LOUD in ED Coaching Session Buprenorphine/Naloxone: Microdosing Induction Strategies

Presented by:
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October 26, 2020

Disclosures

Academic: None

Commercial: None

Financial: None

Questions for the audience

What is your profession? (Nurses or Nurse Practitioners/ Doctors/ Pharmacists/ Social Worker/ Other)

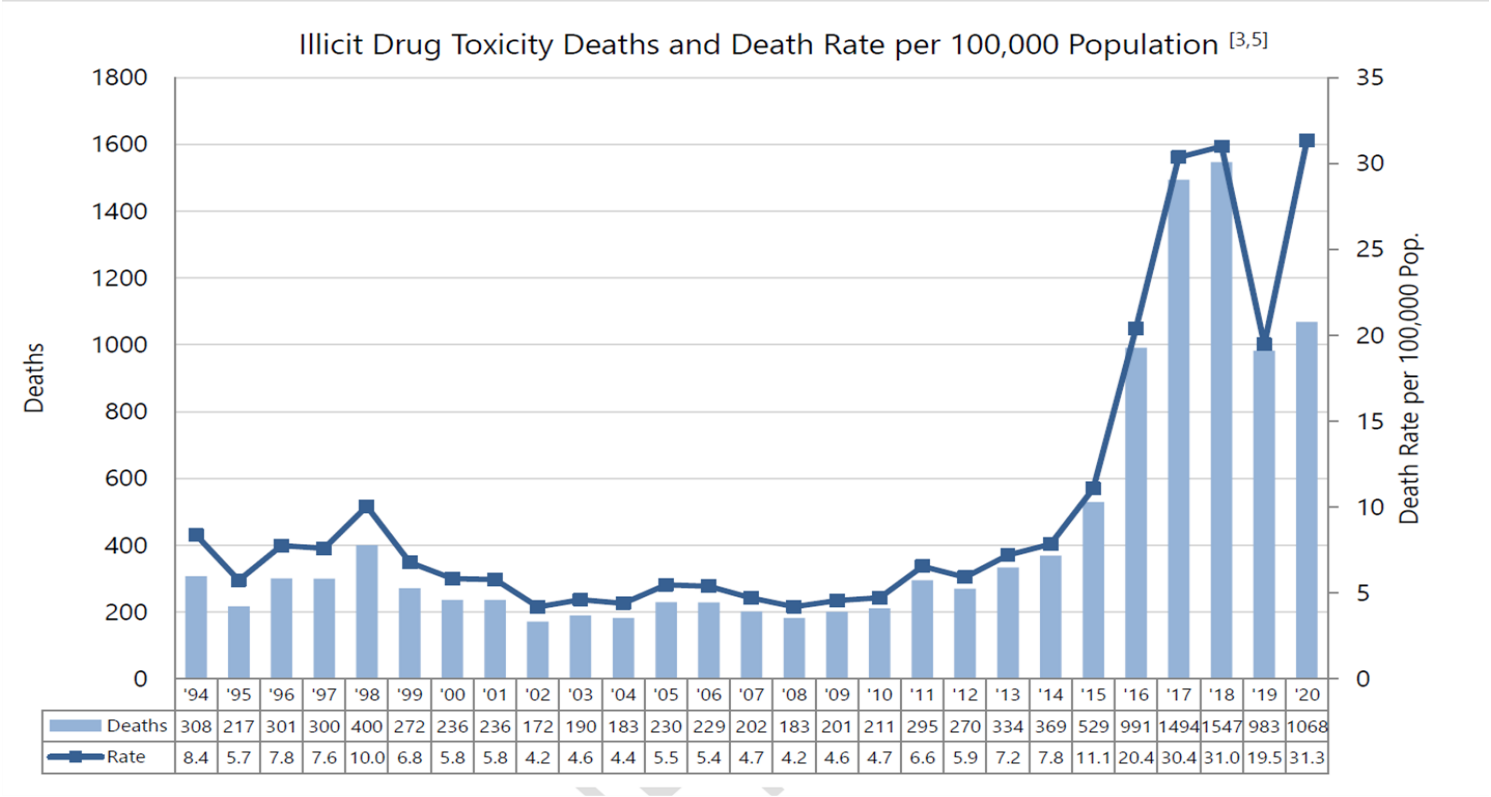
Do you have formal training in addictions? (Yes or No)

Have you been involved in starting a patient on buprenorphine/naloxone microdosing? (Yes or No)

What is your comfort/knowledge level in regards to buprenorphine/naloxone microdosing?

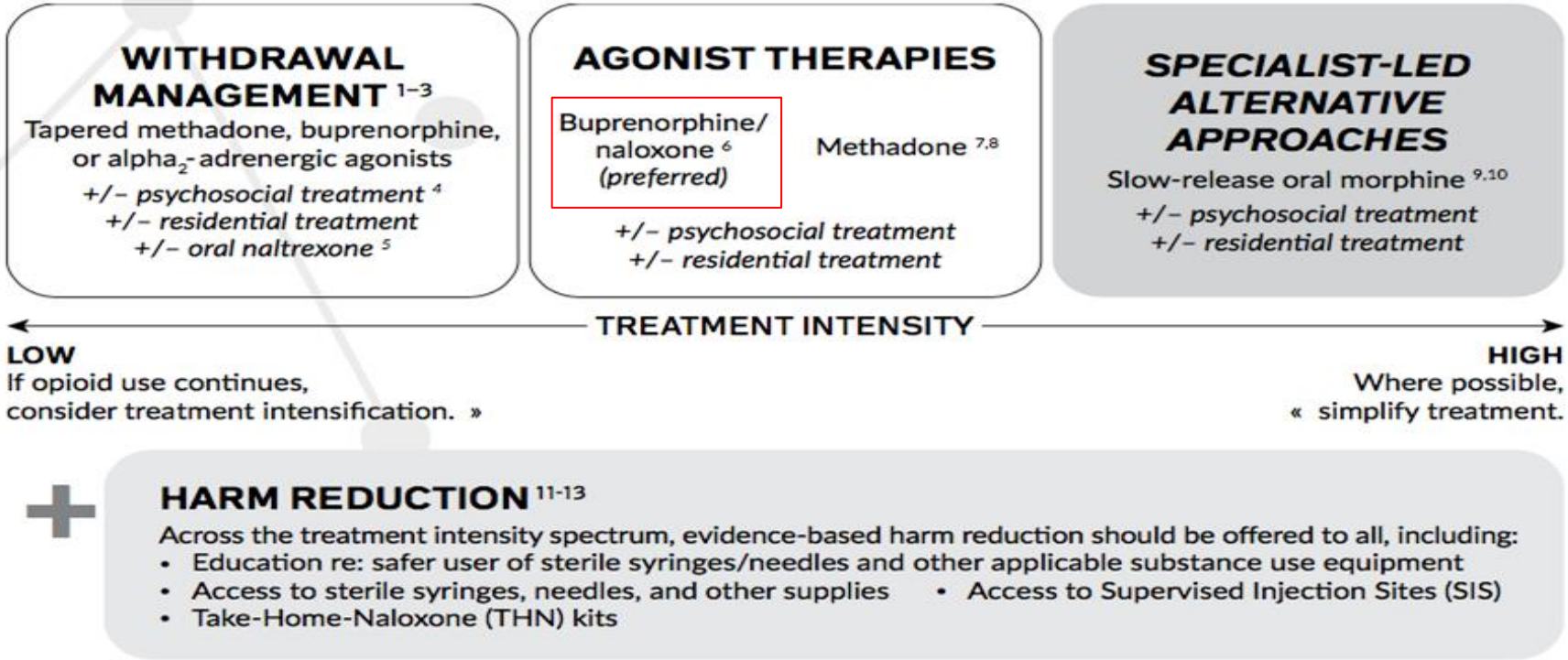
[likert scale 1- no comfort, 2-minimal comfort, 3-somewhat comfortable, 4-very comfortable]

Illicit Drug Toxicity Deaths in BC



	'94	'95	'96	'97	'98	'99	'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13	'14	'15	'16	'17	'18	'19	'20
Deaths	308	217	301	300	400	272	236	236	172	190	183	230	229	202	183	201	211	295	270	334	369	529	991	1494	1547	983	1068
Rate	8.4	5.7	7.8	7.6	10.0	6.8	5.8	5.8	4.2	4.6	4.4	5.5	5.4	4.7	4.2	4.6	4.7	6.6	5.9	7.2	7.8	11.1	20.4	30.4	31.0	19.5	31.3

Continuum of Care

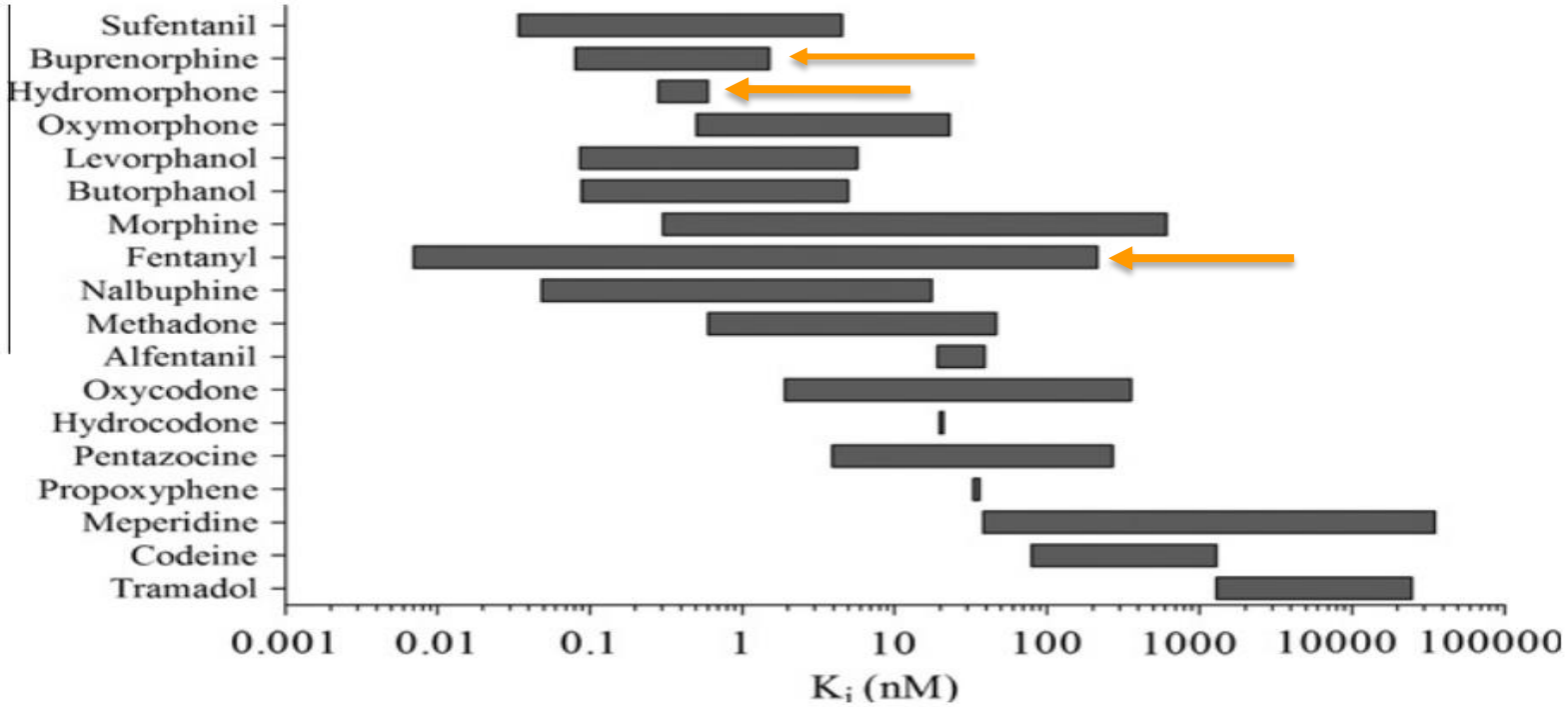


http://www.bccsu.ca/care-guidance-publications/

Buprenorphine

- Partial opioid receptor agonist
- High receptor binding affinity
- Various formulations (patch, sublingual tablets, injectable)
  - Often coupled with naloxone
- Target dose: 12-32mg
- Duration of action dose dependent
  - Typically reported as 32-36 hours
  - Low doses (1.2mg or less) reported as 3-16 hours

Binding Affinity



Regulatory Toxicology and Pharmacology 59 (2011) 385–390

Traditional Induction

1. Taper/stop prescribed/illicit opioids
2. Wait until moderate withdrawal
3. Administer first dose buprenorphine 2-4mg
4. If no precipitated withdrawal in 30-60 minutes, administer additional doses every 1-2 hours until comfortable to a max dose of 12-16 mg on day 1
5. Follow up on day 2 and titrate as needed

Traditional Induction: Potential Issues

- Risk of treatment destabilization
- Patients need to undergo withdrawal
  - Moderate-to-severe withdrawal required
  - **Long process**

Case1: Rob

- 33 year old male presented to ED for fentanyl overdose
- Previously successful with suboxone for about 10 months
- Stopped suboxone 2 weeks ago (didn’t get in for a refill)

Case 1: Rob

How would you start the conversation?

What are some conversational points you can have with a patient who says they don’t want to start suboxone?

What can you say to this patient?

Case 1: Rob

Upon further discussion you discover Rob is willing to restart suboxone, but he does not want to go through withdrawal.

What are your options?

Alternative Induction Strategy

Buprenorphine Microdosing

Buprenorphine Microdosing

- Induction using small, increasing doses
- Generally takes 7-10 days
- Overlapping with full opioid agonists
- Pharmacology:
  - Slow displacement of other opioids
  - Gradual, increasing occupancy of receptors

Substance Abuse and Rehabilitation

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CASE SERIES

Use of microdoses for induction of buprenorphine treatment with overlapping full opioid agonist use: the Bernese method

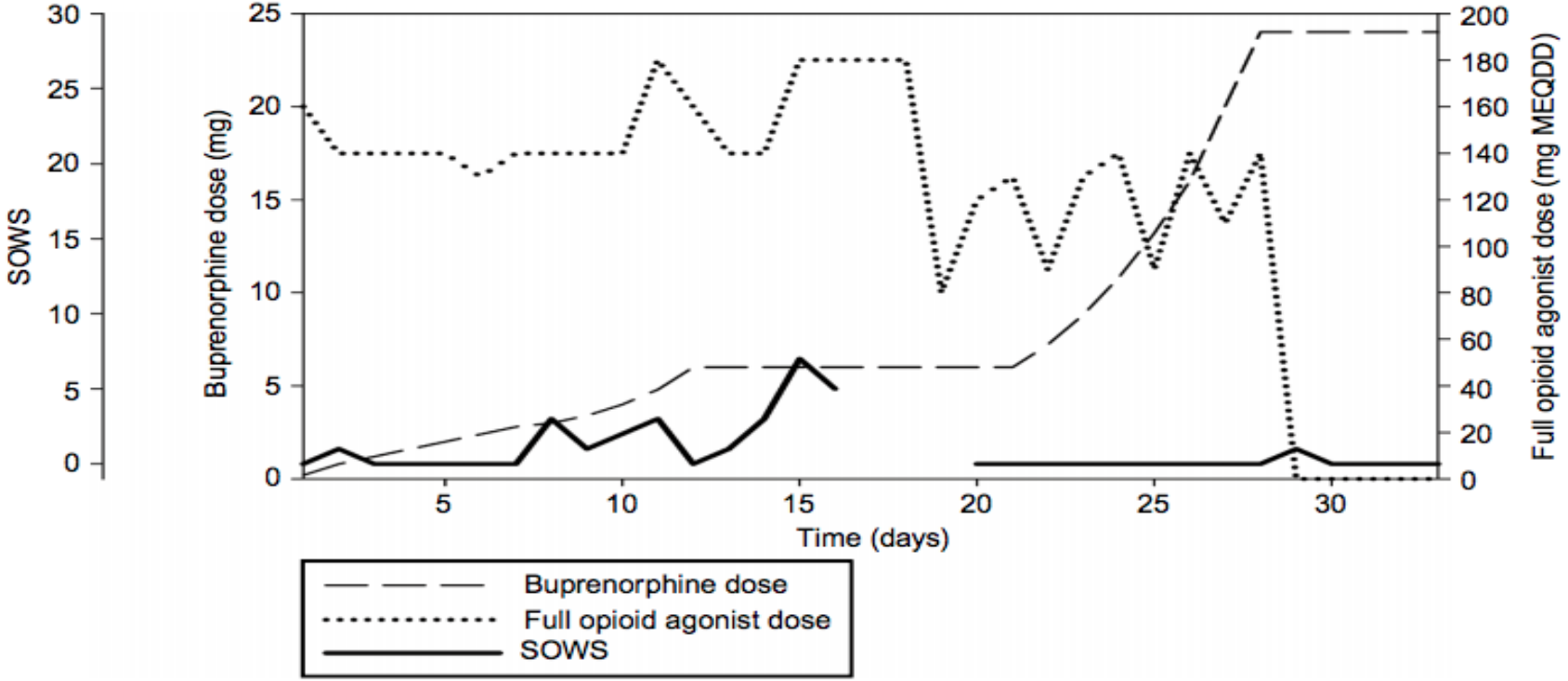
Buprenorphine Microdosing: Bernese Method

Table 1 Buprenorphine dosing and use of street heroin in case 1

Day	Buprenorphine (sl)	Street heroin (sniffed)
1	0.2 mg	2.5 g
2	0.2 mg	2 g
3	0.8+2 mg	0.5 g
4	2+2.5 mg	1.5 g
5	2.5+2.5 mg	0.5 g
6	2.5+4 mg	0
7	4+4 mg	0
8	4+4 mg	0
9	8+4 mg	0

Abbreviation: sl, sublingual.

Buprenorphine Microdosing: Bernese Method



Buprenorphine Microdosing: Advantages

- Can be initiated immediately
  - Less risk of treatment destabilization
- Can be prescribed quickly
- No withdrawal required

Buprenorphine Microdosing: Disadvantages

- Unclear risk of precipitated withdrawal
- Longer period of subtherapeutic doses
- Relatively new intervention, not all care providers understand

Drug and Alcohol REVIEW APSAD

Brief Report

Use of a novel prescribing approach for the treatment of opioid use disorder: Buprenorphine/naloxone micro-dosing – a case series

Rupinder Brar, Nadia Fairbairn, Christy Sutherland, Seonaid Nolan

7 Case reports

- 1 on Methadone (30 mg)
- 3 Sustained release oral morphine (150-300 mg)
- 3 illicit fentanyl/heroin

Induction Dosing

Day 1: 0.5 mg SL Daily
Day 2: 0.5 mg SL BID
Day 3: 1mg SL BID
Day 4: 2 mg SL BID
Day 5: 3 mg SL BID
Day 6: 4 mg SL BID
Day 7: 12 mg SL daily
Day 8: 16-24 mg (variable)

> BMJ Case Rep. 2020 Mar 25;13(3):e233715. doi: 10.1136/bcr-2019-233715.

Transitioning a patient from injectable opioid agonist therapy to sublingual buprenorphine/naloxone for the treatment of opioid use disorder using a microdosing approach

Mackenzie Duncan Gregory Caulfield [1], Rupinder Brar [2], Christy Sutherland [3], Seonaid Nolan [4] [5]

Addict Sci Clin Pract. 2020; 15: 2.
Published online 2020 Jan 15. doi: 10.1186/s13722-020-0177-x
PMCID: PMC6964069
PMID: 31941547

Case report: Successful induction of buprenorphine/naloxone using a microdosing schedule and assertive outreach

Jennifer Rozylo,[1] Keren Mitchell,[1,2,3,5] Mohammadali Nikoo,[1,4] S. Elise Durante,[2,3] Skye P. Barbic,[1,2,3,5,7,8] Daniel Lin,[1,2,3,5] Steve Mathias,[1,2,3,5,7] and Pouya Azar[1,2,3,5,6]

Buprenorphine Microdosing schedule

Schedule	Dose
Day 1	0.5 mg SL BID
Day 2	1 mg SL BID
Day 3	2 mg SL BID
Day 4	3 mg SL BID
Day 5	4 mg SL BID
Day 6 until R/A	12 mg SL daily

Schedule	Dose
Day 1	0.25mg SL
Day 2	0.25 mg SL BID
Day 3	0.5mg SL BID
Day 4	1 mg SL BID
Day 5	2 mg SL BID
Day 6	4 mg SL BID
Day 7 until R/A	12 mg SL daily

https://www.bccsu.ca/wp-content/uploads/2020/04/Risk-Mitigation-in-the-Context-of-Dual-Public-Health-Emergencies-v1.5.pdf

Feasibility Study ED Outpatient Microdosing vs Standard Dosing

Outpatient Prescription:
* Dose based on buprenorphine component

Day	buprenorphine dose*	Number of tablets per dose. Use only buprenorphine-naloxone 2 mg-0.5 mg tablets
1	buprenorphine 0.5 mg sublingual BID	One quarter tablet
2	buprenorphine 1 mg sublingual BID	One half tablet
3	buprenorphine 2 mg sublingual BID	1 tablet
4	buprenorphine 3 mg sublingual BID	One and a half tablet
5	buprenorphine 4 mg sublingual BID	2 tablets
6	buprenorphine 12 mg sublingual daily	6 tablets

****Nurse to FAX this page and completed ALLERGY STATUS to SOT pharmacy fax: 604-875-4475 once buprenorphine-naloxone patient pack removed from Omnicell****

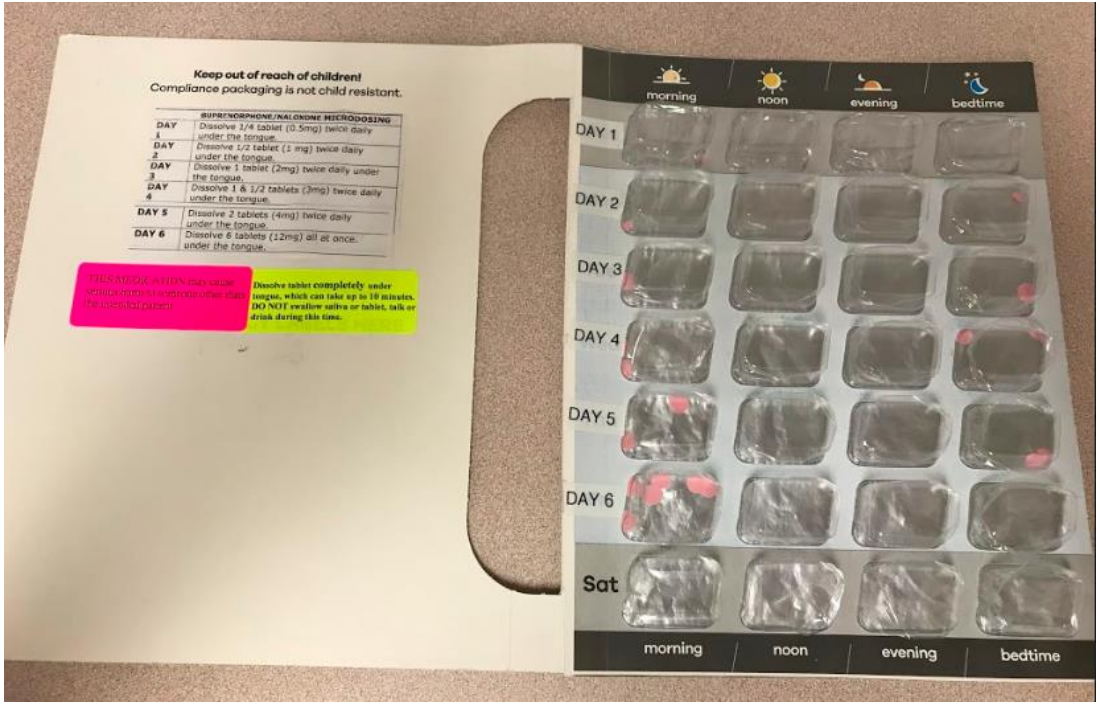
Microdosing Patient Pack Omnicell item name:

buprenorphine-naloxone 2 mg-0.5mg 16.5 TAB 33 mg PT PACK

_____ _____

RN initials Time removed from Omnicell

Feasibility Study: Microdosing



Hospital supplied

Cost (16.5 tablets) =$23.76

Time to make 4 kits:

- 1h to make
- 15 minutes to check

Including printing and cut labels and patient info sheet

- 1.5 hours to make
- 15 minutes to check

Expiry issues

Feasibility study
ED
Outpatient
Microdosing patient information sheet

Suboxone® Microdosing To Go

- You may feel a bit of withdrawal when you start taking Suboxone®- this is ok! You will probably need to keep using opioids when you start taking Suboxone®, but you will feel better as the dose increases over the 6-day course.
- To help manage withdrawal symptoms, you may take Advil®/Motrin® (ibuprofen) for body aches, Gravol® (dimenhydrinate) for nausea and vomiting, and Imodium® (loperamide) for diarrhea.

- Allow the tablets to completely dissolve under your tongue for 10 minutes. Don't swallow, talk or drink during this time.

- Allow 8-12 hours in between the two daily doses of Suboxone®.

- If you feel lots of withdrawal after a dose of Suboxone®, stop and **get help** (St. Paul's Rapid Access Addictions Clinic, Emergency Department).
- If you miss a dose of Suboxone®, stop and **get help** (St. Paul's Rapid Access Addictions Clinic or Emergency Department).

Feasibility Study ED Outpatient Microdosing patient information sheet

Day	Suboxone® Dose*	First Dose		Second Dose (8-12 hours after the first dose)
Day 1 Date: _____	0.5 mg twice	1/4 tablet	8-12 hrs	1/4 tablet
Day 2 Date: _____	1 mg twice	1/2 tablet	8-12 hrs	1/2 tablet
Day 3 Date: _____	2 mg twice	1 tablet	8-12 hrs	1 tablet
Day 4 Date: _____	3 mg twice	1 ½ tablets	8-12 hrs	1 ½ tablets
Day 5 Date: _____	4 mg twice	2 tablets	8-12 hrs	2 tablets
Day 6 Date: _____	12 mg once	6 tablets all at once		

Each full tablet contains buprenorphine/naloxone 2 mg/0.5 mg and Suboxone® is dosed based on the buprenorphine component.

Go to St. Paul's Rapid Access Addictions Clinic (RAAC) on _____ [date] for a new Suboxone® prescription.

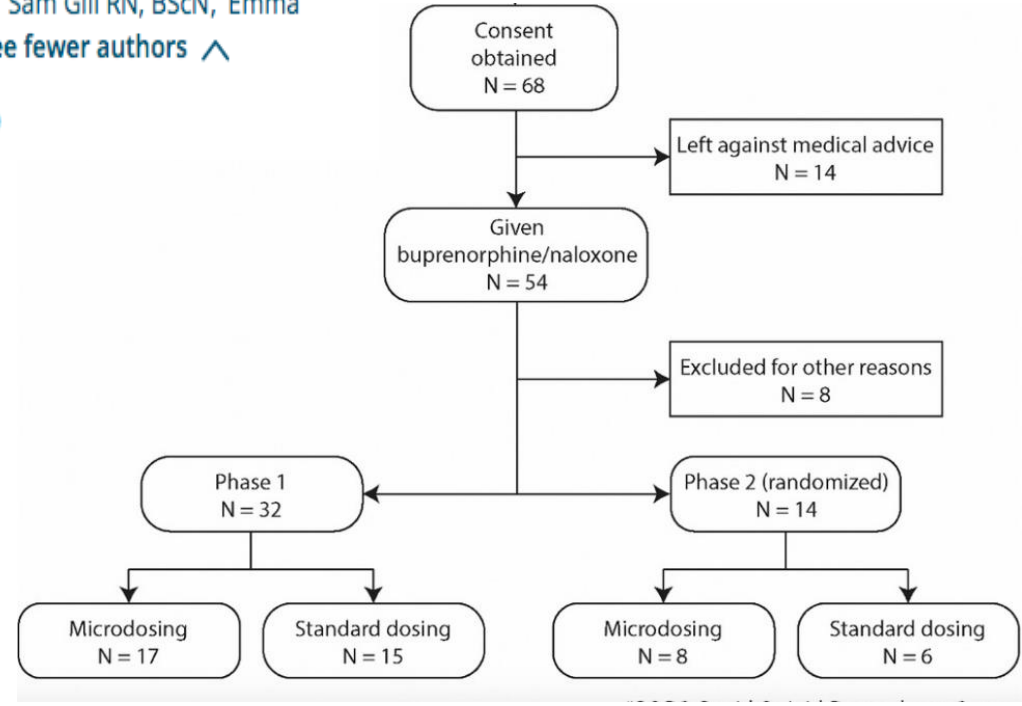
By Day 5, check in with any of these sites - No appointment required		
Rapid Access Addictions Clinic (RAAC) St. Paul's Hospital (2nd Floor Burrard Building) Open 7 days/week 9:00 am - 4:00 pm 604-806-8867	**Connections Clinic (For Downtown East Side residents only)** 623 Powell Street (entrance in alley) Monday - Friday 8:30 am-7:30 pm Saturday and Sunday 8:30 am-5:30 pm 604-675-3600	**Emergency Department** St. Paul's Hospital or Vancouver General Hospital 24 hours/day

BRIEF RESEARCH REPORT | Open Access

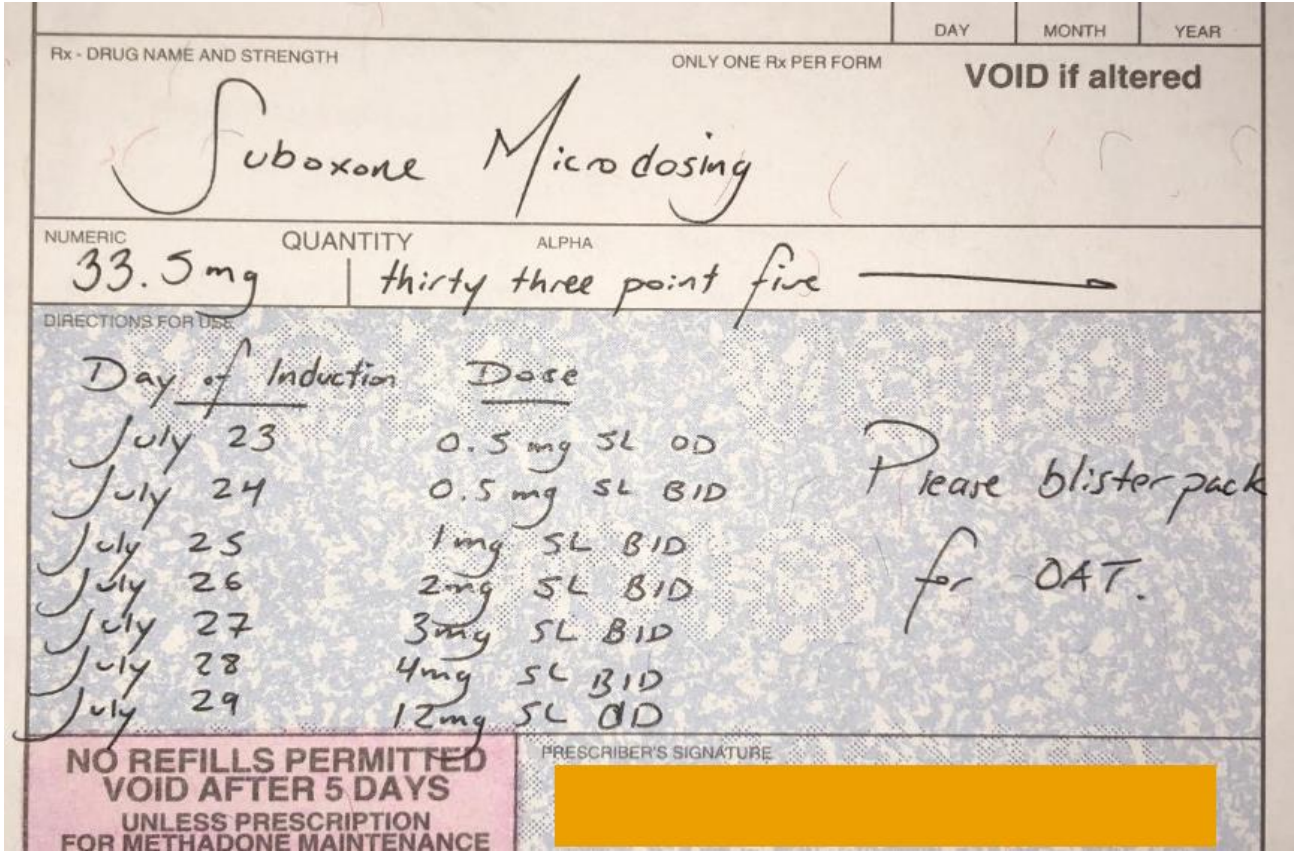
Microdosing and standard-dosing take-home buprenorphine from the emergency department: A feasibility study

Jessica Moe MD, MSc, Katherin Badke PharmD, BScPharm, Megan Pratt MSW, RSW, Raymond Y Cho MD, BSc, Pouya Azar MD, Heather Flemming MD, K. Anne Sutherland MD, MSc, Barbara Harvey MScN, JD, Lara Gurney MSN, RN, Julie Lockington MN, RN, Penny Brasher PhD, Sam Gill RN, BScN, Emma Garrod MSN, RN, Misty Bath MScPH, BSN, Andy Kestler MD, MScPH ... See fewer authors

First published: 20 October 2020 | https://doi.org/10.1002/emp2.12289



Case 1: Back to Rob….



DAY | MONTH | YEAR

Rx - DRUG NAME AND STRENGTH

ONLY ONE Rx PER FORM

VOID if altered

Suboxone Microdosing

NUMERIC: 33.5 mg | QUANTITY | ALPHA: thirty three point five

DIRECTIONS FOR USE

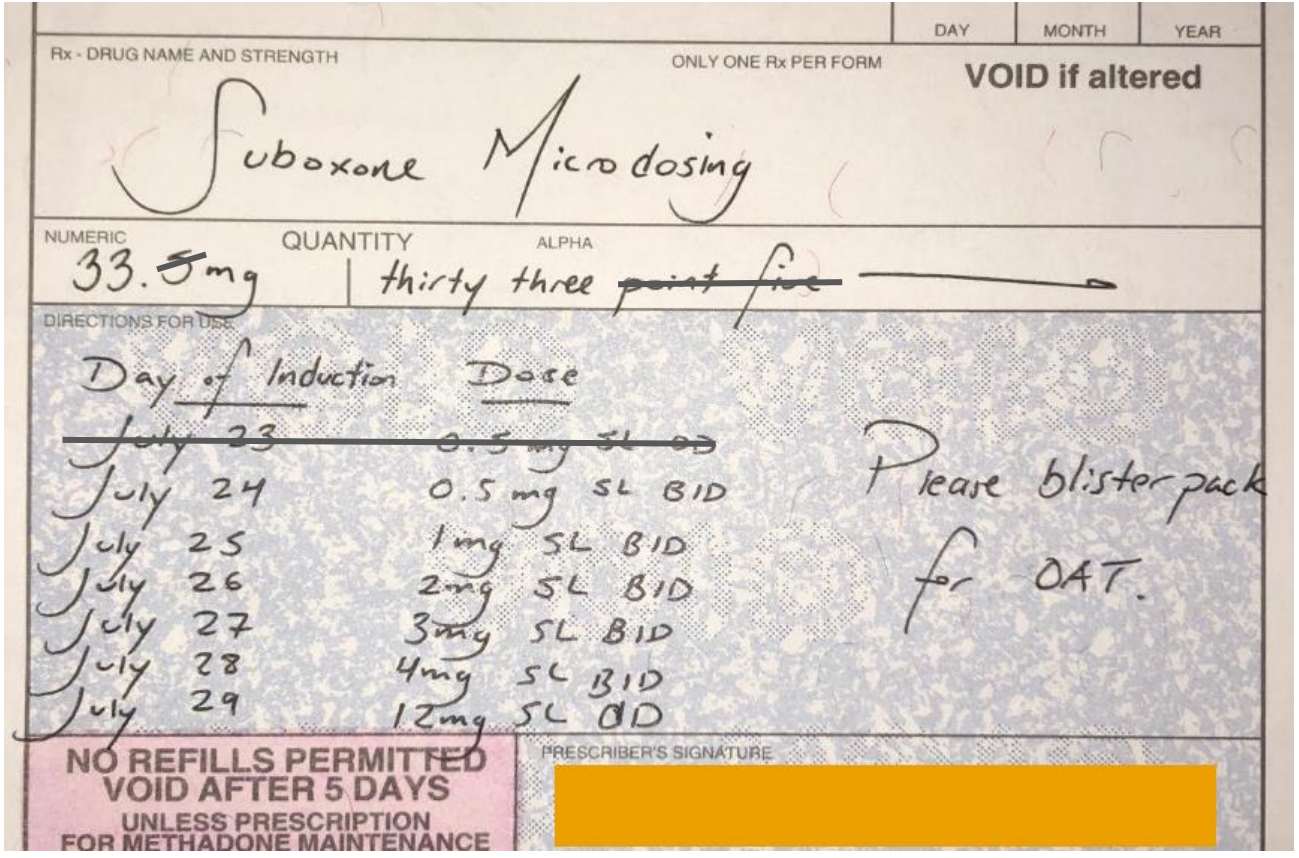
Day of Induction	Dose
July 23	0.5 mg SL OD
July 24	0.5 mg SL BID
July 25	1 mg SL BID
July 26	2 mg SL BID
July 27	3 mg SL BID
July 28	4 mg SL BID
July 29	12 mg SL OD

Please blister pack for OAT.

NO REFILLS PERMITTED
VOID AFTER 5 DAYS
UNLESS PRESCRIPTION FOR METHADONE MAINTENANCE

PRESCRIBER'S SIGNATURE

Case 1: Back to Rob….



DAY MONTH YEAR

Rx - DRUG NAME AND STRENGTH

ONLY ONE Rx PER FORM

VOID if altered

Suboxone Microdosing

NUMERIC 33.~~5~~mg

QUANTITY thirty three ~~point five~~

ALPHA

DIRECTIONS FOR USE

Day of Induction	Dose
~~July 23~~	~~0.5 mg SL OD~~
July 24	0.5 mg SL BID
July 25	1mg SL BID
July 26	2mg SL BID
July 27	3mg SL BID
July 28	4mg SL BID
July 29	12mg SL OD

Please blister pack for OAT.

NO REFILLS PERMITTED
VOID AFTER 5 DAYS
UNLESS PRESCRIPTION FOR METHADONE MAINTENANCE

PRESCRIBER'S SIGNATURE

Case 2: Morley

Presented to ED due to an altercation, now cleared for discharge

- No fixed address, spends time bouncing between family and shelters
- Last used heroin this morning
- Due to acute pain opioid withdrawal is not an option
- Previous good experience with suboxone, but stopped because he started smoking heroin again
- After discussion and the understanding that he can continue to use heroin for the next few days until his injury from altercation is more healed, patient is willing to start microdosing

RISK MITIGATION

IN THE CONTEXT OF DUAL PUBLIC HEALTH EMERGENCIES

In order to avoid the need for moderate withdrawal, consider using a microdosing protocol to initiate patients onto buprenorphine/naloxone, see Appendix 1. To avoid withdrawal and patient discomfort, consider co-prescribing hydromorphone, slow-release oral morphine (Kadian), or sustained-release oral morphine (M-Eslon) during microinduction

Ie. hydromorphone 8mg tablets 1-3 tabs q1h as needed up to 14 tablets, provided daily

Case 2: Morley's plan

1. Microdosing induction kit
2. **Hydromorphone 8 mg tablets= 1-2 tablets qid prn Daily Dispense (provide each day buprenorphine/naloxone dose below 12 mg)**
    a. **If dose is not managing pain/withdrawal follow up at RAAC/ GP/Addictions specialist**
3. Acetaminophen 1000 mg po qid
4. Ibuprofen 600 mg po qid

Case 3: Charles

- 29 y/o presenting to ED with worsening leg abscess
  - Failed OPAT
  - Lost suboxone-to-go packages
  - AMA after 1 day admission
  - Severe OUD
    - Frequent AMA due to pain and opioid withdrawal
    - Uses IV illicit drugs in the hospital

Rapid Micro-Induction

- Variation of standard micro-dosing
- Pharmacological basis
  - Buprenorphine time to peak plasma concentration is approximately 1 hour
- Preferred for inpatient setting

THE AMERICAN JOURNAL ON ADDICTIONS

AAP American Academy of Addiction Psychiatry

Case-Series | Full Access

Rapid Micro-Induction of Buprenorphine/Naloxone for Opioid Use Disorder in an Inpatient Setting: A Case Series

Sukhpreet Klaire MD, CCFP, Rebecca Zivanovic Bsc, MD, Skye Pamela Barbic PhD, OT, Raman Sandhu MD, Nickie Mathew MD, FRCPC, Pouya Azar MD, FRCPC

Klaire et al.

TABLE 2. Titration schedule

	Buprenorphine/Naloxone*		Hydromorphone	
	Dosing	Total Daily Dose	Dosing	Total Daily Dose
Day 0	N/A		3 mg PO q4h regular 2-4 mg PO q4h PRN	24 mg
Day 1	0.5 mg SL q3h	2.5 mg	3 mg PO q4h regular 2-4 mg PO q4h PRN	26 mg
Day 2	1 mg SL q3h	8 mg	3 mg PO q4h regular 2-4 mg PO q4h PRN	24 mg
Day 3	12 mg SL daily	12 mg	Discontinued	

*Expressed as milligrams of buprenorphine in buprenorphine/naloxone sublingual tablet.

Case 3: Charles’ Plan

- Recommend CTU readmission
- Recommend addictions team consult

Case 3: Charles' Plan with Addictions Consult

	Buprenorphine/Naloxone		Hydromorphone	
	Dosing	**Total Daily Dose**	**Dosing**	**Total Daily Dose**
Day 0	N/A		3mg PO q4h regular 2-4mg PO q4h PRN	24mg
Day 1	0.5mg SL q3h	2.5mg	3mg PO q4h regular 2-4mg PO q4h PRN	26mg
Day 2	1mg SL q3h	8mg	3mg PO q4h regular 2-4mg PO q4h PRN	24mg
Day 3	12mg SL daily	12mg	Discontinued	

Case 4: Monty

On Methadone 120 mg po once daily and lenvatinib (QTc-560 ms)

Both methadone and lenvatinib prolong QTCs

Requires change to suboxone and Monty is agreeable

J Addict Med. Sep/Oct 2020;14(5):e271-e273. doi: 10.1097/ADM.0000000000000618.

Rapid Transition From Methadone to Buprenorphine Utilizing a Micro-dosing Protocol in the Outpatient Veteran Affairs Setting

Joao P De Aquino [1], Christopher Fairgrieve, Sukhpreet Klaire, Gabriela Garcia-Vassallo

THE AMERICAN JOURNAL ON ADDICTIONS

Case-Series

Methadone to buprenorphine/naloxone induction without withdrawal utilizing transdermal fentanyl bridge in an inpatient setting—Azar method

Pouya Azar MD, Mohammadali Nikoo MD, Isabelle Miles MD

First published: 02 November 2018 | https://doi.org/10.1111/ajad.12809 | Citations: 6

PHARMACOTHERAPY

Brief Report

Transitioning Hospitalized Patients with Opioid Use Disorder from Methadone to Buprenorphine without a Period of Opioid Abstinence Using a Microdosing Protocol

Dale Terasaki, Christopher Smith, Susan L. Calcaterra

First published: 26 July 2019 | https://doi.org/10.1002/phar.2313 | Citations: 9

Monty’s Plan
Other alternative Micro-induction strategies

1) Fentanyl bridge
2) Kadian bridge
3) Methadone cross taper

Conclusion

- There is a role for microdosing in patients who have difficulty starting buprenorphine
    - Based on case reports and case series
    - Follow-up assessments and education are the utmost importance for patient and practitioners
- No one size fits all formula in microdosing
- **24/7 Addiction Medicine Clinician Support Line** and speak to an Addiction Medicine Specialist, call 778-945-7619

Extra slides

Inpatient- Buprenorphine Microdosing in Vancouver

BUPRENORPHINE-NALOXONE (SUBOXONE) MICRODOSING INDUCTION ORDERS

Chronic Pain and Addiction Services (CPAS) - VGH

☐ **STANDARD MICRODOSING INDUCTION** **Start on:** _____ **(date) at** _____ **(hours)**

Day	buprenorphine dose and interval*	buprenorphine - naloxone strength to use	Quantity per dose
1	0.5 mg sublingual daily	buprenorphine 2 mg - naloxone 0.5 mg	1/4 tab
2	0.5 mg sublingual BID	buprenorphine 2 mg - naloxone 0.5 mg	1/4 tab
3	1 mg sublingual BID	buprenorphine 2 mg - naloxone 0.5 mg	1/2 tab
4	2 mg sublingual BID	buprenorphine 2 mg - naloxone 0.5 mg	1 tab
5	4 mg sublingual BID	buprenorphine 2 mg – naloxone 0.5 mg	2 tabs

Starting on Day 6, give buprenorphine-naloxone* 12 mg (1 tab) sublingual once daily ***AND*** start buprenorphine-naloxone _____ mg sublingual Q3H PRN withdrawal symptoms ***AND*** discontinue all opioids other than buprenorphine-naloxone.

Rapid Buprenorphine Microdosing in Vancouver

BUPRENORPHINE-NALOXONE (SUBOXONE) MICRODOSING INDUCTION ORDERS

Chronic Pain and Addiction Services (CPAS) - VGH

☐ **RAPID MICRODOSING INDUCTION** **Start on:** _____ **(date) at** _____ **(hours)**

Doses	buprenorphine dose and interval*	buprenorphine - naloxone strength to use	Quantity per dose
1 to 8	0.5 mg sublingual Q3H x 8 doses	buprenorphine 2 mg - naloxone 0.5 mg	1/4 tab
9 to 16	1 mg sublingual Q3H x 8 doses	buprenorphine 2 mg - naloxone 0.5 mg	1/2 tab

Starting 3 hours after the last dose (i.e. dose number 16), give buprenorphine-naloxone* _____ mg sublingual once daily ***AND*** start buprenorphine-naloxone _____ mg sublingual Q3H PRN withdrawal symptoms ***AND*** discontinue all opioids other than buprenorphine-naloxone.

* Buprenorphine-naloxone is dosed based on buprenorphine component.

BUPRENORPHINE-NALOXONE (SUBOXONE) MICRODOSING INDUCTION ORDERS

Chronic Pain and Addiction Services (CPAS) - VGH

Other as needed opioid medication for withdrawal symptoms:

Hold PRN opioid if sedated, respiratory rate below 12 per minute, or SpO_2 below 92%.
Discontinue PRN opioid: see instructions on page 1 for timing of discontinuation.

☐ morphine _____ mg PO or _____ mg SUBCUT Q3H PRN

*** OR ***

☐ HYDROmorphone _____ mg PO or _____ mg SUBCUT Q3H PRN

*** OR ***

☐ oxyCODONE _____ mg PO Q3H PRN

BUPRENORPHINE-NALOXONE (SUBOXONE) MICRODOSING INDUCTION ORDERS
Chronic Pain and Addiction Services (CPAS) - VGH

Adjunct medications for withdrawal management:

- ☐ dimenhyDRINATE 50 mg PO/IV Q6H PRN nausea/vomiting (maximum 400 mg per day)
- ☐ ondansetron 4 mg PO/IV Q8H PRN nausea/vomiting
- ☐ acetaminophen 325 to 650 mg PO Q4H PRN pain (maximum 4 g per 24 hour period from all sources)
- ☐ ibuprofen 200 to 400 mg PO Q6H PRN pain (maximum 2.4 g per 24 hour period)
- ☐ clonidine 0.1 mg PO Q1H PRN withdrawal symptoms (maximum 0.8 mg per day). Hold if SBP less than 100 mmHg or DBP less than 70 mmHg.
- ☐ loperamide 2 mg PO QID PRN diarrhea (Maximum 16 mg per 24 hours)
- ☐ zopiclone 3.75 mg PO QHS PRN insomnia. May repeat x 1 dose