10-item Q&A for using buprenorphine/naloxone
Dr. Valerie Primeau, MD FRCPC
November 2, 2017

1) What are the DSM-5 criteria for Opioid Use Disorder?

Criteria for diagnoses of substance use disorders	Severity of disorder
Used more than intended	
Unsuccessful attempts to discontinue use	
Increased time spent acquiring and using the substance	Mild 2-3 criteria are met
Cravings	
Failure to fulfill major role obligations	Moderate
Use despite social or interpersonal problems	4-5 criteria are met
Given up activities	
Use in hazardous situations	Severe
Use despite consequences	6-11 criteria are met
Tolerance (not counted if prescribed)	
Withdrawal (not counted if prescribed)	

2) What is buprenorphine?

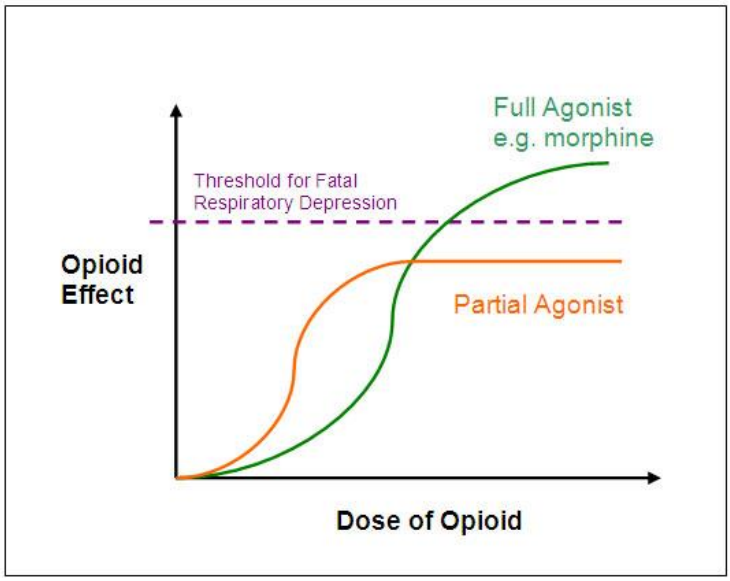
Buprenorphine is a partial opioid agonist used to treat opioid use disorder.

It has been available in Canada since November 2007 as a combination product with the opioid antagonist naloxone (under the brand name "Suboxone"). There are now two additional generic forms of buprenorphine/naloxone available in Canada. Both generic drugs have the same dosage forms of sublingual tablets that come in 2/0.5mg and 8/2mg buprenorphine/naloxone ratio.

Buprenorphine has a high affinity to the opioid receptor. It binds tightly to the receptor and dissociates slowly from it. As a result, buprenorphine's half-life is 24-60 hours with the average being around 32 hours. Because of its slow onset, opioid-dependent patients should not experience sedation or euphoria at the appropriate sublingual dose. Buprenorphine reaches a peak serum level and peak effect in 1-4 hours.

3) What are the advantages and benefits of initiating buprenorphine?

- ✓ Attenuation of symptoms of opioid withdrawal for 24 hours
- ✓ Significant reduction in cravings for opioids
- ✓ Lower risk of relapse compared to an abstinent-based approach
- ✓ Buprenorphine blocks some or all of the effects of other opioids such as morphine, oxycodone, heroin
- ✓ Lower attributable death than methadone
- ✓ Lower risk of overdose and fatal respiratory depression (ceiling effect due to being a partial agonist) and therefore more suitable for older patients, patients using sedating drugs or medications and patients with severe respiratory disease
- ✓ Faster titration compared to methadone
- ✓ More flexible dosing regime where it can be dosed every other day as it has a longer half-life
- ✓ Better cognitive performance than patients on methadone
- ✓ Less sexual dysfunction than methadone
- ✓ Easier than taper off compared to methadone



4) What are the potential disadvantages of starting buprenorphine over methadone?

- ✓ More risk of misuse by injection than methadone (which is mixed in a liquid) with naloxone acting as an imperfect deterrent
- ✓ Precipitated withdrawal reaction when buprenorphine induction is done too soon
- ✓ In rare cases, even at maximal doses, buprenorphine may not be sufficient to manage withdrawal for a full 24 hours. This is due to the ceiling effect. Methadone does not have these same ceiling effect.
- ✓ Dissolution of the sublingual tablets usually takes 2 to 10 minutes and an area needs to be provided in the pharmacy for patients to have their dose supervised

5) Which laboratory investigations are recommended before starting buprenorphine?

- ✓ Urine Drug Test
- ✓ Pregnancy or BHCG Test (opioid withdrawal can precipitate spontaneous abortion)
- ✓ Complete Blood Count
- ✓ Liver Function Tests (could be contraindicated if more than 3-5x the normal values)
- ✓ Blood-borne Viruses Testing (higher risk of hepatitis B, C and HIV infection in intranasal and IV users)

6) What are the contraindications to starting buprenorphine?

- ✓ Allergy or sensitivity to buprenorphine or naloxone
- ✓ Opioid-naïve patients
- ✓ Severe liver dysfunction
- ✓ Acute severe respiratory illness
- ✓ Decreases in level of consciousness
- ✓ Paralytic ileus
- ✓ Inability to provide informed consent
- ✓ During pregnancy, there used to be a concern as naloxone's safety in pregnancy had not been established but experts are routinely using it in pregnancy across Canada at this time

7) What are the potential side effects of buprenorphine?

Buprenorphine has side effects similar to other opioids. These effects include:

- ✓ Sedation
- ✓ Constipation
- ✓ Headaches
- ✓ Nausea/vomiting
- ✓ Dizziness
- ✓ Sweating

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8) How is the buprenorphine induction done?
First, we need to know which type of opioids was used and the date and time of the last dose. Patients need to be in moderate withdrawal (COWS of 13 or more). Otherwise, a precipitated withdrawal reaction can be triggered.

Short-acting opioids:
Abstain for 6 hours as a minimum, but 12 or more hours are preferable

- ✓ Heroin
- ✓ Oxycodone (immediate release and/or in combination with acetaminophen or acetylsalicylic acid)
- ✓ Hydromorphone immediate release
- ✓ Codeine immediate release
- ✓ Controlled-release products that are chewed or crushed

Longer-acting opioids:
Abstain for 12 hours as a minimum, but 24 or more hours are preferable

- ✓ Oxycodone controlled release
- ✓ Hydromorphone controlled release
- ✓ Other slow-release opioids that are swallowed whole

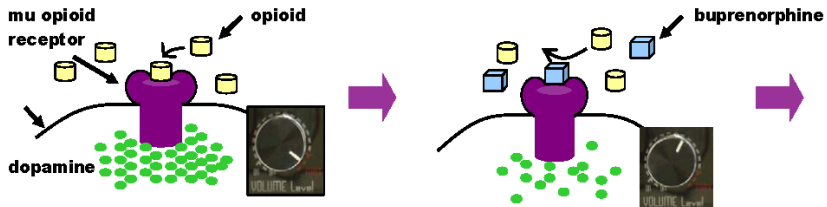
Methadone:
Abstain for 24 hours as a minimum, but 36-72 hours are preferable

When the patient is ready, the first dose can be either 2 mg or 4 mg based on the patient's presentation. The patient can receive further 2 mg doses up to 8 mg on day 1. On day 2, the patient would receive the total from day 1 and can also receive further 2 mg doses up to 16 mg on day 2. The average dose is 8-12 mg, with a maximum of 24 mg per day.

9) How do we know if the dosage of buprenorphine is adequate?
The physician can titrate buprenorphine daily if necessary, keeping in mind that the full effect of a particular dose of buprenorphine cannot be known until a patient has received that dose for three days or more.
Good indicators include:

- ✓ The patient has not experienced opioid withdrawal for 24 hours
- ✓ The patient experiences a reduction in cravings
- ✓ The patient has ceased abusing opioids
- ✓ A slip or relapse to opioids does not result in a euphoric effect due to opioid receptor blockade with buprenorphine
- ✓ The patient does not experience sedation, and opioid side-effects are minimal

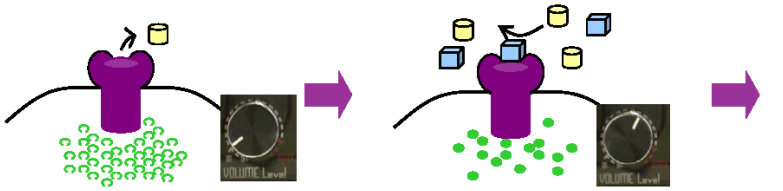
10) Special circumstances:
Vomiting after buprenorphine dosing:
When this happens, no replacement dose is required. Vomiting does not affect buprenorphine doses because sublingual buprenorphine is absorbed via oral mucosa, not the gastrointestinal tract.
Swallowed buprenorphine doses:
Due to the difficulty in establishing how much (if any) of a dose of buprenorphine may have been swallowed rather than absorbed sublingually, swallowed buprenorphine doses should not be replaced.



Full mu agonist (i.e. heroin)
Significant amount of opioid bound to receptors
"Volume" on max

Buprenorphine
Binds preferentially to receptors
"Volume" on medium

Precipitated Withdrawal
Relative to a full mu agonist, **buprenorphine** "turns on" receptors less patient feels withdrawal



Withdrawal
Most receptors unbound
"Volume" on low

Buprenorphine
Binds preferentially to receptors
"Volume" on medium

Induction
Relative to withdrawal, **buprenorphine** "turns on" receptors more ∴ patient feels better

Graphics adapted from NAABT, Inc. (naabt.org)