



Treatment of Opioid Use Disorder During

# Pregnancy

Guideline Supplement



## **A Guideline for the Clinical Management of Opioid Use Disorder—Pregnancy Supplement**

The **BC Centre on Substance Use (BCCSU)** is a provincially networked platform mandated to develop, implement, and evaluate evidence-based approaches to substance use and addiction. The BCCSU's focus is on three strategic areas including research and evaluation, education and training, and clinical care guidance. With the support of the province of British Columbia, the BCCSU aims to help establish world leading educational, research and public health, and clinical practices across the spectrum of substance use. Although physically located in Vancouver, the BCCSU is a provincially networked resource for researchers, educators, and care providers as well as people who use substances, family advocates, support groups, and the recovery community.

**Perinatal Services BC (PSBC)**, a part of the Provincial Health Services Authority, provides leadership, support, and coordination for the strategic planning of perinatal services in British Columbia. PSBC collaborates with the Ministry of Health, health authorities, and other key stakeholders across British Columbia. PSBC is the central source in the province for evidence-based perinatal information.

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## AUTHORS AND CONTRIBUTORS

### Guideline Development Committee

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**Ronald Abrahams** (Committee Co-chair), MD, CCFP, FCFP, M.S.C.; Clinical Professor, Dept. Family Practice, UBC; Medical Director, Perinatal Addictions, BCWH

**Andrea Ryan** (Committee Co-chair), MD, CCFP, Dip. ISAM; Clinical Instructor, Department of Family Medicine, University of British Columbia; Consultant Physician, Addiction Medicine Consult Service, St. Paul's Hospital

**Jola Berkman**, RN, BScN, BSc(med)Hons; Coordinator, Neonatal Care, Perinatal Services BC, Provincial Health Services Authority

**Eric Cattoni**, MD, CCFP; Perinatal Addictions, Physician Co- Lead, BCWH; Clinical Instructor, Dept of Family Medicine, University of British Columbia; Medical Clinic Physician, Sheway

**Sonia Habibian**, MD, CCFP, FASAM, MRO; Canadian Addiction Medicine Research Fellow; Clinical Instructor, Dept. Family Practice, University of British Columbia.

**Janine Hardial**, MD, CCFP; Medical Coordinator, Sheway, Vancouver Coastal Health; Consultant Physician, Perinatal Addictions Service, BC Women's Hospital; Clinical Instructor, UBC

**Georgia Hunt**, MD, CCFP; Assistant Head, Quality, Department of Family Practice Children's and Women's Hospital of British Columbia

**Cheyenne Johnson**, RN, MPH, CCRP; Director, Clinical Activities and Development and Director, Addiction Nursing Fellowship, BC Centre on Substance Use

**Tamil Kendall**, PhD; Interim Provincial Executive Director at Perinatal Services BC, Provincial Health Services Authority

**Annabel Mead**, MBBS, Dip. ABAM, FACHAM; Director, St Paul's Goldcorp Addiction Medicine Fellowship; Consultant Physician, Complex Pain and Addiction Service, Vancouver General Hospital; Physician, St Paul's Hospital Addiction Medicine Consult Service; Clinical Assistant Professor, University of British Columbia

**Jill Pascoe**, MSW, RSW; Program Manager, Oak Tree Clinic HIV Program, Complex Chronic Diseases Program, Fir Square Combined Care Unit

**Nitasha Puri**, MD, CCFP, dip. ABAM; Physician Consultant, Fraser Health and Vancouver Coastal Health; Clinical Instructor, University of British Columbia

**Nancy Poole**, PhD; Director, Centre of Excellence for Women's Health, hosted by BC Women's Hospital + Health Centre; Prevention Lead, CanFASD Research Network

**Christy Sutherland**, MD, CCFP, Dip. ABAM; Medical Director, PHS Community Services Society; Physician Education Lead, BC Center on Substance Use; Clinical Assistant Professor, University of British Columbia

**Meaghan Thumath**, RN, BSN, MScPH; Trudeau Scholar, Department of Social Policy and Intervention, University of Oxford; Addiction Nursing Fellow, St Paul's Goldcorp Addiction Medicine Fellowship

**Lani Wittmann**, RN, MN, IBCLC, PNC(C); Senior Practice Leader – Perinatal, BC Women's Hospital

## External Reviewers

---

**Kate Bodkin**, BA, MD, CCFP; Clinical Lead, Fir square combined care unit; Physician, Sheway Medical Services; Clinical Instructor, University of British Columbia

**Andrew Gaddis**, M.H.S., Fulbright Independent Scholar, British Columbia Centre on Substance Use

**Hendrée Jones**, PhD; Executive Director, UNC Horizons; Professor, Department of Obstetrics and Gynecology

**Lenora Marcellus**, RN,BSN, MN, PhD; Associate Professor, University of Victoria

**Alice Ordean**, MD, CCFP, MHSc, FCFP, FASAM; Medical Director, Toronto Center for Substance Use in Pregnancy, Department of Family Medicine, St. Joseph's Health Center, Toronto

**Launette Rieb**, MD, MSc, CCFP, FCFP, Dip. ABAM, CCSAM; Medical Consultant, St Paul's Hospital; Physician, Orchard Recovery Centre; Physician, Orion Health (Vancouver Pain Clinic); Clinical Associate Professor, University of British Columbia

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## Disclaimer for Health Care Providers

The recommendations in this guideline supplement represent the view of the Pregnancy Supplement Committee, arrived at after careful consideration of the available scientific evidence and external expert peer review. When treating pregnant patients with opioid use disorder, health care professionals are expected to consider this guideline supplement alongside the recommendations articulated in [A Guideline for the Clinical Management of Opioid Use Disorder](#). These guidelines should be considered and interpreted in the context of the individual needs, preferences, and values of patients, their families and other service users, and with adherence to the fundamental principles and values of the Canadian Medical Association Code of Ethics, especially compassion, beneficence, non-maleficence, respect for persons, justice and accountability, as well as the required standards for good clinical practice of the College of Physicians and Surgeons of BC, the College of Registered Nurses of British Columbia, and any other relevant governing bodies. The application of the recommendations in this guideline does not override the responsibility of health care professionals to make decisions appropriate to the circumstances of an individual patient, in consultation with that patient and their guardian(s) or family members, and, when appropriate, external experts (e.g., specialty consultation). Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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The Pregnancy Supplement is intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The Pregnancy Supplement is not intended as a substitute for the advice or professional judgment of a health care professional, nor is it intended to be the only approach to the management of a clinical problem. We cannot respond to patients or patient advocates requesting advice on issues related to medical conditions. If you need medical advice, please contact a health care professional.

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## Executive Summary

This document is intended to supplement the BCCSU [Guideline for the Clinical Management of Opioid Use Disorder \(“Guideline”\)](#) with an overview of care principles and treatment options specifically pertaining to pregnant individuals\*. This guideline recognizes persisting misconceptions about pregnant people who use substances as a primary barrier to accessing treatment for opioid use disorder during pregnancy, and emphasises the need for a non-judgmental, trauma-informed and culturally safe approach to care that accommodates patients’ individual choices and circumstances. Within this framework, the present document recommends a holistic and integrated care plan with appropriate use of the full range of available long-term treatment options and harm reduction services. A summary of the clinical recommendations outlined in this supplement is provided below.

\* While the majority of pregnant individuals identify as women, this term does not reflect the identities and experience of all pregnant people. In recognition of this fact, authors have made an effort to use gender-neutral language where possible. Respect for individual identities and the use of corresponding pronouns is vital when treating all patients.

## Summary of Clinical Recommendations

**Table 1- Summary of recommendations**

### *Prenatal screening and assessment*

1. All individuals who are or may become pregnant should be offered regular screening for alcohol, tobacco, and non-medical drug use, and informed about relevant risks and available risk reduction strategies. Screenings should be accompanied by brief support. (See *Screening and Assessment*.)

### *Pharmacological treatment*

2. Withdrawal management alone is NOT recommended due to high rates of relapse and subsequently elevated risk of fatal and nonfatal overdose, infections, and negative pregnancy outcomes. (See *Withdrawal Management*.)
3. All pregnant individuals with opioid use disorder should be offered opioid agonist treatment (OAT). OAT has been shown to eliminate or substantially reduce non-medical opioid use, leading to improved maternal and neonatal outcomes in comparison to untreated opioid use disorder and/or withdrawal management strategies. (See *Opioid Agonist Treatment*.)
4. The type of OAT to be initiated should be selected based on patients' individual circumstances and with consideration of access and availability.
  - i. Methadone is traditionally recognized as the first-line option for OAT during pregnancy. (See *Methadone*.)
  - ii. Buprenorphine/naloxone is an alternative first-line medication for this population. Recent studies have found this medication to be as safe and effective as methadone and buprenorphine monotherapy during pregnancy. (See *Buprenorphine/naloxone*.)
  - iii. Slow-release oral morphine may be considered for patients who are not successfully retained in treatment with buprenorphine/naloxone or methadone. (See *Slow-release oral morphine*.)
  - iv. Injectable opioid agonist treatment (iOAT) has not been studied in the context of pregnancy. Caution should be exercised when prescribing iOAT for individuals who are pregnant or may become pregnant. This caution should be exercised with consideration of the potential harms of denying access to iOAT for a pregnant person who otherwise meets eligibility criteria. (see *Injectable opioid agonist treatment*.)
5. Unless clinically indicated, transitioning between methadone, buprenorphine/naloxone, and slow-release oral morphine during pregnancy and postpartum periods is not recommended for patients who are stable on one of these medications prior to becoming pregnant. (See *Opioid Agonist Treatment*.)
6. For patients stable on buprenorphine/naloxone prior to becoming pregnant, transition to buprenorphine monotherapy during pregnancy is not necessary. (See *Buprenorphine*.)

### *Postpartum considerations*

7. Rooming-in is recommended as the standard of care for opioid-exposed infants as it facilitates care for the mother-child dyad as one unit while alleviating neonatal opioid withdrawal symptoms. Assessment and treatment of neonatal opioid withdrawal symptoms should be conducted in rooming-in settings (See *Rooming-in and Breastfeeding*.)
8. Breastfeeding should be encouraged in mothers who are stable on OAT. (See *Rooming-in and Breastfeeding*.)

Also refer to the [Summary of Recommendations of the Guideline](#) for contextualizing information.

## Introduction

Obtaining accurate prevalence data on substance use during pregnancy is particularly difficult primarily due to the stigma and prejudice against pregnant women who use substances. While non-medical opioid use during pregnancy is less frequently self-reported than alcohol and tobacco use, it is recognized by the Public Health Agency of Canada as a significant concern across all socioeconomic groups.<sup>1</sup> In addition to risks of overdose and infection, untreated opioid use disorder in pregnant individuals is associated with increased likelihood of adverse obstetrical outcomes including fetal growth restriction, fetal demise, and neonatal opioid withdrawal.<sup>2,3</sup> On the other hand, increased frequency of healthcare service use in the prenatal period and elevated motivation for delivering a healthy baby present a unique opportunity to engage and retain pregnant individuals with opioid use disorder in treatment and to support women's health and family stability in the long-term.<sup>4,5</sup>

Appropriate care for opioid use disorder during pregnancy, intrapartum, and the postpartum periods has been shown to eliminate or substantially reduce nonmedical opioid use and significantly improve pregnancy outcomes.<sup>6</sup> Specifically, the benefits of opioid agonist treatment (OAT) during pregnancy are well-documented and have been shown to outweigh any neonatal risks associated with opioid agonists, notwithstanding the lack of sufficient consensus to definitively rule out the teratogenicity of opioids.<sup>7,8</sup> Yet stigma against opioid use during pregnancy and lack of knowledge regarding appropriate treatment options for this population are frequently cited as barriers to seeking this treatment for substance use disorders.<sup>4</sup> Pregnant individuals who do seek treatment are often prescribed pharmacological interventions that are insufficient in dose and/or duration.<sup>4,9</sup> In addition to outlining available treatment options for pregnant people and their newborns, this guideline underscores the essential role of non-judgmental, patient-centered, and trauma-informed care and promotes an approach that also aims to address issues affecting patients' social determinants of health.

## Care principles

### Establishing Collaboration and Trust at Intake

Establishing a trusting, collaborative, and empowering relationship with patients is a cornerstone of treating opioid use disorder during pregnancy. Upon intake, patients should be assured of the confidentiality of the information they disclose. Clinicians should inform patients of the relevant aspects of their duty to report and emphasize that there is no legal obligation to report substance use and risks to the fetus during the course of pregnancy (see the [Child Protection](#) section). This is an important detail to include in the initial discussion as, according to numerous studies, the fear of intervention by child welfare services and losing custody of a child is a major barrier to seeking treatment for pregnant people who use substances.<sup>10,11</sup>

### Trauma-informed Care

Opioid use disorder has been associated with a high lifetime prevalence of trauma including physical and sexual abuse, and pregnancy is a period of particular vulnerability for individuals who have experienced trauma.<sup>12,13</sup> It is also noteworthy that women are at increased risk of intimate partner violence during pregnancy, particularly in the case of unintended pregnancies.<sup>14</sup> Clinicians involved in the care of pregnant patients with opioid use disorder should be familiar with the principles of trauma-informed practice (e.g., trauma awareness; safety and trustworthiness; choice, collaboration and connection; strengths-based approaches and skill building). The provincial [Trauma-informed Practice \(TIP\) Guide](#) may be a useful resource when working with this patient population.<sup>15</sup>

### Integrated Medical Management

Care for pregnant individuals with opioid use disorder should reach beyond a strictly substance-focused approach in order to improve long-term outcomes for the mother-infant dyad. As the standard of care for the management of any complex or chronic medical condition, thorough medical management should be provided to pregnant patients with opioid use disorder. In this context, medical management is defined as informal medically-focused counselling that includes, but is not limited to, conducting health and mental wellness checks; offering non-judgmental support and advice; assessing motivation and exploring ideas for change; developing a holistic treatment plan; promoting alternative strategies for managing stress; and providing appropriate referrals to health and social services with the consent and input of the patient. Clinicians should also ascertain patients' nutritional, housing, and security needs, making necessary referrals to address them.<sup>12,13</sup>

### Harm Reduction During Pregnancy

Pregnant individuals with opioid use disorder should have access to the full range of harm reduction supplies and services available to the general patient population, including supervised consumption sites, overdose prevention sites, sterile consumption supplies, take-home naloxone kits and education on safer use. Substantial evidence has associated the use of harm reduction services with a significant reduction in substance use-related harms, including HIV and hepatitis C infection and overdose death, while providing a point of access to care and promoting engagement in treatment.<sup>16-19</sup> Additionally, harm reduction during pregnancy has been associated with improved neonatal outcomes, such as fewer preterm births, higher birth weights, and increased likelihood of babies being discharged from hospitals with their mothers following birth.<sup>20,21</sup>

For additional information on these harm reduction strategies, this document recommends the [BC Women's Harm Reduction in Pregnancy: Community Based Approaches to Pre-natal Substance Use in Western Canada](#).

**Table 2- Summary of care principles**

1.	Establishing a trusting and collaborative relationship with the patient is paramount. To this end, patients should be assured of the confidentiality of the information they disclose in a clinical setting.
2.	Clinicians caring for pregnant individuals with opioid use disorder should apply the principles of trauma-informed and culturally safe practice.
3.	Clinicians should assess each patient's basic medical and psychosocial needs (e.g., mental wellness, security, stable housing) and make necessary referrals to secure social determinants of health.
4.	Integrated and individualized care programs are essential to fostering stability and improving treatment and pregnancy outcomes.
5.	All pregnant people with opioid use disorder should have access to the full scope of harm reduction supplies and services available to the general patient population.

## Clinical Recommendations

### Screening and Assessment

While this supplement focuses on opioid use disorder, it emphasizes the importance of obtaining a comprehensive account of patients' substance use history so that a care plan for problematic substance use can be developed collaboratively. As a standard of care, all patients who are pregnant or may become pregnant should be offered regular screening for alcohol, tobacco, and other non-medical drug use, and engaged in discussion about the risks of substance use during pregnancy and how to reduce them.

Clinicians should also obtain a thorough record of current prescribed medication use and be mindful of the maternal and neonatal risks associated with the concurrent use of opioids and other psychotropic drugs during pregnancy. While the elevated risk of accidental overdose among adults who use opioids and other psychotropic medications is well-documented, more recent research also demonstrates that in-utero co-exposure to these drugs increases the severity and duration of neonatal withdrawal symptoms.<sup>22-25</sup> For example, a large cohort study involving pregnant participants who use prescription opioids showed a 30-60% increase in the risk of neonatal drug withdrawal associated with co-exposure to antidepressants, benzodiazepines, or gabapentin compared with opioids alone.<sup>23</sup> Healthcare providers should review patients' current medication use through PharmaNet, consult with relevant specialists and other care providers (with the patients consent), and take necessary measures to minimize the use of these medications if possible and appropriate. For more information on safe prescribing guidelines, refer to CPSBC's [Professional Standards and Guidelines for Safe Prescribing of Drugs with the Potential for Misuse/Diversion](#).

In alignment with guidance from Perinatal Services BC, substance use screening should be included in the first prenatal assessment and conducted periodically throughout pregnancy and postpartum when clinically relevant and necessary.<sup>26-28</sup> Alongside patient reports, urine drug testing (UDT) is typically the preferred drug screening method.<sup>29</sup> Refer to Appendices 1 and 4 of the [Guideline](#) for detailed guidelines on utilizing UDT as an assessment and monitoring tool. Clinicians should be sensitive to specific vulnerabilities of this population and clearly describe the purpose of each test. The patient's informed consent should be sought prior to performing point-of-care UDT or ordering laboratory tests. Patients who self-report ongoing substance use, test positive for substance use, or those who decline or are unable to provide a urine sample, should receive brief intervention and support and be encouraged to continue to engage in treatment.<sup>6,30</sup> Depending on the substance (e.g., tobacco, alcohol, pharmaceutical or illegal drugs) and diagnosis (e.g., high-risk use, substance use disorder), treatment for this group of patients may involve pharmacotherapy, and/or appropriate referrals to specialist care as required or requested.<sup>6,28</sup>

All patients of childbearing capacity starting OAT should be offered screening for pregnancy at intake, and contraceptive counselling and supplies should be offered as appropriate. This is in consideration of the fact that the majority of pregnancies among individuals with substance use disorders are unplanned.<sup>5</sup> Also, pregnant individuals with substance use disorders may present for prenatal care relatively late in their term due to various social and personal barriers such as fear of losing custody of their children. Contraceptive counselling services and supplies should also be offered to patients who are currently pregnant in order to reduce the likelihood of a subsequent unplanned pregnancy as short intervals between pregnancies may disrupt ongoing treatment and amplify potential risks to recovery and long-term health.<sup>5</sup>

### Prenatal Treatment Considerations

#### Opioid Agonist Treatment

OAT has long been the standard of pharmacological care for pregnant individuals with opioid use disorder, as it has been shown to eliminate or substantially reduce non-medical opioid use and associated health risks, leading to improved neonatal outcomes in comparison to untreated opioid use disorder and/or rapid withdrawal

management.<sup>8,9,31,32</sup> For a review of evidence pertaining to the efficacy and safety of OAT in adults with opioid use disorder, refer to the corresponding chapter of the [Guideline](#). Abundant supporting evidence has rendered methadone the most frequently prescribed OAT during pregnancy; however, a growing body of research supports the equal efficacy, and potentially superior safety, of buprenorphine and buprenorphine/naloxone for the treatment of opioid use disorder in pregnancy.<sup>8,9,32-34</sup>

It is important to note that, unless clinically indicated, transitioning between methadone, buprenorphine/naloxone, and slow-release oral morphine is NOT advisable for patients who are stable on one of these agents during pregnancy and postpartum; the process of reducing and titrating medication dosage during transition may result in the re-emergence of withdrawal symptoms and increased risk of relapse. Research has consistently shown that continuity of care and adequate suppression of withdrawal symptoms during pregnancy are the most important factors associated with improved maternal and neonatal outcomes.<sup>5,27</sup>

### *Methadone*

Compared to untreated opioid use disorder and medically managed withdrawal, methadone treatment is associated with improved neonatal outcomes including longer gestation, higher live birth rates, greater birth weights, and earlier discharge of infants from hospital.<sup>29</sup> In addition to preventing relapse, methadone has been shown to minimize the sharp fluctuations in maternal serum opioid levels that occur with ongoing use of short-acting opioids. As a result, OAT using an appropriate therapeutic dose of methadone can eliminate fetal stress that may be caused by cyclical intoxication and withdrawal.<sup>4,8</sup>

Like other opioids, methadone can cause neonatal opioid withdrawal symptoms (NOWS), a treatable constellation of withdrawal symptoms that, in some cases, can require extended hospitalization and pharmacological treatment. Neonatal withdrawal is not equivalent to substance use disorder or opioid addiction in infants and can be medically treated (see the [Neonatal Opioid Withdrawal Symptoms](#) section). Neonatal methadone withdrawal lasts longer than withdrawal symptoms attributed to shorter acting opioids such as heroin (due to the long half-life of methadone).<sup>9,34</sup> Nevertheless, these symptoms are treatable, and the risks of maternal methadone treatment to the neonate are proven to be far fewer and less severe than those associated with untreated opioid use and acute withdrawal.<sup>4,34,35</sup>

### Dosing:

Methadone dosing principles for pregnant individuals do not differ from the general adult patient population (i.e., individually titrated doses that eliminate or sufficiently reduce withdrawal symptoms). Refer to [Appendix 1 of Guideline](#) for induction and dosing guidelines for methadone.

There are contrasting findings in the literature concerning the possibility of correlation between methadone dose and the severity of NOWS; however the one meta-analysis published on this topic has found no significant association between these factors.<sup>24,36-39</sup> While patients should always be maintained on the lowest effective dose of methadone, it is important to keep in mind that the potential harms of relapse resulting from sub-optimal treatment surpass those of NOWS. Thus, as with non-pregnant patients, individualized dose titration to an optimal dose that sufficiently reduces cravings is strongly recommended. In the process of gauging the effectiveness of the methadone dose, care must be taken to distinguish between symptoms of opioid withdrawal and pregnancy symptoms. For some pregnant patients on methadone, the acceleration of maternal metabolism in the course of pregnancy may require an increase in daily dose to address emergent withdrawal symptoms and prevent fetal stress, particularly in the second or third trimesters.<sup>4,40</sup> If needed, gradual dose increases can be made by increments of 5 mg to 10 mg. Due to the increased hepatic metabolism of methadone in pregnancy, split dosing may be considered to prevent withdrawal symptoms.<sup>4,40</sup>

For case-specific assistance, clinicians may consult the [RACE line](#). This service provides specialized consultation in Perinatal Addictions and Addiction Medicine specialty areas.

### *Buprenorphine*

While the neonatal outcomes associated with buprenorphine and methadone exposure in pregnancy are similar, research shows that NOWS resulting from buprenorphine may be less severe due to its partial agonist characteristics, requiring a shorter treatment period.<sup>34,35</sup> A recent systematic review (three RCTs, n=223; 15 observational cohort studies, n=1923) comparing the maternal and neonatal outcomes of buprenorphine and methadone found that buprenorphine treatment resulted in lower risk of preterm labour, larger head circumference, and greater birth weight in comparison to methadone.<sup>8</sup> The authors noted no significant differences between the two treatments in terms of spontaneous fetal loss (i.e., spontaneous miscarriage) and congenital abnormalities.<sup>8</sup> Moreover, a systematic review of opioid OAT options for pregnant individuals in rural areas found that, due to its superior safety profile, buprenorphine may be advantageous compared to methadone in locations where access to specialized care, including daily dispensing requirements for methadone, is limited.<sup>41</sup>

Transitioning pregnant individuals from buprenorphine/naloxone to buprenorphine monotherapy is unnecessary unless clinically indicated or requested by the patient. This is due to the growing evidence demonstrating the equal safety of buprenorphine/naloxone during pregnancy (see the Buprenorphine/naloxone section below) and potential delays in obtaining this medication which is not approved in Canada. The buprenorphine-only formulation is currently available via authorization through Health Canada's [Special Access Programme](#) and can often take up to 2 weeks to import once authorization and medication coverage have been secured.

### *Buprenorphine/naloxone*

In comparison to treatment with buprenorphine-only, there are fewer studies that investigate the efficacy and safety of buprenorphine/naloxone during pregnancy; this is arguably due to the theoretical risk that naloxone may pose to the fetus by elevating maternofetal cortisol levels. However, several recent studies have found no statistically significant differences between the two formulations in terms of pregnancy and treatment outcomes.<sup>8,42-45</sup> For example, a 2013 study compared the maternal and neonatal outcomes of 10 participants treated with buprenorphine/naloxone to the corresponding statistics presented in 7 previously published studies examining methadone and buprenorphine treatments in pregnancy.<sup>46</sup> While the authors emphasized the need for more extensive research to fully characterize the impact of buprenorphine/naloxone on the fetus, they reported similar results for maternal outcomes, gestation period, and the incidence and severity of NOWS.<sup>46</sup>

Parallel with evidence supporting the safety and effectiveness of buprenorphine/naloxone, pregnancy was recently removed as a contraindication in the product monograph of the Health Canada-approved buprenorphine/naloxone (brand name Suboxone®).<sup>43,47</sup> In view of these developments, initiation of buprenorphine/naloxone treatment may be considered on a case-by-case basis by the treating clinician with appropriate monitoring.

In cases where patients have achieved clinical stability on buprenorphine/naloxone prior to pregnancy, continuation of this treatment is recommended.<sup>5</sup> Transition to buprenorphine monotherapy during pregnancy is not necessary, but may be offered to a patient who is fully informed of treatment options and wishes to proceed with buprenorphine.

#### Dosing:

Buprenorphine/naloxone dosing principles for pregnant individuals do not differ from the general adult patient population (i.e., individually titrated doses that eliminate or sufficiently reduce withdrawal symptoms). Refer to [Appendix 2 of Guideline](#) for induction and dosing guidelines for buprenorphine/naloxone. For case-specific assistance, clinicians may consult the [RACE line](#) Perinatal Addiction service.



Buprenorphine/naloxone is somewhat less likely than methadone to require significant dose changes during pregnancy, since its extended half-life renders changes in maternal blood volume less concerning. However, studies on buprenorphine treatment during pregnancy report that, in some cases, a slight increase (0.5 – 3.3 mg) in the mean dose during pregnancy may be required based on clinical judgement.<sup>35,48,49</sup> Adequate doses of buprenorphine/naloxone can help address the risk of attrition associated with this medication.<sup>4,9</sup> Inpatient induction may be beneficial for preventing precipitated withdrawal.

#### *Slow-release oral morphine*

Slow-release oral morphine as a treatment option for opioid use disorder was originally studied in the context of pregnancy in a 1999 randomized controlled trial (n=48) with the hypothesis that it may cause milder neonatal withdrawal symptoms than methadone.<sup>50</sup> The authors did not find any significant differences between the duration or severity of NOWS caused by methadone and slow-release oral morphine, and concluded that the two medications were equally effective in terms of maternal and neonatal outcomes.<sup>50</sup> The study also found that participants receiving slow-release oral morphine were marginally less likely to use benzodiazepines and non-medical opioids in the course of treatment.<sup>50</sup> This is in line with the preliminary findings concerning non-pregnant patients, which also indicate that slow-release oral morphine is as effective as methadone with respect to treatment retention and safety while potentially providing comparatively reduced opioid cravings and superior treatment satisfaction.<sup>51,52</sup>

However, the body of evidence supporting the safety and efficacy of slow-release oral morphine for treating opioid use disorder during pregnancy is limited. This medication option may be considered at the discretion of the treating clinician, particularly for patients who have not benefited from first- and second-line treatment options (i.e., methadone and buprenorphine/naloxone) or in areas where access to other OAT options are not readily available.

Opioid use disorder treatment with slow-release oral morphine is considered off-label and should be prescribed by, or in consultation with, an addiction specialist and with the patient's written consent and treatment agreements. See [Appendix 8 of the BCCSU Guideline](#) for agreement and consent forms.

#### Dosing:

Dosing pregnant individuals should follow dosing recommendations for non-pregnant adults.<sup>50,53</sup> Refer to [Appendix 3 of Guideline](#) for induction and dosing guidelines for slow-release oral morphine. As per all other opioid agonists, clinicians should prescribe the lowest effective dose of slow-release oral morphine. For case-specific assistance, clinicians may consult the [RACE line](#) Perinatal Addiction service.

#### *Injectable opioid agonist treatment*

Injectable opioid agonist treatment (iOAT) with diacetylmorphine or hydromorphone is an established evidence-based treatment option in multiple jurisdictions for non-pregnant individuals with severe long-term opioid use disorder for whom other available treatments have proven ineffective.<sup>54,55</sup> To date, published evidence on the feasibility and safety of iOAT during pregnancy is limited to two European case reports both of which attribute positive pregnancy outcomes to the continuation of treatment with diacetylmorphine in the case of patients with severe opioid use disorder and multiple comorbidities.<sup>56,57</sup> In light of the paucity of evidence supporting the safety of iOAT for this population, oral treatment options should always be offered before contemplating the initiation or continuation of iOAT. For transition from iOAT to oral OAT, methadone or slow-release oral morphine may be preferable to buprenorphine/naloxone, as they do not require a period of detoxification prior induction.

However, in the context of the current overdose crisis, the potential harms of initiating iOAT should be weighed against the considerable risk of morbidity and mortality associated with untreated opioid use disorder in the case of patients with severe opioid use disorder who have not benefited from other options. Similarly, for individuals who are stable on iOAT prior to pregnancy, the likelihood of relapse to non-medical opioid use and associated harms should be carefully assessed when considering treatment de-intensification. There are a number of recorded cases of successful iOAT continuation through pregnancy provided by services across Europe (Vogel, M. Personal communication, 22, Nov., 2017).<sup>58</sup> Decisions concerning the initiation and continuation of iOAT should be made with caution and in consultation with an addiction specialist. The patient's informed consent should be obtained and documented prior to initiating this treatment.

For more information regarding the eligibility criteria for iOAT, see BCCSU's guidance document for [Injectable Opioid Agonist Treatment for Opioid Use Disorder](#).

### Residential treatment

Although the evidence supporting the efficacy of residential treatment for substance use disorder is relatively limited, guidelines pertaining to pregnant individuals cite this setting as potentially beneficial for patients who require more intensive medical care and support to improve health and pregnancy outcomes.<sup>59,60</sup> Residential programs may also be appropriate for patients with comorbidities and complex medical and psychosocial needs, as well as those who unstable housing and social circumstances.<sup>59</sup> Residential treatment should be considered in collaboration with, and with the consent of, the patient. The following factors should be considered when selecting a residential facility for pregnant patients:

- Capacity to provide OAT as directed by the patient's prescriber
- Capacity to provide wraparound medical and psychosocial support
- Access to comprehensive specialist pregnancy and prenatal care
- If applicable, access to postpartum and neonatal care, as well as onsite accommodation or visitation provision for patient's child(ren).<sup>61</sup> Keeping mothers and children together should be among primary considerations when selecting a treatment setting for this population.

Effective discharge planning is also crucial to ensure positive long-term residential treatment outcomes.<sup>59,62</sup> The residential facility should communicate outpatient care providers and relevant community-based services to ensure the continuation of care after discharge. It may be necessary to intensify support and monitoring during transition between settings as patients are particularly vulnerable to relapse to nonmedical opioid use in these periods. Every effort should be made to ensure patient's access to safe and stable housing prior to discharge.<sup>61</sup>

### Withdrawal management (i.e., detoxification)

Withdrawal management alone is not a recommended approach during pregnancy primarily due to the high rates of relapse, which are similar to those in the general population of patients with opioid use disorder.<sup>2</sup> Relapse following detoxification can lead to increased risk of morbidity (e.g., infections, non-fatal overdose) and mortality (e.g., fatal overdose).<sup>29,63</sup> Moreover, numerous studies demonstrate that sharp physiological fluctuations associated with rapid withdrawal from opioid use and subsequent relapse can lead to adverse outcomes for the fetus that are more severe and lasting than NOWS, such as maternal and fetal distress, fetal demise, fetal hypoxia, preterm labor, and long-term developmental issues.<sup>4</sup>

If a patient expressly wishes to discontinue opioid use after being informed of the risk of relapse and associated harms, slow withdrawal management (i.e. prolonged OAT taper over months) should be devised combined with intensive long-term monitoring and psychosocial treatment interventions and support.<sup>2,64,65</sup>



## Naltrexone

The meager volume of research on the use of naltrexone for treating opioid use disorder in pregnancy focuses on the extended-release injectable or implantable formulations of this agent.<sup>66</sup> Available evidence does not endorse the use of naltrexone during pregnancy mainly due to the period of detoxification and abstinence required prior to treatment initiation, which poses a high risk of relapse and, in turn, fetal distress, infection, and fatal and nonfatal overdose.<sup>66</sup> Also, by blocking the effect of opioid pain medication, naltrexone significantly limits pain management options, necessitating a tailored non-opioid pain management plan.<sup>66</sup>

While naltrexone is currently not associated with severe negative neonatal or long-term developmental effects,<sup>67,68</sup> the human data evaluating the neonatal outcomes of this medication is sparse, and there are no human studies on the developmental effect of this medication on developmental factors. Moreover, the extent to which naltrexone affects the production of breast milk and the safety of breastfeeding is not currently known.<sup>66</sup>

However, in the interest of maintaining patient stability and preventing relapse, the continuation of treatment in the case of patients who are stable on naltrexone may be considered with extreme caution.<sup>66</sup>

## Intrapartum considerations

OAT should be continued through labour and considered separate from any pain management strategies employed during labour and delivery. If liquids are contraindicated during labour (e.g., if the risk of needing anesthesia is high) parenteral opioids (e.g., injectable hydromorphone) may replace methadone.

Regular pain management for labour and delivery may be provided alongside OAT.<sup>69,70</sup> While epidural anesthesia is often the preferred pain management analgesic method for this population, the full range of pain management options (including non-pharmacological and non-analgesic options) may be considered to accommodate each patient's circumstances and preferences.<sup>71,72</sup> If opioid analgesics are used for labour pain management, higher doses may be required to compensate for increased tolerance, and the patient must be monitored for respiratory depression and somnolence.<sup>72</sup> It should be noted that opioid-dependent patients may be hyperalgesic and may require a multimodal approach to pain treatment involving additional pain treatment medications.<sup>72,73</sup> Good communication between the clinical care team and patient is essential throughout pregnancy to devise an appropriate pain management strategy.

For patients with a history of sexual trauma and post-traumatic stress disorder, labour may trigger symptoms that, in turn, intensify labour pain.<sup>12,13</sup> Informed consent prior to every exam, particularly vaginal exam, should be sought as an essential aspect of patient-centered and trauma-informed care.

## Postpartum considerations

### Adjustment of OAT and pain medication

After childbirth, methadone doses may be lowered in response to the decrease in blood volume and metabolism, and split dosing should be discontinued. For example, a common dose reduction immediately post-partum for patients taking methadone is 20% of the total daily dose; however, empirical evidence supporting this pre-determined dose reduction convention is limited.<sup>74,75</sup> Endorsing frequent visits for monitoring for at least 12 weeks post-partum, a number of studies demonstrate that gradual and individualized dose reductions informed by observed signs of over-sedation may more suitable for maintaining the mother's stability during this period.<sup>75-77</sup> In some cases, it may be safe to continue split dosing until a new stable dose is determined.<sup>76</sup> The dosage of other OAT medications (i.e. buprenorphine/naloxone, slow release oral morphine, and injectable opioid agonists) may also be adjusted if necessary.

Moderate levels of postpartum pain for individuals who deliver vaginally can be managed using a combination of NSAIDs and acetaminophen, as clinically indicated. Additional use of short-acting opioids may be considered for some patients, particularly in cases of caesarean delivery.<sup>71,72</sup>

### Rooming-in and Breastfeeding

Keeping mothers and infants together following delivery (i.e., rooming-in) is associated with healthy mother-infant bonding leading to improved long-term developmental outcomes, higher likelihood of breastfeeding, improved access to integrated care and initial childcare education in a family-centered setting, reduced need for pharmacological treatment for NOWS, and fewer neonates discharged to foster care.<sup>36,78-81</sup> A long-established standard in maternity settings for the general population, rooming-in has been successfully adopted for mothers with opioid use disorder and their infants in a number of in a number of jurisdictions; Vancouver's Fir Square, a combined evidence-based care unit within BC Women's Hospital, serves as a pioneering example for this development.<sup>36</sup> In light of the significant emerging evidence supporting the safety and effectiveness of rooming-in, this guideline recommends rooming in as the standard of care for opioid exposed infants.

Breastfeeding while maintained on methadone is safe regardless of dose, and may help decrease NOWS while facilitating maternal/infant bonding.<sup>82,83</sup> Although the human data on the safety of buprenorphine and buprenorphine/naloxone for breastfeeding is limited, the amounts of these substances secreted in human milk are believed to be too small to affect the health of the infant.<sup>84,85</sup> The impact of slow-release oral morphine on human milk has not yet been adequately studied. Breastfeeding is not recommended for HIV-positive patients and patients who are actively using non-medical substances or alcohol.<sup>9</sup>

### Neonatal Opioid Withdrawal Symptoms

Neonatal opioid withdrawal symptoms (NOWS) refers to a constellation of possible postnatal opioid withdrawal symptoms experienced by newborns whose mothers used opioids during pregnancy. Between 48% and 94% of newborns exposed to opioids in utero experience opioid withdrawal symptoms.<sup>85</sup> NOWS is best characterized by dysregulation of central and automatic nervous systems and the gastrointestinal systems.<sup>86</sup> While NOWS is highly variable in its clinical manifestations, its common symptoms include inconsolable high pitch crying, fever, tremors, irritability, poor feeding, vomiting, diarrhea, weight loss, and convulsions.<sup>85,86</sup> It is important to emphasize that NOWS is a treatable syndrome that should not be construed as addiction in infants.

The discussion in this section is in line with Canadian Paediatric Society's recently released practice guideline for [Management of Infants born to Mothers who have used Opioids during Pregnancy](#).

## *Screening and Assessment*

All infants with known in utero opioid exposure should undergo inpatient monitoring for a minimum of 72 hours.<sup>87,88</sup> The onset age of NOWS depends largely on the half-life of the opioid used by the mother; neonatal heroin withdrawal typically presents within 24-48 hours while methadone withdrawal symptoms generally occur within 48-72 hours, and buprenorphine withdrawal symptoms take longer to appear.<sup>89</sup> Other possible causes, such as infection and hypoglycemia, for observed symptoms should be ruled out before commencing treatment for NOWS.<sup>90</sup>

Traditionally, the Finnegan scoring system has been the most common assessment tool for detecting NOWS and assessing their severity over time in order to determine the need for pharmacological treatment as well as dose escalation and weaning schedules.<sup>91,92</sup> Consisting of 21 items assessed in 3-4 hour intervals, the traditional Finnegan scoring is prone to subjective inter-observer error and may be disruptive to the infant's sleeping and feeding patterns.<sup>87,89,93</sup> The [Canadian Paediatric Society guidelines](#) has featured a modified Finnegan scoring tool as a widely used example. However, emerging evidence has propelled a shift towards a novel simplified scoring method that focuses on objective factors such as adequate weight gain and ability to sleep.<sup>89,93</sup> For example, a recent study (n=50) demonstrated that observing the infant's ability to feed, sleep, and be consoled is an effective method for assessing neonatal withdrawal, leading to fewer infants requiring pharmacological NOWS management.<sup>94</sup> [Appendix 1](#) contains an example of a NOWS assessment protocol predominantly based on these measures.

The factors that affect the onset and severity of NOWS are not yet fully understood; information regarding the type and dose of opioid used by the mother should not be relied on exclusively as predictors of the onset or severity of NOWS.<sup>87,91</sup>

PSBC's upcoming practice tools for the assessment and treatment of NOWS will be appended to the present text upon release.

## *Treatment*

Pharmacological treatment for NOWS involves the administration of an opioid for symptom control with subsequent tapering over the course of days to weeks.<sup>92</sup> The current first line treatments for NOWS are oral morphine and methadone. Oral morphine is the most commonly prescribed agent for NOWS; however, studies comparing the two first line agents have found no evidence that would promote one agent over the other.<sup>92,95</sup>

In the recent years, sublingual buprenorphine has also been increasingly considered as a potentially advantageous treatment option for NOWS. For example, a 2017 clinical trial including 63 opioid-exposed term infants found that buprenorphine treatment resulted in shorter duration of treatment and hospital stay than treatment with oral morphine, with no significant difference in adverse events.<sup>92</sup>

Historically, standard care for newborns with in utero opioid exposure has involved admission to an intensive care nursery where the infant can be monitored and, if needed, treated for symptoms of NOWS in an isolated environment where exposure to sensory stimuli is minimized.<sup>78,79,91</sup> However, there is no evidence supporting the effectiveness of sensory deprivation in reducing symptoms of NOWS.<sup>78,89</sup> Conversely, studies conducted on rooming-in practices for substance-exposed newborns have demonstrated that NOWS treatment can be provided successfully in this setting, resulting in fewer admissions to the neonatal intensive care unit, shorter pharmacological treatment at lower doses, and earlier discharge of infants from hospital.<sup>78,79,85</sup> Rooming-in also facilitates breastfeeding and skin-to-skin contact, and other bonding and soothing measures which have been recognized as effective nonpharmacological approaches to treating NOWS.<sup>88,93</sup> Thus, this guideline recommends rooming in as the standard setting for the treatment of NOWS.

## Child Protection

### The prenatal period:

Clinicians in Canada do not have a legal obligation to report prenatal substance use or other risks to the fetus during the course of pregnancy. Any antenatal referrals or reports require the informed consent of the patient.

Integrated care programs and collaborative long-term support planning in the course of pregnancy may foster family stability and enable the new mother to play an active role in her child's care with the help of resources available in her family and community.<sup>36,96</sup> The involvement of the mother, supportive family members, public health and community-based resources, and services provided by the Provincial Ministry of Children and Family Development (MCFD) prior to childbirth can help improve pregnancy outcomes. However, the involvement of these services should be considered with the collaboration and consent of the pregnant patient.

### The neonate (and other children in the custody of patient):

Maternal substance use alone is not grounds for the apprehension of the infant or even referral to MCFD. However, the health care team is legally obligated under Section 14 of the [Child and Family and Community Service Act \(CFCSA\)](#) to report child protection concerns to the MCFD. Prior to making a report, clinicians should refer to [Section 13 of CFCSA](#) for a comprehensive outline of circumstances under which notifying MCFD is warranted. The decision to report should be made on a case-by-case basis in consultation with the full health care team. It should be noted that the apprehension of infants is associated with a range of negative long-term social and health outcomes for the mother and child.<sup>97-99</sup> If a child is temporarily apprehended during the immediate postpartum period, mothers should be offered appropriate supports to ensure that the outcomes they experience after the loss of their child do not become barriers to reunification.<sup>97</sup>

Healthcare providers may consult the [RACE line](#) Perinatal Addiction Service for ascertaining whether notifying MCFD is appropriate.

## **Evidence Gaps for Future Work**

There is a relative dearth of research focused on managing substance use disorders among pregnant individuals, partly due to the ethical complexity of conducting clinical trials involving this population. However, in the context of the current opioid overdose crisis, excluding pregnant patients from clinical studies and practices for the management opioid use disorder may no longer qualify as a prudent measure. Potential priorities for future investigation include research to clearly characterise risks and benefits associated with iOAT and slow-release oral morphine for pregnant patients with severe opioid use disorder, and to describe optimal treatment conditions and factors for this population. Further research is also needed to unequivocally establish the safety of slow-release oral morphine and buprenorphine/naloxone for breastfeeding.

While the benefit of rooming-in for the mother and infant are well-documented, implementation science research is needed to support the broad implementation of this setting in both rural and urban jurisdictions. Finally, further research into nonpharmacological approaches to treating NWS and supporting mother-infant bonding would help create a solid evidence base for standardizing practices that promote long term health.



## Summary

Within the framework of a non-judgmental, trauma-informed, culturally safe, and collaborative approach to care, this guideline recommends a comprehensive integrated care plan for pregnant patients with appropriate use of the full range of available treatment options and harm reduction services. The care plan for pregnant individuals should reach beyond substance-focused approaches and include collaboration with relevant resources to secure patients' social determinations of health, such as adequate nutrition, housing, and other psychosocial supports.

In line with recommendations pertaining to the general population, this guideline recommends against a strategy involving withdrawal management alone and strongly endorses OAT with methadone or buprenorphine/naloxone as the first line pharmacological treatment option for opioid use disorder during pregnancy. Methadone and buprenorphine/naloxone treatments have been shown to eliminate or substantially reduce non-medical opioid use and prevent relapse, leading to improved maternal and neonatal outcomes in comparison to untreated opioid use disorder and rapid withdrawal management. Buprenorphine monotherapy has also been reviewed as an OAT option that may be considered on a case-by-case basis to accommodate patients preference. This document also includes a review of slow-release oral morphine and injectable OAT as higher intensity alternatives that may be considered with caution for specific patients with severe opioid use disorder who have been unsuccessful with first and second line treatments. For dosing and other treatment considerations, clinicians are referred back to the BCCSU [Guideline for the Clinical Management of Opioid Use Disorder](#).

This document strongly emphasises the importance of treatment consistency and continuity through pregnancy and after delivery. Unless clinically indicated or requested by the patient, patients who are stable on an OAT medication prior to pregnancy should not be transitioned to another medication once they become pregnant as the transition period poses a substantial risk of treatment destabilization. OAT should be continued through labour and considered separate from pain management medication which should be provided as needed throughout intrapartum and postpartum periods.

Finally, in view of the importance of breastfeeding and sustained mother-infant contact to the infant's long-term developmental outcomes, this supplement also emphasises the safety recommends the adoption of rooming-in as the standard maternity setting for opioid exposed neonates.

## Appendix 1: Sample Rooming-In protocol for opioid-exposed neonates (Adapted from the Fir Square Protocol)

### General Considerations

- Infants room-in with their mothers at the hospital for at least 7-8 days, so that they are monitored for NOWS and thriving is established according to the assessment measures below.
- The Rooming-in model views continuous parental involvement in the neonate's care as a key component of effective treatment for NOWS. Mothers should be encouraged and taught to hold their infants and maintain skin-to-skin contact, which has been shown to soothe the baby and decrease the severity of withdrawal symptoms.
- Where possible, assessment procedures should be performed without disrupting the infant's sleep or the mother-infant contact.
- Mothers should be encouraged and taught to breastfeed.

### Assessment for neonatal opioid withdrawal

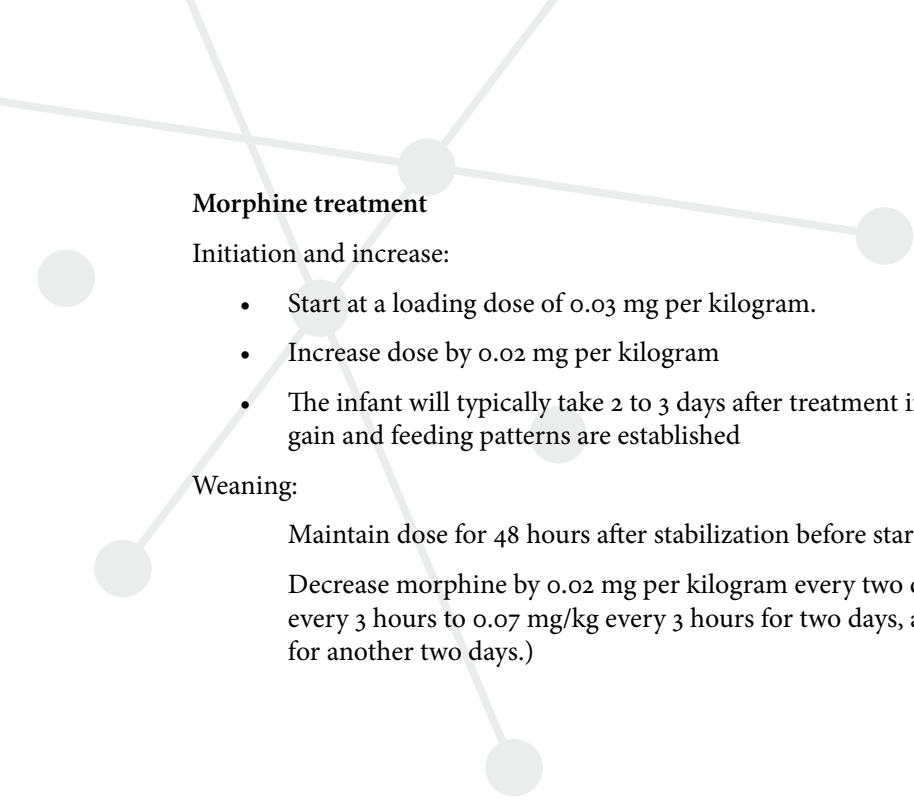
In order to minimize intra-observer error and disruption to the infant's sleep and feeding cycles, Finnegan's scoring is discarded for a simplified and more objective assessment method focused on two major factors: 1) adequacy of weight gain and 2) ability to sleep and be consoled

#### 1) Weight gain:

- Babies should be weighed daily.
- Up to 10% weight loss within the first 72 hours (i.e., the length of time it generally takes for routine feeding patterns to get established) is acceptable and does not require initiation of morphine. In this case, clinicians should identify and address the potential causes of weight loss in communication and collaboration with the mother:
  - a) Insufficient breast milk or the infant's tendency to fall asleep during breastfeeding are common causes of inadequate weight gain in newborns and can be addressed by supplementing breastfeeding with formula or donated breast milk. Supplementary bottle feeding may help avoid treatment with morphine.
  - b) Causes other than neonatal opioid withdrawal for diarrhea and vomiting should be considered and addressed.
- Morphine initiation or increase may be considered if adequate weight gain is not established despite these measures after the first 72 hours.

#### 2) Ability to sleep and be consoled:

- Rooming-in and continuous skin-to-skin contact with the mother has been shown to significantly ameliorate neonatal distress, eliminating or considerably decreasing the need for morphine treatment. These nonpharmacological measures should be taken to address high pitched crying and inability to sleep prior to considering morphine.
- Morphine may be considered if the infant cannot be consoled and high pitched crying does not subside within 10 minutes or sleep undisturbed for at least 1 hour.



## Morphine treatment

### Initiation and increase:

- Start at a loading dose of 0.03 mg per kilogram.
- Increase dose by 0.02 mg per kilogram
- The infant will typically take 2 to 3 days after treatment initiation to stabilize (i.e., satisfactory weight gain and feeding patterns are established)

### Weaning:

Maintain dose for 48 hours after stabilization before starting to wean

Decrease morphine by 0.02 mg per kilogram every two days (e.g., decrease dose from 0.09 mg/kg every 3 hours to 0.07 mg/kg every 3 hours for two days, and then decrease to 0.05 mg/kg every 3 hours for another two days.)

## REFERENCES

- Public Health Agency of Canada. What Mothers Say: The Canadian Maternity Experiences Survey. Ottawa, 2009.
- Lund IO, Fitzsimons H, Tuten M, Chisolm MS, O'Grady KE, Jones HE. Comparing methadone and buprenorphine maintenance with methadone-assisted withdrawal for the treatment of opioid dependence during pregnancy: maternal and neonatal outcomes. *Substance abuse and rehabilitation*. 2012;3(Suppl 1):17-25.
- Maeda A, Bateman BT, Clancy CR, Creanga AA, Leffert LR. Opioid abuse and dependence during pregnancy: temporal trends and obstetrical outcomes. *Anesthesiology*. 2014;121(6):1158-1165.
- McCarthy JJ, Leamon MH, Finnegan LP, Fassbender C. Opioid Dependence and Pregnancy: Minimizing Stress on the Fetal Brain. *American journal of obstetrics and gynecology*. 2016.
- American Society of Addiction Medicine. Substance Use, Misuse, and Use Disorders During and Following Pregnancy, with an Emphasis on Opioids. January 18, 2017. Available from: <http://www.asam.org/advocacy/find-a-policy-statement/view-policy-statement/public-policy-statements/2017/01/19/substance-use-misuse-and-use-disorders-during-and-following-pregnancy-with-an-emphasis-on-opioids>
- WHO Guidelines Approved by the Guidelines Review Committee. In: Guidelines for the Identification and Management of Substance Use and Substance Use Disorders in Pregnancy. Geneva: World Health Organization. Copyright (c) World Health Organization 2014.; 2014.
- Lind JN, Interrante JD, Ailes EC, et al. Maternal Use of Opioids During Pregnancy and Congenital Malformations: A Systematic Review. *Pediatrics*. 2017.
- Zedler BK, Mann AL, Kim MM, et al. Buprenorphine compared with methadone to treat pregnant women with opioid use disorder: a systematic review and meta-analysis of safety in the mother, fetus and child. *Addiction (Abingdon, England)*. 2016.
- Jones HE, Martin PR, Heil SH, et al. Treatment of Opioid Dependent Pregnant Women: Clinical and Research Issues. *Journal of substance abuse treatment*. 2008;35(3):245-259.
- Poole N, Isaac B. Apprehensions: Barriers to Treatment for Substance Using Mothers. Vancouver, BC: BC Centre of Excellence for Women's Health, 2001.
- Finnegan L. Substance abuse in Canada: Licit and illicit drug use during pregnancy: Maternal, neonatal and early childhood consequences. Ottawa, ON: Canadian Centre on Substance Abuse, 2013.
- Leeners B, Richter-Appelt H, Imthurn B, Rath W. Influence of childhood sexual abuse on pregnancy, delivery, and the early postpartum period in adult women. *Journal of Psychosomatic Research*.61(2):139-151.
- Najavits LM, Weiss RD, Shaw SR. The link between substance abuse and posttraumatic stress disorder in women. A research review. *The American journal on addictions / American Academy of Psychiatrists in Alcoholism and Addictions*. 1997;6(4):273-283.
- Preventing Violence Across the Lifespan Research Network. Research Brief: Identifying and Responding to Intimate Partner Violence. Fall 2016. Available from: <http://prevail.wp.fims.uwo.ca/wp-content/uploads/sites/10/2016/11/IPV-Research-Brief-2016.pdf>.
- BC Centre of Excellence in Women's Health. Trauma-Informed Practice Guide. May 2013. Available from: [http://bccewh.bc.ca/wp-content/uploads/2012/05/2013\\_TIP-Guide.pdf](http://bccewh.bc.ca/wp-content/uploads/2012/05/2013_TIP-Guide.pdf) In.
- DeBeck K, Kerr T, Bird L, et al. Injection drug use cessation and use of North America's first medically supervised safer injecting facility. *Drug and alcohol dependence*. 2011;113(2-3):172-176.
- Strathdee SA, Celentano DD, Shah N, et al. Needle-exchange attendance and health care utilization promote entry into detoxification. *Journal of urban health : bulletin of the New York Academy of Medicine*. 1999;76(4):448-460.
- McDonald R, Strang J. Are take-home naloxone programmes effective? Systematic review utilizing application of the Bradford Hill criteria. *Addiction (Abingdon, England)*. 2016;111(7):1177-1187.
- Marshall BD, Milloy MJ, Wood E, Montaner JS, Kerr T. Reduction in overdose mortality after the opening of North America's first medically supervised safer injecting facility: a retrospective population-based study. *Lancet*. 2011;377(9775):1429-1437.
- Nathoo, T., Marcellus, L., Bryans, M., Clifford, D., Louie, S., Penalosa, D., Seymour, A., Taylor, M., and Poole, N. Harm Reduction and Pregnancy: Community-based Approaches to Prenatal Substance Use in Western Canada. Victoria and Vancouver, BC: University of Victoria School of Nursing and British Columbia Centre of Excellence for Women's Health. 2015. Available from: [http://bccewh.bc.ca/wp-content/uploads/2015/02/HReduction-and-Preg-Booklet.2015\\_web.pdf](http://bccewh.bc.ca/wp-content/uploads/2015/02/HReduction-and-Preg-Booklet.2015_web.pdf).
- Marshall SK, Charles G, Hare J, Ponzetti JJ, Jr, Stokl M. Sheway's services for substance using pregnant and parenting women: evaluating the outcomes for infants. *Canadian journal of community mental health = Revue canadienne de sante mentale communautaire*. 2005;24(1):19-34.

22. Hwang CS, Kang EM, Kornegay CJ, Staffa JA, Jones CM, McAninch JK. Trends in the Concomitant Prescribing of Opioids and Benzodiazepines, 2002-2014. *American journal of preventive medicine*. 2016;51(2):151-160.
23. Huybrechts KF, Bateman BT, Desai RJ, et al. Risk of neonatal drug withdrawal after intrauterine co-exposure to opioids and psychotropic medications: cohort study. *BMJ*. 2017;358.
24. Dryden C, Young D, Hepburn M, Mactier H. Maternal methadone use in pregnancy: factors associated with the development of neonatal abstinence syndrome and implications for healthcare resources. *BJOG : an international journal of obstetrics and gynaecology*. 2009;116(5):665-671.
25. Wachman EM, Newby PK, Vreeland J, et al. The relationship between maternal opioid agonists and psychiatric medications on length of hospitalization for neonatal abstinence syndrome. *Journal of addiction medicine*. 2011;5(4):293-299.
26. ACOG Committee Opinion No. 524: Opioid abuse, dependence, and addiction in pregnancy. *Obstetrics and gynecology*. 2012;119(5):1070-1076.
27. Wright TE, Terplan M, Ondersma SJ, et al. The role of screening, brief intervention, and referral to treatment in the perinatal period. *American journal of obstetrics and gynecology*. 2016;215(5):539-547.
28. Perinatal Services BC. Provincial Perinatal Guidelines: Population and Public Health Prenatal Care Pathway. March 2014. Available from: <http://www.perinatalservicesbc.ca/Documents/Guidelines-Standards/HealthPromotion/PrenatalCarePathway.pdf>.
29. Wong S, Ordean A, Kahan M. SOGC clinical practice guidelines: Substance use in pregnancy: no. 256, April 2011. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*. 2011;114(2):190-202.
30. Chang G, McNamara TK, Orav EJ, et al. Brief intervention for prenatal alcohol use: a randomized trial. *Obstet Gynecol* 2005;105:991-8.
31. WHO Guidelines Approved by the Guidelines Review Committee. In: *Clinical Guidelines for Withdrawal Management and Treatment of Drug Dependence in Closed Settings*. Geneva: World Health Organization. Copyright (c) World Health Organization 2009.; 2009.
32. Minozzi S, Amato L, Bellisario C, Ferri M, Davoli M. Maintenance agonist treatments for opiate-dependent pregnant women. *Cochrane Database Syst Rev*. 2013(12):Cd006318.
33. Noormohammadi A, Forinash A, Yancey A, Crannage E, Campbell K, Shyken J. Buprenorphine Versus Methadone for Opioid Dependence in Pregnancy. *The Annals of pharmacotherapy*. 2016;50(8):666-672.
34. Jones HE, Kaltenbach K, Heil SH, et al. Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure. *New England Journal of Medicine*. 2010;363(24):2320-2331.
35. Jones HE, Johnson RE, Jasinski DR, et al. Buprenorphine versus methadone in the treatment of pregnant opioid-dependent patients: effects on the neonatal abstinence syndrome. *Drug and alcohol dependence*. 2005;79(1):1-10.
36. Hodgson ZG, Abrahams RR. A Rooming-in Program to Mitigate the Need to Treat for Opiate Withdrawal in the Newborn. *Journal of Obstetrics and Gynaecology Canada*.34(5):475-481.
37. Dashe JS, Sheffield JS, Olscher DA, Todd SJ, Jackson GL, Wendel GD. Relationship between maternal methadone dosage and neonatal withdrawal. *Obstetrics and gynecology*. 2002;100(6):1244-1249.
38. Lim S, Prasad MR, Samuels P, Gardner DK, Cordero L. High-dose methadone in pregnant women and its effect on duration of neonatal abstinence syndrome. *American Journal of Obstetrics & Gynecology*.200(1):70.e71-70.e75.
39. Cleary BJ, Donnelly J, Strawbridge J, et al. Methadone dose and neonatal abstinence syndrome-systematic review and meta-analysis. *Addiction (Abingdon, England)*. 2010;105(12):2071-2084.
40. Bogen DL, Perel JM, Helsel JC, et al. Pharmacologic Evidence to Support Clinical Decision Making for Peripartum Methadone Treatment. *Psychopharmacology*. 2013;225(2):441-451.
41. Jumah NA. Rural, Pregnant, and Opioid Dependent: A Systematic Review. *Substance Abuse: Research and Treatment*. 2016;10(Suppl 1):35-41.
42. Wiegand SL, Stringer EM, Stuebe AM, Jones H, Seashore C, Thorp J. Buprenorphine and naloxone compared with methadone treatment in pregnancy. *Obstetrics and gynecology*. 2015;125(2):363-368.
43. Dooley J, Gerber-Finn L, Antone I, et al. Buprenorphine-naloxone use in pregnancy for treatment of opioid dependence: Retrospective cohort study of 30 patients. *Canadian Family Physician*. 2016;62(4):e194-e200.
44. Debelak K, Morrone WR, O'Grady KE, Jones HE. Buprenorphine + naloxone in the treatment of opioid dependence during pregnancy-initial patient care and outcome data. *The American journal on addictions / American Academy of Psychiatrists in Alcoholism and Addictions*. 2013;22(3):252-254.
45. Wiegand S, Stringer E, Seashore C, et al. 750: Buprenorphine/naloxone (B/N) and methadone (M) maintenance during pregnancy: a chart review and comparison of maternal and neonatal outcomes. Vol 2102014.
46. Lund IO, Fischer G, Welle-Strand GK, et al. A Comparison of Buprenorphine + Naloxone to Buprenorphine and Methadone in the Treatment of Opioid Dependence during Pregnancy: Maternal and Neonatal Outcomes. *Substance Abuse: Research and Treatment*. 2013;7:61-74.

47. Suboxone product monograph including patient medication information. Indivior UK Limited: Berkshire, UK. Control No. 195433. December 20, 2016. Available from: [https://pdf.hres.ca/dpd\\_pm/00037755.PDF](https://pdf.hres.ca/dpd_pm/00037755.PDF).
48. Jones HE, Dengler E, Garrison A, et al. Neonatal outcomes and their relationship to maternal buprenorphine dose during pregnancy. *Drug and alcohol dependence*. 2014;134:414-417.
49. Fischer G, Ortner R, Rohrmeister K, et al. Methadone versus buprenorphine in pregnant addicts: a double-blind, double-dummy comparison study. *Addiction (Abingdon, England)*. 2006;101(2):275-281.
50. Fischer G, Jagsch R, Eder H, et al. Comparison of methadone and slow-release morphine maintenance in pregnant addicts. *Addiction*. 1999;94(2):231-239.
51. Verthein U, Beck T, Haasen C, Reimer J. Mental Symptoms and Drug Use in Maintenance Treatment with Slow-Release Oral Morphine Compared to Methadone: Results of a Randomized Crossover Study. *European Addiction Research*. 2015;21(2):97-104.
52. Beck T, Haasen C, Verthein U, et al. Maintenance treatment for opioid dependence with slow-release oral morphine: a randomized cross-over, non-inferiority study versus methadone. 2014.
53. Metz VE, Comer SD, Wuerzl J, Pribasnik A, Fischer G. Characteristics and quality of life of opioid-dependent pregnant women in Austria. *Archives of Women's Mental Health*. 2014;17(6):529-539.
54. Haasen C, Verthein U, Degkwitz P, Berger J, Krausz M, Naber D. Heroin-assisted treatment for opioid dependence: randomised controlled trial. *The British journal of psychiatry : the journal of mental science*. 2007;191:55-62.
55. Oviedo-Joekes E, Guh D, Brissette S, et al. Hydromorphone Compared With Diacetylmorphine for Long-term Opioid Dependence A Randomized Clinical Trial. *Jama Psychiatry*. 2016;73(5):447-455.
56. Hartwig C, Haasen C, Reimer J, et al. Pregnancy and birth under maintenance treatment with diamorphine (heroin): a case report. *European addiction research*. 2008;14(2):113-114.
57. Groh A, Urlichs F, Hillemacher T, Bleich S, Heberlein A. Case report: Pregnancy and birth under heroin-assisted treatment (HAT) Heroin Addiction and Related Clinical Problems. March 2014, 16(2): 47-52.
58. Uchtenhagen, Ambros. The role and function of heroin assisted treatment at the treatment system level. *Heroin Addiction and Related Clinical Problems*. 19(2); 2017. Available at:[http://www.zora.uzh.ch/id/eprint/133002/1/HAT\\_at\\_system\\_level.pdf](http://www.zora.uzh.ch/id/eprint/133002/1/HAT_at_system_level.pdf).
59. British Columbia Ministry of Health. Service Model and Provincial Standards for Adult Residential Substance Use Services. September 011. Available at: <http://www.health.gov.bc.ca/library/publications/year/2011/adult-residential-treatment-standards.pdf>.
60. Substance Abuse and Mental Health Services Administration. A Collaborative Approach to the Treatment of Pregnant Women with Opioid Use Disorders. HHS Publication No. (SMA) 16-4978. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2016. Available at: <http://store.samhsa.gov/>.
61. Mandell, Kara, and Werner, Deborah. Guidance to States: Treatment Standards for Women with Substance Use Disorders. National Association of State Alcohol and Drug Abuse Directors, 2008. Available at: <http://nasadad.org/wp-content/uploads/2010/12/Guidance-to-States-Treatment-Standards-for-Women.pdf>.
62. Carter RE, Haynes LF, Back SE, et al. Improving the transition from residential to outpatient addiction treatment: gender differences in response to supportive telephone calls. *The American journal of drug and alcohol abuse*. 2008;34(1):47-59.
63. Terplan M. The obstetric and neonatal impact of maternal opioid detoxification in pregnancy. *American journal of obstetrics and gynecology*. 2014;210(4):375-376.
64. Dashe JS, Jackson GL, Olscher DA, Zane EH, Wendel GD, Jr. Opioid detoxification in pregnancy. *Obstetrics and gynecology*. 1998;92(5):854-858.
65. Bell J, Towers CV, Hennessy MD, Heitzman C, Smith B, Chattin K. Detoxification from opiate drugs during pregnancy. *American journal of obstetrics and gynecology*. 2016;215(3):374.e371-376.
66. Tran TH, Griffin BL, Stone RH, Vest KM, Todd TJ. Methadone, Buprenorphine, and Naltrexone for the Treatment of Opioid Use Disorder in Pregnant Women. *Pharmacotherapy*. 2017.
67. Hulse G, O'Neil G. Using naltrexone implants in the management of the pregnant heroin user. *The Australian & New Zealand journal of obstetrics & gynaecology*. 2002;42(5):569-573.
68. Hulse GK, O'Neil G, Arnold-Reed DE. Methadone maintenance vs. implantable naltrexone treatment in the pregnant heroin user. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*. 2004;85(2):170-171.
69. Meyer M, Paranya G, Keefer Norris A, Howard D. Intrapartum and postpartum analgesia for women maintained on buprenorphine during pregnancy. *European Journal of Pain*. 2010;14(9):939-943.
70. Meyer M, Wagner K, Benvenuto A, Plante D, Howard D. Intrapartum and postpartum analgesia for women maintained on methadone during pregnancy. *Obstetrics and gynecology*. 2007;110(2 Pt 1):261-266.

71. Safley RR, Swietlikowski J. Pain Management in the Opioid-Dependent Pregnant Woman. *The Journal of perinatal & neonatal nursing*. 2017;31(2):118-125.
72. Pan A, Zakowski M. Peripartum Anesthetic Management of the Opioid-tolerant or Buprenorphine/Suboxone-dependent Patient. *Clinical obstetrics and gynecology*. 2017;60(2):447-458.
73. Sen S, Arulkumar S, Cornett EM, et al. New Pain Management Options for the Surgical Patient on Methadone and Buprenorphine. *Current pain and headache reports*. 2016;20(3):16.
74. Helmbrecht GD, Thiagarajah S. Management of addiction disorders in pregnancy. *Journal of addiction medicine*. 2008;2(1):1-16.
75. Albright B, de la Torre L, Skipper B, Price S, Abbott P, Rayburn W. Changes in methadone maintenance therapy during and after pregnancy. *Journal of substance abuse treatment*. 2011;41(4):347-353.
76. Pace CA, Kaminetzky LB, Winter M, et al. Postpartum changes in methadone maintenance dose. *Journal of substance abuse treatment*. 2014;47(3):229-232.
77. Mattocks KM, Clark R, Weinreb L. Initiation and Engagement with Methadone Treatment among Pregnant and Postpartum Women. *Women's Health Issues*. 2017.
78. Abrahams RR, Kelly SA, Payne S, Thiessen PN, Mackintosh J, Janssen PA. Rooming-in compared with standard care for newborns of mothers using methadone or heroin. *Canadian Family Physician*. 2007;53(10):1722-1730.
79. Holmes AV, Atwood EC, Whalen B, et al. Rooming-In to Treat Neonatal Abstinence Syndrome: Improved Family-Centered Care at Lower Cost. *Pediatrics*. 2016;137(6).
80. McKnight S, Coe H, Davies G, et al. Rooming-in for Infants at Risk of Neonatal Abstinence Syndrome. *American journal of perinatology*. 2016;33(5):495-501.
81. Saiki T, Lee S, Hannam S, Greenough A. Neonatal abstinence syndrome--postnatal ward versus neonatal unit management. *European journal of pediatrics*. 2010;169(1):95-98.
82. Jansson LM, Choo R, Velez ML, et al. Methadone maintenance and breastfeeding in the neonatal period. *Pediatrics*. 2008;121(1):106-114.
83. Wilbourne P, Wallerstedt C, Dorato V, Curet LB. Clinical management of methadone dependence during pregnancy. *The Journal of perinatal & neonatal nursing*. 2001;14(4):26-45.
84. Lindemalm S, Nydert P, Svensson JO, Stahle L, Sarman I. Transfer of buprenorphine into breast milk and calculation of infant drug dose. *Journal of human lactation : official journal of International Lactation Consultant Association*. 2009;25(2):199-205.
85. Abrahams RR, MacKay-Dunn MH, Nevmerjitskaia V, MacRae GS, Payne SP, Hodgson ZG. An evaluation of rooming-in among substance-exposed newborns in British Columbia. *Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC*. 2010;32(9):866-871.
86. McQueen K, Murphy-Oikonen J. Neonatal Abstinence Syndrome. *N Engl J Med*. 2016;375(25):2468-2479.
87. Stover MW, Davis JM. Opioids in pregnancy and neonatal abstinence syndrome. *Seminars in perinatology*. 2015;39(7):561-565.
88. Lacaze, T; O'Flaherty, P. Management of infants Born to Mothers Who Have Used Opioids During Pregnancy. *The Canadian Paediatric Society*; Jan 11, 2018. Available at: <https://www.cps.ca/en/documents/position/opioids-during-pregnancy>.
89. Kaltenbach K, Jones HE. Neonatal Abstinence Syndrome: Presentation and Treatment Considerations. *Journal of addiction medicine*. 2016;10(4):217-223.
90. Lazic Mitrovic T, Mikovic Z, Mandic V, et al. Neonatal Abstinence Syndrome - Diagnostic Dilemmas in the Maternity Ward. *Srpski arhiv za celokupno lekarstvo*. 2015;143(9-10):573-577.
91. Logan BA, Brown MS, Hayes MJ. Neonatal abstinence syndrome: treatment and pediatric outcomes. *Clinical obstetrics and gynecology*. 2013;56(1):186-192.
92. Kraft WK, Adeniyi-Jones SC, Chervoneva I, et al. Buprenorphine for the Treatment of the Neonatal Abstinence Syndrome. *N Engl J Med*. 2017;376(24):2341-2348.
93. Grossman MR, Berkwitz AK, Osborn RR, et al. An Initiative to Improve the Quality of Care of Infants With Neonatal Abstinence Syndrome. *Pediatrics*. 2017;139(6).
94. Grossman MR, Lipshaw MJ, Osborn RR, Berkwitz AK. A Novel Approach to Assessing Infants With Neonatal Abstinence Syndrome. *Hospital pediatrics*. 2018;8(1):1-6.
95. Osborn DA, Jeffery HE, Cole MJ. Opiate treatment for opiate withdrawal in newborn infants. *Cochrane Database Syst Rev*. 2010(10):Cd002059.
96. Ordean A, Kahan M, Graves L, Abrahams R, Kim T. Obstetrical and neonatal outcomes of methadone-maintained pregnant women: a canadian multisite cohort study. *Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC*. 2015;37(3):252-257.
97. Wall-Wieler E, Roos LL, Bolton J, Brownell M, Nickel NC, Chateau D. Maternal health and social outcomes after having a child taken into care: population-based longitudinal cohort study using linkable administrative data. *Journal of Epidemiology and Community Health*. 2017;71(12):1145.
98. Turney K, Wildeman C. Mental and Physical Health of Children in Foster Care. *Pediatrics*. 2016;138(5).
99. Vinnerljung B, Hjern A, Lindblad F. Suicide attempts and severe psychiatric morbidity among former child welfare clients – a national cohort study. *Journal of Child Psychology and Psychiatry*. 2006;47(7):723-733.

