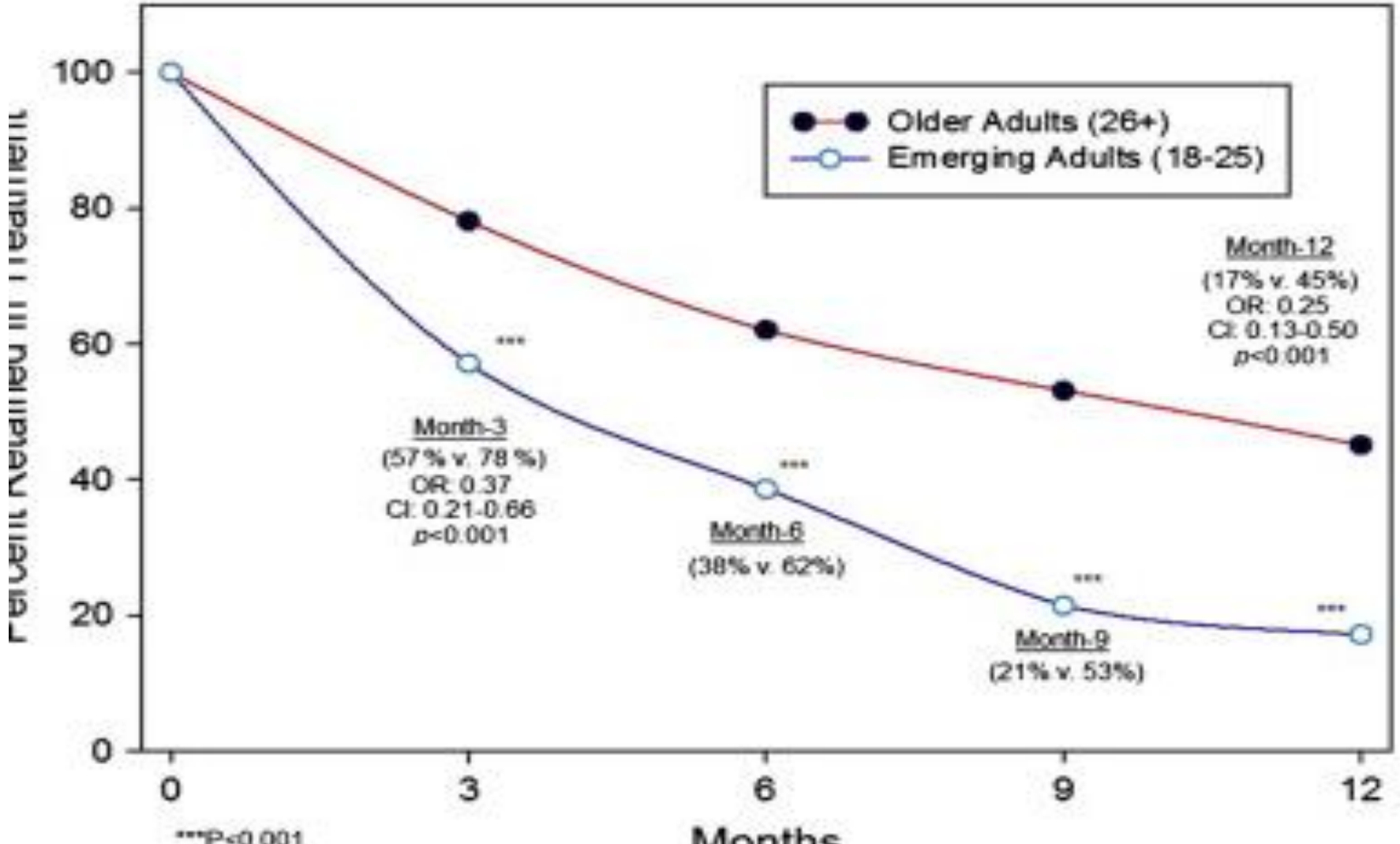
Fig. 2. Survival analysis showing retention in treatment for methadone versus buprenorphine.

The SUMMIT Trial: A field comparision of buprenorphine versus methadone maintenance treatment Pinto H, et al., Journal of Substance Abuse Treatment (39) 2010

Emerging adult age status predicts poor buprenorphine retention. Schuman-Oliver Z, et al Journal of Substance Abuse Treatment (47) 2014



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

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

- 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?

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

1 Week Taper
2 Week Taper
4 Week Taper
Buprenorphine Dose (mgs)
CINA Severity Score
VAS "Withdrawal"
Mean CINA Ratings (range 0-31), Mean Buprenorphine dose (mgs)
Mean VAS Ratings (range 0-100)
Study Day

At some point they will want to wade into that water

FEAR/ANXIETY

- Leaving something comfortable, life saving
- Pain of withdrawal

ANTICIPATORY WITHDRAWAL

Is the patient psychologically prepared to be abstinent

- Do they have the “recovery capital”

The more severe the addiction to opioids the more likely the patient will remain on long term MAT

- A True
- B. False
- C. It does not matter

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

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/popular final dose was .063mg

Buprenorphine weaning strategies

- Discuss reasons
- Informed shared decision
- Agree upon strategy
- Start after achieving lowest dose maintenance dose
- Increase support
- Taking buprenorphine once in AM so blood levels are lowest during sleep
- Initial increments can be larger (4mg)
- The percent decrease is more important than the total decrease

Buprenorphine weaning strategies

- The hardest part may be the 2mg – 0mg
  (2mg of buprenorphine may be = 80mg morphine equivalent)
- 2mg dose may occupy up to 48% mu receptors
- Pause the taper when a dose decrease causes unacceptable discomfort
- Allow the patient some level of control
- Expect overtaking during a taper
- Adjuvant medications??

Adjuvant pharmacology during taper?

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

Buprenorphine weaning strategies

- Exercise
- Frequent support and visits
- The door remains open to increase or come back (home induction)
- Have a plan for post taper (Naltrexone)

- Chronic pain patients not likely to do well
- Follow up after the taper is over

- CAUTION THE PATIENT ABOUT LOSS OF TOLERANCE

USING BUPRENORPHINE INJECTABLE AS A WEANING TOOL ?

- More steady state which reaches very low serum levels
- Long half life (40-60 days)
- Removes the “pill taking” response to stress or withdrawal
- Somewhat “blind” dosing to the patient
- Can get

Using Extended Release Buprenorphine Injection to Discontinue Sublingual Buprenorphine: A Case Series Ritvo, A., et al., Journal of Addiction Med, 15(3), June 2021

- Case study of 3 patients
- Case 1 : Patient was on 4 mg, given 100mg injection
- Case 2: Patient was on 2 mg given 100 mg injection
- Case 3: Patient was on 6 mg, given 100mg injectinon

2 of the 3 patients were more chronic pain pts with dependence
all the patients were stable at least one year

Patient with opioid use disorder presents wanting a short term “detox”. Do you offer it?

- A. Yes
- B. No

- SHOULD WE OFFER A TREATMENT THAT IS NOT LIKLEY TO BE SUCCESSFUL AND MAY EVEN CARRY RISK WHEN THERE IS A MUCH BETTER ALTERANTIVE

FUTURE EXPLORATIONS

- Use of injectable as part of a tapering protocol
- :Microweaning” using buccal or patch formulations
- Ultrarapid detoxifications
- Ketamine

SUMMARY

- There should be no pressure to taper off buprenorphine if it is working
- To optimize success, > 1 year of abstinence, lowest dose possible for maintenance, slow taper (months), increase support
- Always keep the door open