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CASE STUDY

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

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## Abstract

**Background:** The requirement for moderate withdrawal prior to initiation can be a barrier to buprenorphine/naloxone induction.

**Case presentation:** We aimed to use a microdosing regimen to initiate regular dosing of buprenorphine/naloxone in a high-risk patient with a history of failed initiations due, in part, to withdrawal symptoms. Using an assertive outreach model and a buprenorphine/naloxone microdosing schedule, we initiated treatment of an individual's opioid use disorder. There was a successful buprenorphine/naloxone microdosing induction as the team reached a therapeutic dose of buprenorphine/naloxone. Including the induction period, the medication was used consistently for 4 weeks.

**Conclusions:** A microdosing schedule can be used to induce a patient onto buprenorphine/naloxone with no apparent withdrawal; gradually reducing illicit substance use. This case report builds on previous literature, highlighting ways to minimize barriers to induction of buprenorphine/naloxone, using a microdosing schedule and assertive outreach. Given the safety profile of buprenorphine and its potential to be a lifesaving intervention, a larger study of microdosing is indicated.

**Keywords:** Opioid use disorder, Buprenorphine/naloxone, Microdosing, Bernese method, Induction method

## Background

Over the past 10 years, rates of opioid-related overdose deaths and opioid-related harms have drastically increased in British Columbia [1]. Since 2015, illicit drug use has surpassed suicide as the major cause of unnatural deaths in BC, with fentanyl-related overdoses implicated as the leading cause of illicit drug overdoses [1]. This public health crisis of historical scale has taken more lives than the HIV epidemic in the early 1990's [2]. The latter at its peak (1995) was identified as the cause of a total of 1764 mortalities in Canada [3] compared to 4588 reported apparent opioid-related deaths in Canada in 2018 [4] when, approximately four people lost their lives to overdose every day in BC [1].

Opioid agonist treatment (OAT) has been shown to reduce morbidity and mortality among patients with opioid use disorder (OUD) [5–10]. Buprenorphine/naloxone has become the recommended first-line OAT in Canada based on its preferable safety profile and efficacy [11, 12].

Buprenorphine is a partial μ agonist, with high receptor affinity resulting in a slow dissociation from the receptor and prolonged activity. Naloxone has minimal effect when taken orally and is introduced to the formula to minimize diversion. The pharmacokinetics of buprenorphine/naloxone result in a favourable safety profile due to

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a ceiling effect on respiratory depression and the ability for rapid titration. Precipitated withdrawal can result if buprenorphine/naloxone is introduced in the presence of other opiates with lesser-binding affinities, such as heroin or methadone; therefore, patients are required to be in moderate withdrawal prior to induction.

Need for withdrawal prior to induction is acknowledged as a challenge for choosing OAT with buprenorphine/naloxone (BUP/NLX). This requirement mandates the patients to time their withdrawal to match an office-based appointment, and to be supervised for several hours. This is a barrier for a variety of reasons, such as lack of clinic space or staffing to monitor the induction, and also patients' anxiety, impulsivity, work or school commitments interfering with such a long stay in the clinic. In addition to the fluctuating level of consciousness associated with high opioid use, tolerating the high cravings to use during the timed withdrawal which is required for office induction is another inherent challenge for this method. While home BUP/NLX induction strategies have offered an alternative to the need for withdrawal in clinic, there remains a selected patient population for whom the requirement for moderate withdrawal prior to initiation will remain a barrier regardless of the setting [13, 14]. Patients may also be fearful of precipitated withdrawal, which is associated with usual induction starting before adequate withdrawal. Moreover, precipitated withdrawal is perceived by some providers a barrier for adopting home induction with buprenorphine [15]. These barriers may encourage patients towards other OAT medications with less favourable safety profile such as methadone or slow-release oral morphine. Microdosing inductions can preclude the requirement for the withdrawal prior to induction and also may decrease the risk of precipitated withdrawal. Ultimately, it will also provide patients keen on starting OAT with BUP/NLX with more options.

A microdosing schedule for buprenorphine was first introduced and trialed in 2010 by Hamming et al. in Bern, Switzerland [16], followed by a more recent report of two cases of successful induction of buprenorphine/naloxone in 2016 [17]. The first case was induction of buprenorphine/naloxone using a microdosing schedule starting at 0.2 mg daily and titrated up to 12 mg daily over 9 days, with gradual reduction and eventual cessation of illicit heroin use over this time [16]. The second case was a gradual cross-titration of methadone and diacetylmorphine to buprenorphine/naloxone starting at 0.2 mg and titrated up to 24 mg over 28 days [17]. Both patients tolerated this induction without reporting the experience of precipitated withdrawal or need for withdrawal from opiates prior to induction. This method has been coined "The Bernese Method" [16]. The pharmacological hypothesis tested in the Bernese Method is that small amounts of buprenorphine doses should not precipitate opioid withdrawal, but because of its relatively long half-life, accumulates at the receptor gradually replacing the full μ-agonist (e.g. fentanyl, heroin) at the opioid receptor. This was successfully shown with these two cases presented by Hamming; however, this has not been replicated in the current practice literature [16, 17].

There has been growing interest in the Bernese Method in Vancouver, BC, Canada, as healthcare providers struggle to find ways to reduce mortality in the context of a public health emergency. To date, there has been considerable effort to engage individuals who use opioids in opioid agonist treatment, as well as to provide overdose response kits and personnel to manage acute overdoses [18]. The Bernese Method is a potential compliment to patients who want treatment with buprenorphine/naloxone, but are adverse to the traditional induction method because of the need for withdrawal and/or have difficulty attending scheduled appointments. This method has also shown promise for other indications such as pain management [19].

Apart from above-mentioned barriers, there remains other challenges for home induction with BUP/NLX. Home induction works best for patients who have stable housing, relatively good cognitive function, and are organized enough to reliably follow instructions. Unfortunately, this is not the case for most of patients who are served by the outreach programs, patients with severe opioid use disorder, high rates of cognitive impairment and major mental health illness in the most vulnerable opioid using population i.e. homeless population that can interfere with their ability to come to a clinic, tolerate withdrawal, and stay for induction and as a result precludes them often from successful home induction. Provision of microdosing within an outreach program can make buprenorphine/naloxone treatment accessible to high-risk patients who have difficulty attending office-based appointments or complying with a home-based protocol. Assertive outreach, part of this model of care, involves flexible delivery of integrated health services by an interdisciplinary team and is an established model for engaging patients with complex needs that have not been met in traditional office-based settings [20, 21]. The Inner City Youth Program (ICYP) uses this approach with high-risk youth who are living with moderate to severe mental illness and/or substance use disorders, and psychosocial and/or medical complexities. The ICYP is located at Foundry Vancouver Granville, which is a "one-stop shop" health centre in downtown Vancouver for young people aged 12–24, which includes support to family members and caregivers. Care is provided by an interdisciplinary

team of peers and professionals through clinic-based and outreach services.

In February 2018, we began using a microdosing regimen to initiate regular dosing of buprenorphine/naloxone in ICYP patients with significant barriers to induction, such as developmental disabilities, homelessness, and psychosis. We used assertive outreach to identify and locate patients with OUD who were not receiving OAT and offer them buprenorphine/naloxone microdosing induction on the spot. OAT prescribers offered weekly outreach, and interdisciplinary team members provided case management and supported patients with their OAT and other related goals. Patients were linked to primary care, psychiatry, peer support and other services.

In the first 6 months of this program, 14 people, 18–25 years-old with severe disordered use of multiple substances and comorbid mental illness, and history of residential instability and poverty were engaged in care with 8 successful inductions and no instances of precipitated withdrawal. This method has also attracted growing interest among other clinics in our community. As there are limited published reports on this topic, we present a case report for discussion to contribute to the body of evidence. Specifically, we present a case of a patient successfully completing buprenorphine/naloxone induction, without reporting a period of withdrawal, using a microdosing schedule delivered via assertive outreach. Success was defined as reaching a therapeutic dose of Suboxone for a minimum of 30 consecutive days.

## Case presentation

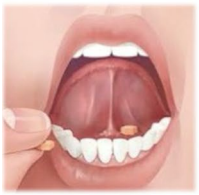
The patient was a 55-year-old male, a parent of one of our youth outreach patients. He reported being First Nations, living in a single-room-occupancy hotel, and supported by income assistance. He had a long history of opioid and stimulant use disorders. Given the incredible urgency and need for flexibly service delivery in the context of OAT, he was taken as a patient in our youth outreach program to help family members in innovative ways. His presentation was complicated by an evolving left leg cellulitis, untreated hepatitis C, and a history of gout. At the time of initial assessment, he was not taking any medications. Our team was consulted to see him for buprenorphine/naloxone microdosing induction in his residence. Visiting the patient in his residence was used as a measure to lower the threshold for access to care and improve his engagement with the treatment.

On initial assessment, the patient self-reported injecting 200 mg of heroin daily 200 mg of crystal methamphetamine every 3 days. The actual amounts used was difficult to measure given the variability in chemical make-up and potency of heroin and other street drugs in Vancouver, including their adulteration with fentanyl and other contaminants [22, 23].

The patient had previously trialed methadone but had relapsed. He had multiple trials of traditional buprenorphine/naloxone inductions but was unable to complete them due to his intolerance of withdrawal symptoms. He had experienced at least one overdose requiring resuscitation with naloxone.

Outreach visits to this patient began February 28, 2018 and he was seen four times (out of five attempted visits) over 3 weeks at his residence. The patient was prescribed a buprenorphine/naloxone microdosing regimen (see Fig. 1). The BUP/NLX tablets were split by the local pharmacy for off-label administration of small doses in microdosing protocol. Since the smallest available dose in Canada is 2 mg, it was more practical to split the tablets into 0.25 mg as opposed to 0.2 mg, which was prescribed in Bernese Method. The patient was instructed to use decreasing doses of heroin as buprenorphine/naloxone doses increased, then to stop heroin once the buprenorphine dose reached 12 mg. He completed the microdosing regimen and over the course of 7 days his dose was titrated to 12 mg daily. On day 8 the dose was increased to 16 mg daily and the patient abstained from illicit drugs. Despite the team offering to deliver the medication to the patient's home, he chose to pick them up himself daily from the pharmacy. The outreach team supported him with reminders to pick up his medications regularly. Due to a prescription error, he missed 3 days of his buprenorphine/naloxone (March 20–23, 2018), and a relapse of heroin and crystal methamphetamine ensued. A subsequent retrial of buprenorphine/naloxone microdosing induction was prescribed, but the patient did not pick up his medications, and was difficult to find for follow up.

The patient was seen again on outreach visits to his residence and neighbourhood starting on May 14, 2018. He was contemplative about quitting heroin. He wanted to retrial the microdosing induction method. We conducted a medical history, screening for major health concerns, liver failure, other medications and allergies. Blood work from December 2017 showed normal complete blood count, electrolytes, blood urea nitrogen, and creatinine. December 2016 liver function tests were normal. A microdosing buprenorphine/naloxone regimen was re-prescribed, along with a blood requisition for updated liver function tests, human immunodeficiency virus, treponema pallidum, hepatitis B virus, complete blood count, electrolytes, blood urea nitrogen, and creatinine. Medication was dispensed daily to the patient at a pharmacy situated across the street from his residence. The prescriber and the pharmacy stayed in close phone and



| Day | Total dose |
|---|---|
| 1 | 0.25 mg |
| 2 | 0.5 mg |
| 3 | 1 mg |
| 4 | 2 mg |
| 5 | 4 mg |
| 6 | 8 mg |
| 7 | 12 mg |




**Fig. 1** Buprenorphine/naloxone microdosing regimen (daily witness ingestion). The team partnered with a local pharmacy who were able to split that tablets for microdosing. The tablet splitting may not have been 100% accurate, however it was effective for this patient, given that the technique is to start low and gradually increase and best practice for dosing has yet to be established

in-person connection regarding dosage adjustments and medication adherence.

The patient picked up and took all but two doses in the first week.

There were no symptoms of withdrawal throughout the induction. This was documented via the patients self-report and the clinicians' overall assessment of the patient's withdrawal symptoms as the use of standardized tools was neither feasible nor necessary given that withdrawal prior to induction is not a requirement in microdosing technique. The patient reduced illicit heroin use to 200 mg every 2 days during the week of the microdosing. The patient had mild cravings when he reached 12 mg, though decreased his use to 100 mg every three days. Follow up was challenging because the patient had difficulty keeping appointments, and we were not always able to locate him on outreach. The team looked for the patient in his home and in the neighborhood, and after several attempts assessed him on May 28, 2018. At the time, he was on 12 mg daily. He continued to self-report using heroin 500 mg every 3 days and experiencing cravings, so his dose was increased to 16 mg. He continued to stay on buprenorphine/naloxone 16 mg daily, with no further missed doses.

He was assessed again on June 11, 2018. Notably, a painful left leg cellulitis persisted, and he continued to use heroin 500 mg every 3 days when he felt leg pain. While he reported mild cravings, he reported using heroin to manage pain. The team connected him to a nearby primary care clinic for wound care and antibiotics. The dose of buprenorphine/naloxone was increased to 20 mg daily. He adhered to his agonist medication till August 27, 2018 and reported using 50 mg approximately every 4 days, which he was willing to taper. Interestingly, he reported no longer using any other illicit substances. The outreach team supported him to connect with an adult-oriented primary care and OAT clinic, and his care was transferred accordingly.

## Discussion and conclusions

We presented a case of an induction to buprenorphine/naloxone using a microdosing schedule (Bernese Method) with no apparent withdrawal. The induction was conducted successfully as part of the outreach visits to the patient's residence in a single-room-occupancy hotel in downtown Vancouver. The outreach component, which sets this apart from the Bernese Method alone, aimed to promote adherence and minimize barriers for patients with multiple treatment failures and complex medical comorbidities. The combination of buprenorphine/naloxone safety profile, and flexible microdosing schedule are well suited to the outreach model and a complex patient population. Further studies could study the effectives of microdosing as compared to outreach component towards the effectiveness of the overall model for instance by comparing patients receiving

outreach intervention with microdosing induction or regular buprenorphine dose induction. However such a study will be very challenging because traditional induction methods have been limited in their utility due to the profound executive dysfunction in this population. They are migratory and difficult to locate. They are impulsive in their substance use and struggle so much with their organization and planning that traditional induction methods are for the most part impractical. The flexibility that microdosing affords in the real-world allows induction to occur in a much more resource-efficient and achievable way.

This report shows that a microdosing schedule can be used to induce a patient onto buprenorphine/naloxone, with no apparent withdrawal, and reduced illicit substance use. Secondary benefits included increased connection with the healthcare team, and treatment of the patient's cellulitis.

Further carefully designed research is needed to build evidence regarding the viability and efficacy of the Bernese Method in an outreach setting. The optimum dosing schedule has yet to be defined. A major limitation of this method is the continued illicit opiate use during the initial phases of the induction. The OAT may reduce or stop opioid use, but that is not the only rationale for it. Harm reduction is a pragmatic approach which focuses on immediacy of needs, patient-chosen goals, and on reducing the harms. Individuals with opioid use disorder are at extraordinarily high risk of mortality and morbidity. Opioid agonist therapy can lead to reduced opioid use, but it is also an evidence-based harm- reduction treatment in individuals who are continuing to use opioids. These include a reduction in overdoses, infectious diseases, legal problems, hospitalization and a greater stability and engagement in mental and physical health services. In addition, as in this case, usual induction is not an option for some patients and microdosing technique within the outreach program provides an alternative to ongoing use and not engaging with any sort of treatment. Hence, offering microdosing despite continued use in such cases can be considered a pragmatic harm reduction approach and may even decrease the overall risk of overdose by focussing on patients' chosen goals and immediacy of their needs, engaging them with the treatment, and addressing often multiple concurrent illnesses such as hepatitis C, HIV, and psychosis. These yet need to be evaluated in further studies." Also, given the high initial attrition rate of buprenorphine maintenance treatment ranging between 10 and 24% [24–26] in the first week, it is critical that novel and innovative approaches are used to overcome obstacles to initiation, e.g. requirement for withdrawal prior to induction. The Bernese Method delivered by an outreach team is a promising alternative to overcomes this obstacle while minimizing the risk for overdoses at a critical and vulnerable time. Another limitation is missing standard measurements of withdrawal and urine drug screen for illicit drug use, as the withdrawal was assessed by clinician impression and patient self-report. This could be partly explained by less than ideal setting of an outreach visit requiring optimal use of the time in a short encounter. Such measures would have allowed for a full evaluation and comparison with existing described methods. Also, the splitting of BUN/NLX tablets might not have been 100% accurate in this study; however, it was effective in that the premise is to start low and gradually increase. Best practice for dosing has yet to be established and dosing accuracy would need to be assured for future studies. Further research needs to explore feasibility of the Bernese Method in an outreach setting with a larger group of patients and warrants a comparison of the protocol versus current best practice. Further study is also needed to clarify which interventions may have assisted this patient to discontinue methamphetamine use as part of this intervention.

This case report explores a novel way to minimize barriers to induction of first-line opioid agonist treatment in Canada, buprenorphine/naloxone, by eliminating withdrawal symptoms in this phase, using a microdosing regimen based on the Bernese Method, provided as part of an outreach program.

#### Abbreviations

OAT: opioid agonist treatment; OUD: opioid use disorder; ICY: Inner City Youth Program; ICM: intensive case management.

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#### Authors' contributions

JR: Treatment of patient, data collection, manuscript write up, manuscript review. KM: Treatment of patient, data collection, manuscript write up, manuscript review. MN: Manuscript write up, manuscript review. SED: Treatment of patient, manuscript write up, manuscript review. SPB: Manuscript write up, manuscript review. DL: Manuscript write up, manuscript review. SM: Manuscript write up, manuscript review. PA: Treatment of patient, data collection, manuscript write up, manuscript review. All authors read and approved the final manuscript.

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#### Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

#### Ethics approval and consent to participate

Informed consent was obtained from participant. As per communication with the research board, ethics approval was not required for the case reports.

**Consent for publication**
No personal identifier is included.

**Competing interests**
The authors report no potential conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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

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**Background and Objectives:** Buprenorphine/naloxone has been shown to be effective in the treatment of opioid use disorder. Due to its pharmacological properties, induction can be challenging, time-consuming, and result in sudden onset of withdrawal symptoms.
**Methods:** Retrospective case series ($n = 2$).
**Results:** Two patients with opioid use disorder were successfully started on buprenorphine/naloxone using a rapid micro-induction technique that did not cause precipitated withdrawal or require preceding cessation of other opioids.
**Discussion and Conclusions:** These cases provide an alternative method for starting buprenorphine/naloxone that offers unique benefits compared to protocols previously described in the literature.
**Scientific Significance:** This method can be used to minimize barriers to opioid agonist therapy. (Am J Addict 2019;28:262–265)

## INTRODUCTION

Deaths caused by opioid overdose have been rising in both Canada and the United States.[1,2] This increase has been observed in both illicit and prescription opioid users.[3,4] Overprescribing practices and the availability of inexpensive high-potency synthetic opioids, such as fentanyl, have been implicated in this alarming change.[5–7]

Buprenorphine/naloxone has been shown to effectively treat opioid use disorder and has been recommended as first-line therapy.[8–11] Buprenorphine, a partial mu-opioid receptor agonist, can also be used to provide analgesia while carrying a more favorable safety profile compared to full mu-opioid agonists.[12,13] It is often combined with naloxone, a competitive opioid receptor antagonist with minimal oral and sublingual absorption, to discourage intravenous use.[14] When administered at target doses, buprenorphine/naloxone has been shown to decrease binding of other opioids, thereby decreasing the likelihood of overdose.[15] This is due to buprenorphine's mu-opioid receptor binding affinity, which is significantly higher than other opioids.[16] This high receptor binding affinity is also responsible for buprenorphine's ability to displace other opioids and cause sudden onset of withdrawal symptoms, also known as precipitated withdrawal.[13]

In order to avoid this withdrawal effect, when buprenorphine/naloxone is first administered, patients are required to be in mild-to-moderate withdrawal from all other opioids.[9,10] The recommended period of abstinence can range from 12 to 16 hours for short-acting opioids such as hydromorphone or diacetylmorphine (heroin) and upwards of 48 hours for longer-acting opioids such as methadone.[11] Furthermore, traditional buprenorphine/naloxone induction involves the administration of small doses with an assessment of withdrawal symptoms after each dose.[9,10] For these reasons, traditional induction can be time-consuming and difficult for patients to tolerate.[8,17] A "micro-dosing" regimen which does not require prior withdrawal has been described in the literature in an outpatient setting.[18] However, a limitation of this method is the significant length of time required to reach a therapeutic dose.

Here we present two cases in which inpatients were successfully started on buprenorphine/naloxone using a rapid micro-induction technique that did not require preceding

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withdrawal or cause precipitated withdrawal. Written consent was obtained from both patients.

## CASE 1

A 33-year old woman was brought to the emergency department at a tertiary care hospital in Vancouver, British Columbia after being struck by a vehicle. She was treated surgically for a subdural hematoma and a left proximal humerus fracture was managed conservatively. Her past medical history included severe opioid use disorder, severe alcohol use disorder, fetal alcohol spectrum disorder, hepatitis C virus, right brachial artery aneurysm, and remote left index finger amputation secondary to infection. Prior to admission, she was not taking prescription medications and reported using approximately .5 grams of intravenous heroin per day. During her admission, the patient experienced symptoms of opioid withdrawal and was receiving intravenous hydromorphone for treatment of withdrawal and pain. She also supplemented these medications with illicit intravenous heroin provided to her in hospital by friends. She was then seen by our complex pain and addiction consult team. Physical examination revealed extensive track marks on both of her upper extremities and neck. A urine drug screen (UDS) was positive for opiates and negative for fentanyl and methadone. She expressed interest in starting opioid agonist treatment opioid agonist treatment (OAT) and was assessed to be candidate for buprenorphine/naloxone.

At the time of induction, the patient was experiencing minimal withdrawal symptoms with a clinical opioid withdrawal score clinical opioid withdrawal scale (COWS) of 2.[19] While continuing to receive intravenous hydromorphone, she completed a rapid micro-induction. She was started on buprenorphine/naloxone .25 mg sublingual (SL) every four hours (q4h) and received four doses on Day 1. Her dose was doubled each day until Day 4 when she received 2 mg SL q4h. Her buprenorphine/naloxone was then consolidated to a single daily dose of 16 mg on Day 5. The full titration schedule is detailed in Table 1. The patient experienced no increase in withdrawal symptoms suggestive of precipitated withdrawal. Her dose was continued at 16 mg for the duration of her admission and she continued to endorse no cravings for opioids. She also denied ongoing illicit use of heroin.

## CASE 2

A 40-year old man was brought to the emergency department at the same tertiary care hospital after being found unresponsive in a residential drug treatment facility. He was diagnosed with an opioid overdose and treated successfully with intramuscular naloxone. He was subsequently diagnosed and treated for rhabdomyolysis, aspiration pneumonia, and compartment syndrome of the right forearm. His past medical history was significant for severe opioid use disorder, severe stimulant use disorder, ulcerative colitis, and gastroesophageal reflux disease. He was taking no prescription medications prior to admission and reported that he was previously using intranasal heroin daily. Our complex pain and addiction consult team was asked to see him for post-operative pain management. He was initially treated with intravenous fentanyl, which was transitioned to oral hydromorphone. Approximately 1 week into the admission, the patient had a surgical graft procedure. During this post-operative period, he expressed interest in OAT in the form of buprenorphine/naloxone and was deemed to be an appropriate candidate.

While continuing to receive oral hydromorphone, he completed a rapid micro-induction. On Day 1, he received buprenorphine/naloxone .5 mg SL every three hours (q3h) for a total of five doses. This was doubled on the next day and consolidated in to a single dose of 12 mg on Day 3. The full titration schedule is detailed in Table 2. Prior to induction, the patient had a COWS score of zero. He reported no symptoms suggestive of precipitated withdrawal and both his pain and withdrawal were well controlled after induction was completed. There were no further cravings for opioids and he was discharged to a residential treatment facility on a daily buprenorphine/naloxone dose of 12 mg.

## DISCUSSION

Here we have described two cases in which inpatients with pre-existing opioid use disorder were started on

**TABLE 1.** Titration schedule for Case 1

| | Buprenorphine/Naloxone* | | Hydromorphone | |
|---|---|---|---|---|
| | Dosing | Total Daily Dose | Dosing | Total Daily Dose |
| Day 0 | N/A | | 1-4 mg IV q4h PRN | 3 mg |
| Day 1 | 0.25g SL q4h | 1 mg | 1-4 mg IV q4h PRN | 11 mg |
| Day 2 | 0.5 mg SL q4h | 2.5 mg | 1-4 mg IV q4h PRN | 15 mg |
| Day 3 | 1 mg SL q4h | 5 mg | 1-4 mg IV q4h PRN | 15 mg |
| Day 4 | 2 mg SL q4h | 8 mg | 1-4 mg IV q4h PRN | 4 mg |
| Day 5 | 16 mg SL daily | 16 mg | Discontinued | |

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

**TABLE 2.** Titration schedule for Case 2

| | 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.

buprenorphine/naloxone using a rapid micro-dosing induction protocol. Both required treatment for post-operative pain in addition to withdrawal symptoms. Each patient reached a therapeutic dose of buprenorphine/naloxone without requiring a period of opioid withdrawal prior to initiation. During this time, they continued to receive short-acting opioids without experiencing precipitated withdrawal symptoms. Following induction, both patients were maintained on buprenorphine/naloxone in hospital and did not experience withdrawal symptoms or cravings for illicit opioids.

The strength of this study is the demonstration of an alternative induction technique in a monitored setting that allowed for accurate assessment of therapeutic effect, as well as complications. In the first case, while there were no objective or subjective symptoms of precipitated withdrawal, there was an increase in hydromorphone use on the first day of induction. Initially this was concerning for perhaps masking withdrawal symptoms. However, review of the patient's chart revealed that the majority of the hydromorphone (7 mg out of total daily dose of 11 mg) was received before buprenorphine/naloxone was administered. As well, the total daily dose on Days 1–3 was consistent with hydromorphone use prior to induction, with the minimal use on Day 0 being an anomaly.

To our knowledge, the only known existing micro-dosing protocol for buprenorphine in the literature is the "Bernese method" which has been described in a case series.[18] This protocol utilized the administration of buprenorphine at "micro" doses either daily or twice daily in an effort to avoid precipitated withdrawal. The hypothesis was that small, successive doses of buprenorphine would slowly accumulate at the mu-opioid receptor. Our study postulated that doses could be administered more rapidly given buprenorphine's time to peak plasma concentration of approximately 1 hour.[14] The two patients in the Bernese method study took 10 days or greater to reach a therapeutic dose, whereas our two patients reached therapeutic doses in 3 to 5 days. While both patients in the previously described method started with a single dose of 0.2 mg on the first day, our patients received a higher starting dose that was dosed frequently. This allowed for the total dose on the first day of our method to be much higher. In contrast to the cases presented here, the Bernese method was demonstrated in an outpatient setting. Rapid induction is important in an inpatient setting where discharges are generally not delayed to complete buprenorphine/naloxone induction. The use of this protocol could increase the number of patients leaving hospital on a therapeutic dose.

In the cases presented, a traditional induction would have required the cessation of all opioids, which were serving a dual purpose of treating pain and withdrawal symptoms. It is unlikely that these patients would have been able to tolerate this required period of abstinence, effectively excluding them from this first-line treatment for their opioid use disorder. This can be extrapolated to an outpatient setting, where high-risk patients with opioid use disorder have difficulty initiating buprenorphine/naloxone due to the requirement of being in withdrawal.[17] The complexity of the induction process has been seen as a barrier to buprenorphine/naloxone use among physicians.[20] Eliminating the need for preceding withdrawal and simplifying the induction process could increase the availability of opioid agonist treatment. This protocol may also be applicable in patients with chronic pain who are receiving high doses of prescribed opioids. In addition to being an effective pain medication, buprenorphine/naloxone carries a better safety profile than other opioids.[12,13] Thus, rapid micro-induction of buprenorphine/naloxone could be used to decrease risk of overdose in patients taking prescribed opioids and optimize long-term quality of life.

We would suggest that this protocol be tested in an inpatient setting for patients with opioid use disorder who meet existing criteria for buprenorphine/naloxone treatment.[9–11] Given the strong evidence for buprenorphine/naloxone, it is imperative that research efforts are focused on eliminating barriers to its use. Micro-dosing is a possible solution to the requirement for preceding opioid withdrawal and risk of precipitated withdrawal that deters many patients from utilizing this therapy. Future research is needed to examine the safety and efficacy of micro-dosing inductions in diverse samples. This should be done for patients receiving short-acting opioids, such as in our cases, and also longer-acting opioid formulations such as methadone.

### *Declaration of Interest*

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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ADDRESSOGRAPH

**COMPLETE OR REVIEW ALLERGY STATUS PRIOR TO WRITING ORDERS**

# BUPRENORPHINE-NALOXONE (SUBOXONE) MICRODOSING INDUCTION ORDERS

## Chronic Pain and Addiction Services (CPAS) - VGH

(items with check boxes must be selected to be ordered)



Time Processed
RN/LPN Initials
Comments

**Date:** _____ **Time:** _____

Notes to Prescriber:
**Refer to buprenorphine-naloxone prescribing guidelines from College of Physicians and Surgeons of BC on reverse of page 2 (page 2A).**
The physician ordering buprenorphine-naloxone must call the patient's community pharmacy to discontinue any ongoing provision of opioids in the community.

**LABORATORY:**
☐ Urine drug screen (including methadone metabolites, fentanyl, oxyCODONE and opiates)
☐ Urine HCG for female patients (Emerg only) – notify physician before induction if HCG positive
☐ HCG (blood) for female patients – notify physician before induction if HCG positive

**MEDICATIONS:**

☐ **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 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.

Advise patient to dissolve tablet completely under the tongue, which can take up to 10 minutes.
DO NOT swallow saliva or tablet, talk or drink during this time.

_____ Prescriber's Signature
_____ Printed Name
_____ College ID

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ADDRESSOGRAPH

**COMPLETE OR REVIEW ALLERGY STATUS PRIOR TO WRITING ORDERS**

# BUPRENORPHINE-NALOXONE (SUBOXONE) MICRODOSING INDUCTION ORDERS

## Chronic Pain and Addiction Services (CPAS) - VGH

(items with check boxes must be selected to be ordered)



Time Processed
RN/LPN Initials
Comments

**Date:** _____ **Time:** _____

**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

**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

_____ Prescriber's Signature

_____ Printed Name

_____ College ID

# Buprenorphine-naloxone prescribing guidelines from the College of Physicians and Surgeons of BC:

## BUPRENORPHINE-NALOXONE: PRESCRIBING FOR OPIOID USE DISORDER

### INITIATION, MAINTENANCE OR DOSE INCREASE

**PRESCRIBER SHOULD:**

- complete recognized buprenorphine-naloxone education program such as www.suboxonecme.ca
- have experience or have consulted with a physician experienced in opioid substitution treatment
- prescribe daily dispensing (with daily witnessed ingestion) under supervision of health-care professional, until patient has sufficient clinical stability and is able to safely store carries at home
- be familiar with and follow *the Methadone and Buprenorphine: Clinical Practice Guidelines* and *Safe Prescribing of Drugs with Potential for Misuse/Diversion, including*:
  - PharmaNet access and patient profile review
  - implementation of urine drug testing protocol (supervised and random)
  - documentation of biopsychosocial support discussions

### SHORT-TERM TREATMENT (ONE WEEK OR LESS) FOR CONTINUITY OF CARE

**PRESCRIBER SHOULD:**

- Until consultation with a physician experienced in opioid substitution treatment:
  - maintain the same or lower dose
  - prescribe buprenorphine-naloxone as daily dispensed (with daily witnessed ingestion)

If no addiction specialist is readily available in the community, the RACE line may be consulted:

www.raceconnect.ca
604-696-2131
1-877-696-2131

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# A Case Report: Rapid Micro-Induction of Buprenorphine/Naloxone to Administer Buprenorphine Extended-Release in an Adolescent With Severe Opioid Use Disorder

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**Background and Objectives:** Buprenorphine extended-release (BUP-XR) is a monthly injectable form of opioid agonist therapy. Before its administration, a minimum 7-day induction period with a transmucosal buprenorphine-containing product is recommended.
**Methods:** Case report ($n = 1$).
**Results:** A 16-year-old female with active, severe opioid use disorder (OUD) and stimulant use disorder, hepatitis C virus, co-occurring mental health disorders, and complex social stressors had five recent overdoses requiring naloxone. She had previously been treated with methadone and several trials of sublingual buprenorphine/naloxone, but would quickly discontinue the treatment. Using a rapid micro-induction protocol, buprenorphine/naloxone was administered for 3 days. On day 4, 300 mg BUP-XR was administered subcutaneously. Minimal withdrawal symptoms occurred, despite recent fentanyl use.
**Discussion and Conclusions:** A rapid sublingual buprenorphine/naloxone micro-induction was successfully used to initiate BUP-XR, thereby eliminating the abstinence period prior to buprenorphine/naloxone administration, shortening the induction period, and minimizing withdrawal.
**Scientific Significance:** This is the first reported case of using rapid micro-induction as a bridge to initiate BUP-XR. By reducing the length of induction to 4 days and minimizing withdrawal, this induction method can make BUP-XR more accessible to patients who would otherwise refuse the medication due to concerns of enduring withdrawal. (Am J Addict 2020;29:531–535)

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## INTRODUCTION

North America is experiencing a public health crisis as opioid overdoses and deaths have dramatically increased over recent years. In 2016, the life expectancy in the United States and Canada stopped increasing, attributed to the rising opioid overdose-related deaths.[1,2]

Buprenorphine extended-release (BUP-XR) is a monthly injectable form of opioid agonist therapy (OAT) approved for the management of moderate to severe opioid use disorder (OUD) in adults.[3] BUP-XR is subcutaneously injected, provides sustained exposure of buprenorphine to block the subjective effects (ie, drug liking) of other opioids over a 1-month dosing interval, and reduces withdrawal and craving symptoms[4]—potentially providing protection to individuals at high risk of fatal overdose. Depot injections of buprenorphine can reduce the treatment burden on clinicians and patients by negating the need for adherence to a daily oral medication regimen. In a randomized, double-blind, phase 3 trial conducted comparing the efficacy and safety of BUP-XR with placebo for participants with OUD, the participants' percentage abstinence was significantly higher in the BUP-XR group

than in the placebo group.[4] While still not widely available in Canada, in November 2018, BUP-XR was approved by Health Canada for the treatment of moderate to severe OUD.[5] This followed approval of the drug by the US Food and Drug Administration (FDA) in November 2017.[6]

Before administration of BUP-XR, it is recommended that patients receive a transmucosal buprenorphine-containing product, such as buprenorphine/naloxone, at a dose that controls withdrawal symptoms for a minimum of 7 days.[3] Buprenorphine is a partial μ-opioid receptor agonist with high binding affinity but lower intrinsic activity than other opioids, such as heroin and methadone.[7] Initiation of buprenorphine can result in "precipitated withdrawal" whereby circulating full agonists are rapidly displaced, resulting in relative reduced activity at the opioid receptor. To prevent precipitated withdrawal from occurring, patients are required to be in at least mild to moderate opioid withdrawal and abstinent from all other opioids before buprenorphine-containing products are initiated.[8,9] Traditional buprenorphine induction is thereby often challenging and time-consuming for patients to tolerate, which can be a barrier for many patients who need this potentially life-saving therapy the most.

To overcome these difficulties, novel approaches to induction are currently being explored. These include a transdermal fentanyl bridge, a micro-induction technique, and a rapid micro-induction technique.[10-12] The first method involves the use of a transdermal fentanyl patch to transition patients from methadone to buprenorphine/naloxone.[12] The patch is applied, and all other opioids are discontinued. Once the opioids are completely cleared from the patient, the patch is removed, and a buprenorphine/naloxone induction can begin immediately. Micro-induction, also known as micro-dosing and originally described as the "Bernese method," involves the administration of small buprenorphine doses once to twice daily while overlapping with a full opioid agonist, hydromorphone, so patients reach therapeutic doses in a few days to weeks.[10] Rapid micro-induction builds upon the basis of micro-induction, but the administration of buprenorphine occurs every 3 to 4 hours, resulting in patients reaching therapeutic doses in just 3 to 5 days.[11] Compared with micro-induction, rapid micro-induction significantly reduces the time to induction. These aforementioned induction methods all eliminate the period of abstinence proceeding induction and minimize the withdrawal symptoms experienced by the patient.

Treatment of OUD in youth can be complex due to the scarcity of evidence-based guidelines and youth-focused treatment resources. Furthermore, youth have specific and varied neurodevelopmental challenges that affect the way they interact with the treatment. For instance, the maturation of specific brain regions associated with motivation and impulsivity primarily occurs during adolescence and emerging adulthood.[13] Regardless, medication for OUD endorsed by a growing number of medical associations, such as the American Academy of Pediatrics, is still widely underutilized.[14,15] A monthly injectable formulation of buprenorphine used in combination with a rapid micro-induction protocol can be especially beneficial for youth as this approach can improve adherence by minimizing withdrawal symptoms and reducing the time of induction.

Here, we present a case utilizing a rapid sublingual buprenorphine/naloxone micro-induction to initiate BUP-XR in an adolescent patient with severe OUD admitted to a tertiary pediatric hospital in Vancouver, British Columbia, Canada. Written informed consent was obtained.

## CASE HISTORY

A 16-year-old female was admitted to a pediatric hospital in British Columbia, presenting with hematemesis and cellulitis. Approximately 4 hours prior to admission, she had used fentanyl and crystal methamphetamine by injection. Her initial vitals at admission were the following: blood pressure of 120/84 mm Hg, oxygen saturation of 97% on room air, heart rate of 96 beats per minute, body temperature of 36.8°C, and Glasgow Coma Scale (GCS) score of 15. Physical examination revealed track marks on her arms and cellulitis of her right arm. A urine drug screen (UDS) was positive for opioids, fentanyl, and amphetamines. She was started on cephalexin for cellulitis and treated with omeprazole for hematemesis, which resolved while in hospital.

Her past medical history included severe OUD and stimulant use disorder, generalized anxiety disorder, posttraumatic stress disorder, major depressive disorder, and attention-deficit hyperactivity disorder. She had a significant history of developmental and intergenerational trauma, and a history of suicidal ideation with several previous suicide attempts. Past medications included methadone, buprenorphine/naloxone, and medroxyprogesterone acetate. She also had several medical complications of substance use, which included a recent diagnosis of hepatitis C virus. Due to parent-child relational conflicts, she was under voluntary care through the provincial child protective services, and resided in a group home for youth with high-risk street involvement; however, she frequently did not stay there and was street-involved. She had several community supports, including a child protection social worker, and an outreach concurrent disorders clinician. The patient was also in a romantic relationship with another high-risk youth with OUD, and had reported incidents of intimate partner violence. She demonstrated many strengths at the times her mental status was clear, including insight and motivation to recover, and deep caring and empathy for others.

With regard to her substance use history, the patient, since age 15, has been injecting illicit fentanyl 0.5 to 1 g per day and crystal methamphetamine daily. When not using, she experienced symptoms of withdrawal and cravings. She had multiple recent overdoses requiring administrations of

**TABLE 1.** Rapid micro-induction titration schedule

| | Hydromorphone (oral) | | Buprenorphine/naloxone (sublingual)[a] | | BUP-XR (subcutaneous) |
|---|---|---|---|---|---|
| | Dosing | Total dose received | Dosing | Total dose received | Dose administered |
| Day 1 | 1-3 mg q3h prn | 15 mg | 0.5 mg q3h | 3 mg | |
| Day 2 | 1-3 mg q3h prn | 5 mg | 1 mg q3h | 7 mg | |
| Day 3 | Discontinued | | 8 mg daily | 8 mg | |
| Day 4 | | | Discontinued | | 300 mg |

BUP-XR = buprenorphine extended-release; prn = as needed; q __ h = every __ hours.
[a]Expressed as mg of buprenorphine component.

naloxone, resulting in five inpatient hospitalizations at the pediatric hospital. At her most recent hospitalization 1 month prior to this presentation, she had expressed interest in starting OAT, which was a rare window of opportunity for engagement as she had historically been unwilling to start treatment. Using a 3-day rapid micro-induction protocol, she was initiated on buprenorphine/naloxone and reached a total daily dose of 12 mg, which controlled her cravings and withdrawal symptoms.[11] However, she did not fill her prescription for buprenorphine/naloxone upon discharge.

Considering the patient's previous treatment attempts with daily dosed formulations of methadone and buprenorphine/naloxone had been unsuccessful, along with her multiple psychiatric comorbidities, psychosocial barriers, and overdose history; BUP-XR was obtained through Health Canada's Special Access Program with agreement from the patient. Due to the patient's prior success with a 3-day induction, a buprenorphine/naloxone rapid micro-induction protocol was used to transition her onto 300 mg BUP-XR within 4 days, as seen in Table 1. In addition to short-acting hydromorphone, several ancillary nonopioid drugs were used—clonazepam and dimenhydrinate for anxiety and nausea, respectively, on day 1, clonidine for residual withdrawal symptoms on day 1, quetiapine for sleep, and ibuprofen for the BUP-XR injection on day 4. The maximum Clinical Opiate Withdrawal Scale (COWS) score was 6 throughout induction. The patient's COWS score ranged from 2 to 6 on days 1 and 2, and 2 to 4 on days 3 and 4. There were no signs of precipitated withdrawal at any point during the induction.

While the induction and administration of BUP-XR was successful, the patient did not return for her subsequent dose. She relapsed into illicit fentanyl and crystal methamphetamine use, which was self-reported and confirmed by a positive UDS. The OAT prescribing team made several attempts to reach out to her, but was unsuccessful.

## DISCUSSION

Here we have presented a case of an adolescent inpatient with severe OUD successfully started on BUP-XR using a rapid micro-induction of sublingual buprenorphine/naloxone. The strength of this case is the demonstration of a novel induction protocol to administer BUP-XR, which may be a lower barrier and more tolerable for patients due to the reduced length of time and minimal withdrawal symptoms. BUP-XR may have also helped to keep the patient alive, and reversed her recent pattern of multiple overdoses in rapid succession. Multiple contributing factors may explain why this patient did not return for her second dose of BUP-XR. The patient's underlying mental health concerns and psychosocial challenges were neither adequately nor concurrently addressed. She went back to using illicit fentanyl and crystal methamphetamine, as she reported that she wanted to experience the intoxication effects of these substances and to self-medicate her posttraumatic stress disorder symptoms. Therefore, while the induction itself was successful to initiate BUP-XR, it exists on a spectrum of inter-sectoral therapies to treat addiction. Since this admission with the administration of BUP-XR, the patient has not re-presented herself to the pediatric emergency department with an overdose requiring naloxone. She has been accessing more community harm reduction resources, has continued to follow-up with her mental health clinician, and has been staying at her group home more consistently. All of this have been made possible by providing her the opportunity to remain in the community without the need of multiple emergency room and inpatient admissions.

To our knowledge, there have been two micro-induction protocols published. The "Bernese method" used the administration of sublingual buprenorphine at "microdoses" either once or twice daily to avoid precipitated withdrawal symptoms in an outpatient setting, where the patients reached therapeutic doses in 10 or more days.[10] Based on the hypothesis that buprenorphine's time to reach peak plasma concentrations is approximately 1 hour, a more rapid protocol was developed to be primarily used in an inpatient setting, which has been described in this case report and a previous case series.[11] This protocol, termed "rapid micro-induction" uses small doses of sublingual buprenorphine/naloxone administered every 3 to 4 hours, resulting in patients reaching therapeutic doses in just 3 to 5 days. Rapid micro-induction offers many advantages over standard induction, which has been seen as a hurdle to the use of buprenorphine/naloxone among clinicians.[16] Standard

induction requires the patient to be abstinent from all opioids and thus be subjected to at least mild to moderate withdrawal symptoms. Rapid micro-induction eliminates the abstinence period and reduces the risk of precipitated withdrawal. Furthermore, it minimizes symptoms of withdrawal and craving. While rapid micro-induction is a possible solution in overcoming the barriers patients encounter during standard induction, further research is needed to examine its efficacy and safety in a larger, more diverse patient population and its applicability to an outpatient setting.

The rapid micro-induction used here to initiate BUP-XR was based on clinical experience and a previous case series.[11] The safest starting dose of buprenorphine/naloxone that would not precipitate withdrawal was determined to be 0.5 mg, while the frequency of dosing was based on buprenorphine's time to reach the maximum plasma levels. The hydromorphone was administered as needed to best meet the patient's baseline opioid requirements. It should be noted that as the buprenorphine dosing increased throughout the induction, the use of hydromorphone decreased.

Another important aspect is that the treatment of OUD in adolescents differs from than in adults. OAT is strongly recommended because of the high risk of overdose and death associated with continued opioid use.[14,17,18] Moreover, randomized controlled trials for OAT in adolescents with OUD have only been conducted for buprenorphine.[17] A study examining the youth perspective also found that buprenorphine was perceived to be more effective than methadone in reducing cravings and eliminating withdrawal symptoms, and less stigmatizing.[19] It is thereby recommended that buprenorphine be the OAT of choice in adolescent patients.[17,18] In this case, BUP-XR was chosen due to the patient's previous adherence challenges to daily dosed formulations of methadone and sublingual buprenorphine/naloxone. BUP-XR offers several advantages over sublingual buprenorphine. It does not require daily administration or pharmacy visits, and reduces the risk of diversion and illicit opioid use. It has also been shown to be effective in blocking the subjective pleasurable and reinforcing effects of opioids in individuals with moderate or severe OUD.[4,20]

This case demonstrates a novel approach and application of the rapid micro-induction protocol to initiate BUP-XR. By minimizing withdrawal symptoms and reducing the risk of precipitated withdrawal and length of induction, this innovative method may improve the accessibility of BUP-XR to patients with OUD.

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### *Declaration of Interest*

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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