

Buprenorphine/Naloxone Microdosing: The Bernese Method

A Brief Summary for Primary Care Clinicians

Disclaimer:

Microdosing principles are currently not included in any clinical practice guidelines for the management of Opioid Use Disorder, rather it is an off-label practice that has been included in clinical practice amongst addiction specialists. It is therefore important to obtain informed consent prior to initiating it with a patient. Microdosing is frequently used at the London Rapid Access and Addictions Medicine (RAAM) Clinic with good results.

What is Microdosing?

The Bernese Method uses the principle of Microdosing to initiate a patient onto buprenorphine/naloxone (bup/nlx) maintenance therapy. The theoretical background of this method is based on the following hypotheses:

- 1) Repetitive administration of very small buprenorphine doses with sufficient dosing intervals (e.g. 12 hours) should not precipitate opioid withdrawal
- 2) Because of the long receptor binding time, buprenorphine will accumulate at the opioid receptor
- 3) Over time, an increasing amount of a full μ -agonist will be replaced by buprenorphine at the opioid receptor

Therefore, overlapping induction of buprenorphine with ongoing use of opioids, from the unregulated drug market or prescription, including maintenance doses of a full μ -agonist (e.g. methadone or sustained release oral morphine), should be possible without precipitating severe opioid withdrawal. Mild withdrawal symptoms may be experienced during the induction.

Although dosing schedules vary, principles of the Microdosing method include:

- 1) Prescriber starts with a low dose of buprenorphine, overlapping with other opioid use
- 2) Small daily buprenorphine dose increases
- 3) Abrupt cessation of opioid use at sufficient dose of buprenorphine

Why use it, and who is a good candidate?

Microdosing may have considerable advantages despite taking longer for the overall induction than the traditional protocol. It may be useful for most patients. In more detail:

- It may be helpful for patients fearing withdrawal or experiencing severe symptoms during conventional induction, or who have failed conventional induction due to inability to tolerate withdrawal symptoms

- It may also be beneficial when a switch to buprenorphine is desired for patients maintained on a full μ -agonist such as methadone or slow-release oral morphine (SROM)
- It is no longer necessary to wait for withdrawal before induction, so patients who may not be able to attend daily appointments due to work commitments, etc. are good candidates
- As it negates withdrawal, there may be better treatment retention with buprenorphine/naloxone
- It may have more providers willing to prescribe buprenorphine/naloxone, as the induction is not as complex

Who Should Be Referred to the RAAM Clinic for Induction and Stabilization of Opioid Agonist Therapy (OAT)?

- Patients who are on high dose fentanyl patches of 100mcg/hour or greater
- Patients who are using illicit street fentanyl (due to the uncertain risk of precipitated withdrawal)
- Injection drug users
- Methadone conversions

Monitoring Considerations:

If choosing to use Urine Drug Screens (UDS) to assist with monitoring, emphasize that they are being utilized as a patient safety tool. These may be used with each client visit, or as the practitioner deems appropriate.

Reasons to use a UDS are to ensure client safety, augment honesty and accountability, and to inform treatment. It is often the case that clients are unaware of the mixed components of their drug from the unregulated market, or how combining medications, like benzodiazepines, can put them at further risk. UDS can help us assist them in their recovery.

Using the Microdosing method, follow-up appointments may be at a weekly interval, based on individual client's stability. You may choose to have a few days of brief daily follow-up appointments with opioid cessation, to allow for timely titration of buprenorphine/naloxone to a comfortable dose.

How do you prescribe buprenorphine/naloxone via the *Microdosing Method*?

Short-acting Opioid:

Day	Buprenorphine / Naloxone	Opioid
1	0.5 mg daily	Maintain dose
2	1.0 mg daily	Maintain dose
3	1.5 mg daily	Maintain dose
4	2.0 mg daily	Maintain dose
5	2.5 mg daily	Maintain dose
6	3.0 mg daily	Maintain dose
7	4.0 mg daily	Stop short-acting opioid
See the patient on Day 7, after 4mg of Bup/Nlx, and give another 2mg every 1h until comfortable, to a max of 12mg that day. You may instead choose to give an additional 2mg as needed on Day 7, with daily follow-ups thereafter, and increases of 2mg to 4mg/day as needed, until comfortable. Final maximum dose is typically 16mg/day.		

Long-acting Opioid:

Day	Buprenorphine / Naloxone	Opioid
1	0.5 mg daily	Maintain dose
2	1.0 mg daily	Maintain dose
3	1.5 mg daily	Maintain dose
4	2.0 mg daily	Maintain dose
5	2.5 mg daily	Maintain dose
6	3.0 mg daily	Maintain dose
7	4.0 mg daily	Begin taper of long-acting opioid
If long- AND short-acting opioids, stop short-acting opioids here, and begin taper of long-acting opioid		
8	5.0 mg daily	Continue taper
9	6.0 mg daily	Continue taper
10	7.0 mg daily	Continue taper
11	8.0 mg daily	Continue taper
12	10.0 mg daily	Continue taper
13	12.0 mg daily	Continue taper
14	12.0 mg daily	Stop remaining long-acting opioid
Follow-up appointment at Day 7 to outline taper of long-acting opioid. See the patient on Day 14, after 12mg of Bup/Nlx, and give another 2mg every 1h until comfortable, to a max of 16mg that day.		

Low doses of prescribed- Fentanyl/Fentanyl Patch:

Day	Buprenorphine / Naloxone	Opioid
1	0.5 mg	Maintain dose
2	1.0 mg	Maintain dose
3	1.5 mg	Maintain dose
4	2.0 mg	Maintain dose
5	2.5 mg	Maintain dose
6	3.0 mg	Maintain dose
7	4.0 mg	Begin taper of prescription Fentanyl
8	5.0 mg	Continue taper
9	6.0 mg	Continue taper
10	7.0mg	Continue taper
11	8.0 mg	Continue taper
12	10.0mg	Continue taper
13	12.0mg	Continue taper
14	12.0 mg	Stop remaining Fentanyl
Closer follow-up may be needed with Fentanyl conversions. Suggested follow-up appointment at Day 7 to outline taper of Fentanyl. See the patient on Day 14, after 12mg of Bup/Nlx, and give another 2mg every 1h until comfortable, to a max of 16mg that day.		

Community Pharmacy Considerations:

It is advisable to check with the patient's community pharmacy to ensure they have buprenorphine / naloxone to dispense. If you are unsure if the pharmacy has dispensed it using the Microdosing method previously, it is a general courtesy to forward them a copy of the Microdosing Method along with your prescription. They may need a "heads up" that tablets may need to be split to accommodate the smaller doses required in Microdosing.

Carries and Observed Doses for Microdosing:

In general, inductions involve all observed doses at the pharmacy. Daily dispensing will also ensure accuracy and ease of any associated opioid taper.

Missed Doses During Microdosing Induction:

If one dose is missed during induction, consider repeating the previous day's dose and continue the schedule.

If two doses are missed, consider restarting the schedule.

Withdrawal Management:

Diphenhydramine, loperamide and acetaminophen/ibuprofen may be of benefit for any potential withdrawal.

Local Support for Clinicians:

If you require any assistance or just want to double check your plan, consider contacting the local Rapid Access Addiction Medicine Clinic.

Also consider an e-Consult (<https://otnhub.ca/patient-care/>) with Addiction Specialist Dr. Ken Lee (ken.lee@sjhc.london.on.ca); or Medical Mentoring for Addictions and Pain (<https://ocfp.on.ca/cpd/collaborative-networks/mmap>)

Or consultation with Katie Dunham, NP (katie_dunham04@hotmail.com) or call 519-319-4428

References:

Hämmig, R., Kemter, A., Strasser, J., von Bardeleben, U., Gugger, B., Walter, M., Dürsteler, K.M. and Vogel, M., 2016. Use of microdoses for induction of buprenorphine treatment with overlapping full opioid agonist use: the Bernese method. *Substance abuse and rehabilitation*, 7, p.99.

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