Dartmouth-Hitchcock

Center for Addiction Recovery in Pregnancy + Parenting
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Buprenorphine Initiation and Maintenance in Pregnancy

(Adapted with permission from the D-H Knowledge Map Primary Care Buprenorphine Guidelines)

Assessment

The diagnosis of OUD should be confirmed by DSM-5 criteria, supplemented by urine drug testing. Opioid use often co-occurs with other substance related disorders, and an inventory of past and current substances used and past SUD treatment should be done. Psychiatric co-morbidity (especially depression, anxiety disorders, and PTSD) is common, and needs to be evaluated. An assessment of social and environmental factors including screening for intimate partner violence should be conducted to identify facilitators and barriers to addiction treatment, and specifically to pharmacotherapy. Addiction is a multi-faceted illness, for which the use of medication(s) is but only one component of overall treatment. A physical examination should be completed, with attention to potential sequelae of substance use. The following laboratory tests may be necessary: complete blood count, liver and kidney function, hepatitis C, HIV and sexually transmitted infections, and TB. Hepatitis A and B testing and vaccination should be offered when appropriate.

Deciding on Treatment and Setting

The choice of treatment option and setting should be a shared decision between clinician and patient, taking into account past treatment history, co-morbidity (other substance use, psychiatric, and medical), social and environmental factors, and risk of diversion. *More structured and intensive treatment should be used for more complex patients and those not responding to maternity care based treatment.* Specialty opioid treatment programs may offer daily supervised dosing of methadone, and increasingly of buprenorphine. Intensive Outpatient Programs offer more structure and intensive counseling for the first several months of treatment. Inpatient and residential treatment programs are reserved for the most complex patients who have not responded to less intensive options.

Informed Consent and Treatment Agreements

Informed consent and treatment agreements should be used to clarify expectations of both practitioner and patient and provide a structure for effective monitoring. The treatment agreement should be reviewed and signed by both the practitioner and patient. Informed consent outlines the risks and benefits of buprenorphine and other

treatment options, specifically including methadone which remains the established standard of care for treatment during pregnancy. The treatment agreement includes: identifying one practice and one pharmacy to provide buprenorphine prescriptions, authorization to communicate with other named providers of care, acknowledgement that the prescription drug monitoring program (PDMP) will be used, and agreement to undergo toxicology screens and pill/film counts upon request.

Induction and Stabilization

Women with acute medical or surgical illness, significant polysubstance use, use of long acting opioids or presenting at a gestational age $\geq$23 weeks may require inpatient admission or in-clinic observation for close monitoring of the buprenorphine induction process (see sample inpatient buprenorphine induction policy). Women presenting prior to 23 weeks gestation without complicating factors may be candidates for office or home induction, particularly if they have previous experience with buprenorphine.

Induction may be observed by the clinician in the office setting, with the exception of women who are already taking a stable dose of buprenorphine. Opioid-dependent patients should wait until they are experiencing moderate opioid withdrawal (COWS score of $\geq$ 12; see appendix), usually 12-16 hours after the last dose of short-acting opioid (heroin, hydrocodone, oxycodone IR), 17-24 hours after intermediate acting opioids (Oxycontin), or 30-48 hours after methadone. This should occur before taking the first dose of buprenorphine to reduce the risk of precipitated withdrawal. Induction of buprenorphine should start with a dose of 4 mg (an initial dose of 2mg can be used for women not currently physically dependent on opioids, such as women using opioids only intermittently, who may not display physical symptoms of opioid withdrawal). If the first dose is well tolerated, additional doses of 4 mg are given every 2 hours as needed to treat withdrawal, up to a maximum of 12 mg in the first day. The optimal maintenance dose should suppress craving and withdrawal and hold the patient in treatment, usually 8-16 mg as a single daily dose. Doses above 16 mg may increase risk of diversion, and should only be used in rare instances. The FDA approves dosing up to 24 mg per day, and there is limited evidence regarding the relative efficacy of higher doses. Some women require doses above 16mg (but not generally above 24mg) in the

latter half of pregnancy or may benefit from more frequent dosing, up to three or four times daily, in pregnancy due to changes in pharmacokinetics.

Women who are already taking buprenorphine at a known dose may be candidates to receive a prescription without formal induction.

Special Considerations for Pregnancy and Lactation

A growing body of evidence supports the use of combination buprenorphine/naloxone (Suboxone) in pregnancy in place of buprenorphine monotherapy (Subutex). While previously it was common practice to use the monoproduct in pregnancy, many providers now use the combination buprenorphine/naloxone product for all patients, including pregnant women. This may reduce the risk of diversion as well as patient anxiety associated with making a medication change in the immediate postpartum period. When buprenorphine/naloxone is taken sublingually as directed, naloxone is minimally absorbed and has virtually no effect; its purpose is simply to discourage misuse of the product.

Women should be counseled regarding the use of buprenorphine in pregnancy and the risk of neonatal opioid withdrawal syndrome (NOWS) in their infants.

Buprenorphine and buprenorphine/naloxone are considered compatible with lactation, and women stable on buprenorphine and not using other substances should be encouraged to breastfeed their infants. Breastmilk levels of buprenorphine and metabolites are low, and buprenorphine is poorly bioavailable when ingested orally, leading to minimal drug exposure for breastfeeding infants. The combination buprenorphine/naloxone product is also recommended in breastfeeding women; naloxone is not orally bioavailable and therefore is unlikely to affect a breastfeeding infant.

Psychosocial Treatment

Psychosocial treatment should be implemented in conjunction with the use of buprenorphine in the treatment of opioid use disorder.

Group therapy is commonly used in substance use disorder treatment settings. A group consisting of other pregnant and postpartum women may help women feel more

supported in their recovery and learn skills for managing cravings or difficult interpersonal situations.

In addition to group and/or individual therapy, all patients receiving office based buprenorphine treatment should receive:

- Regular urine drug screens
- Monitoring of adherence, response to treatment, and adverse effects
- Education about OUD consequences and treatments
- Encouragement to abstain from non-prescribed opioids and other addictive substances
- Encouragement to attend community supports for recovery (e.g., mutual help groups) and to make lifestyle changes that support recovery
- Motivational Interviewing
- Screening and treatment or referral for co-occurring psychiatric conditions

Additional individual counseling, onsite or off, should be arranged as needed and desired.

Monitoring of Adherence, Response to Treatment, and Diversion

Effective monitoring of adherence and response to treatment can increase the likelihood of positive clinical outcomes and reduce the possibility of diversion. Monitoring should include frequent office visits (weekly in early treatment), at-visit and unannounced urine toxicology screening, pill/film count, and the use of state prescription drug monitoring programs (PDMPs). Urine toxicology should be able to detect buprenorphine in addition to drugs of concern, and be collected in a manner that ensures it is unadulterated and belongs to the patient. Frequency of testing should be guided by the stability of the patient. The practitioner should have the patient bring his or her medication container to each appointment to show that the medication is being taken as directed. Unannounced inventories can help ensure that medication is not being diverted. Observed ingestion (having the patient take the medication in front of the practitioner or a trained monitor) at the beginning of buprenorphine therapy can help the practitioner ensure that the patient knows how to take the medication. PDMPs help physicians monitor whether patients are obtaining the prescribed medication, obtaining prescriptions for controlled substances from other prescribers, or refilling prescriptions early.

Responding to Patient Behaviors

Practitioners should acknowledge and reinforce a patient's adherence to treatment, reduction of illicit drug use, and positive life changes. Some patients will continue to use illicit opioids and/or other substances or relapse to opioid use after a period of abstinence. Other patients may have trouble adhering to the treatment plan. Diversion or misuse of buprenorphine may also occur. Signs and behaviors suggesting risk of diversion and misuse of buprenorphine products include:

- Unsupported claims of intolerance or allergy to naloxone to obtain the mono-product, which is more subject to misuse.
- Early requests for refills for unsubstantiated reasons (e.g. prescription was "lost" or "stolen").
- Difficulty keeping appointments and/or lack of engagement in psychosocial aspects of care.
- A sudden request for a dose increase by a previously stabilized patient.
- Positive toxicology screens for illicit substance use or negative toxicology screens for buprenorphine.
- Ongoing close ties to individuals (e.g. spouse, partner, significant others, friends) who sell opioids or have opioid use disorder but are not in treatment.
- Somnolence or agitated behavior in group therapy sessions

Relapse or continued substance use are not reasons for automatically discontinuing buprenorphine. Instead, this should prompt discussion with the patient and evaluation of the treatment plan. If the situation is handled well, a stronger patient–provider alliance can be formed. Changes to treatment should be made on an individual basis and could include any combination of the following: adjusting the patient's buprenorphine dosage, increasing the frequency of office visits, requiring periodic supervised administration by having the patient bring her prescription to an office visit, intensifying counseling, or encouraging the patient to engage in more intensive peer support programs. Some patients may require more structured treatment, such as that offered in a residential, intensive outpatient, or daily dosing program.

Duration and Discontinuation of Treatment

Buprenorphine taper and discontinuation is not generally recommended during pregnancy or the early postpartum period due to the risks of relapse to opioid use, although medically supervised withdrawal is not contraindicated if the benefits outweigh the associated risks. The optimal duration of office-based buprenorphine

treatment remains unclear, and may range from a few months to a lifetime depending on the patient. Patients who discontinue buprenorphine should be made aware of the risks associated with an opioid overdose if they relapse, and should be provided access to naloxone, due to reduced tolerance.

Treating Pain

If pharmacological treatment is considered, non-narcotic medications such as acetaminophen and NSAIDs should be tried first. Temporarily increasing buprenorphine dose and dividing the dosing may be effective for mild-moderate acute pain. Because buprenorphine binds more avidly to opioid receptors than most opioids, pain control with other mu agonists requires careful attention and titration. Regional anesthesia or intravenous fentanyl can be used during childbirth. **The opioid agonist-antagonist medications nalbuphine and butorphanol are contraindicated as they will precipitate withdrawal in a patient chronically using opioids.** For post-operative pain, short-acting full opioid agonists can be used, but providers should anticipate that higher than usual doses may be required to achieve adequate pain control. We recommend that women continue buprenorphine or buprenorphine/naloxone during and after delivery in order to prevent the need for a re-induction onto buprenorphine during the immediate postpartum period.

Naloxone

Patients who are being treated for opioid use disorder and their family members/significant others should be given prescriptions for naloxone and should be trained in the use of naloxone in overdose.

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DSM-5 Opioid Use Disorder

Diagnostic Criteria:

A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Opioids are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
10. Tolerance, as defined by either of the following:
    a. A need for markedly increased amounts of opioids to achieve intoxication or desired effect.
    b. A markedly diminished effect with continued use of the same amount of an opioid.
11. Withdrawal, as manifested by either of the following:
    a. The characteristic opioid withdrawal syndrome.
    b. Opioids (or a closely related substance) are taken to relieve or avoid withdrawal symptoms.

Note: The last 2 criteria are not considered to be met for those individuals taking opioids solely under appropriate medical supervision.

Number of criteria:	0-1	2-3	4-5	6+
Interpretation:	No SUD	Mild SUD	Moderate SUD	Severe SUD

Office Induction Instructions

Most non-pregnant patients can be induced at home, but in-office induction is preferable during pregnancy. Inpatient induction may be considered if there are concerns due to anticipation of severe withdrawal symptoms, obstetric comorbidities, or patient adherence.

- Patient is given a prescription for buprenorphine at the prescriber intake visit, and is instructed to fill the prescription and bring the medications to the induction appointment. The patient should abstain from opioids, with the goal of being in early withdrawal for the induction: 12-16 hours for short-acting opioid (heroin, hydrocodone, oxycodone IR), 17-24 hours for intermediate acting opioids (Oxycontin), or 30-48 hours for methadone.
- Patient arrives at clinic with buprenorphine prescription.
- Withdrawal symptoms are assessed with the Clinical Opioid Withdrawal Scale (COWS).
- If/when COWS score is $\geq$12, 4 mg of buprenorphine (2mg for patients not physically dependent on opioids) is administered, with education on proper technique: sublingual (or buccal for Bunavail or Belbuca), holding the pill or film in place without eating or drinking until it completely dissolves. If COWS score is <12 in a patient physically dependent on opioids, patient should be observed until withdrawal symptoms appear.
- Patient is observed for 45-60 minutes after first dose, and COWS is reassessed.
    - If patient is doing better (lower COWS, subjectively feeling better), they may be discharged and should follow the home induction directions (appendix F).
    - If patient is doing worse (increased COWS), give another dose of buprenorphine and observe another 45-60 minutes. If needed, recalcitrant withdrawal symptoms can be treated with:
        - Acetaminophen or ibuprofen for aches and pains

- Loperamide for diarrhea and cramps
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- Diphenhydramine or trazodone for insomnia (do not prescribe benzodiazepines)
- Clonidine 0.1 mg po q 2 hours for severe anxiety or jitters
- Promethazine 25 mg po q 6 for nausea

  - When feeling better, patient may be discharged and should follow the home induction instructions.

Clinical Opiate Withdrawal Scale (COWS)

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Patient's Name:_____ Date and Time ____/_____/____:_____

Reason for this assessment:_____

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying for one minute* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	**GI Upset**: *over last 1/2 hour* 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting
Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.* 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	**Tremor** *observation of outstretched hands* 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds	**Yawning** *Observation during assessment* 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute
Pupil size	**Anxiety or Irritability**

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Buprenorphine: Continuing at Home

Buprenorphine is both a blocker and stimulator (agonist) of the opiate receptor. The opioid agonist effect reduces withdrawal symptoms and craving, while the blocking effect, at higher doses, prevents or lessens the effect (high) of using another opioid drug. This partial opioid blocking effect also means that buprenorphine can cause withdrawal if taken while other opiates are still in your system. Therefore, the first dose should not be taken until you feel significant symptoms of withdrawal: anxiety, restlessness, cramps, nausea, diarrhea, shakes, goosebumps, yawning, sweating, and fast heartbeat. This usually occurs 12-16 hours after the last dose of short-acting opioid (heroin, hydrocodone, oxycodone IR), 17-24 hours after intermediate acting opioids (Oxycontin) or 30-48 hours after methadone. The worse you feel when you begin the medication, the better it will make you feel. Buprenorphine is not absorbed well if swallowed, so it is taken sublingually (allowed to dissolve under the tongue).

Dosing Instructions:

Day 1: Take 4mg of buprenorphine under the tongue if you begin to feel significant withdrawal symptoms again. Be sure to let this dissolve completely under your tongue and DO NOT eat or drink anything while it is dissolving. Wait at least 1 hour. If you still have symptoms of withdrawal you can repeat this dose, but don't take more if you're feeling ok. If withdrawal symptoms are still present after waiting another hour, or if symptoms return later- take another dose. Repeat as needed up to a maximum of 12 mg on day 1.

Day 2: Take the total number of mg used over day one in a single dose when you wake in the morning. If, after an hour or more, you feel withdrawal- take another initial dose (4mg). Maximum total dose for day 2 is 16mg.

Day 3: Take the total number of mg used over day 2 in a single dose when you wake in the morning. If, after an hour or more, you feel withdrawal and your morning dose was under 16mg- take another initial dose (4mg). Maximum total dose for day 3 is 16mg.

Day 4 and beyond: Take the total mg from day 3 in a single dose in the morning.

Caution:

- **If you continue to have withdrawal symptoms in spite of taking buprenorphine as directed above, contact your OB/Gyn clinic. You can take acetaminophen for pain (unless told not to) and loperamide (Imodium) for diarrhea. Clonidine can be prescribed for bad anxiety or jitters.**
- **Do not take other opioids, benzodiazepines (sedating medicine) or drink alcohol while on buprenorphine.**
- **If you feel sleepy or impaired do not drive or operate a mechanical object or vehicle.**
- **Be sure to store your medication in a safe place where children and others will not have access to it.**