

Substance Use in Pregnancy

This clinical practice guideline has been prepared by the Working Group on Problematic Substance Use in Pregnancy, reviewed by the Maternal Fetal Medicine Committee, the Family Physicians Advisory Committee and the Medico-Legal Committee, and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

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Abstract

Objective: To improve awareness and knowledge of problematic substance use in pregnancy and to provide evidence-based recommendations for the management of this challenging clinical issue for all health care providers.

Options: This guideline reviews the use of screening tools, general approach to care, and recommendations for clinical management of problematic substance use in pregnancy.

Outcomes: Evidence-based recommendations for screening and management of problematic substance use during pregnancy and lactation.

Evidence: Medline, PubMed, CINAHL, and The Cochrane Library were searched for articles published from 1950 using the following key words: substance-related disorders, mass screening, pregnancy complications, pregnancy, prenatal care, cocaine, cannabis, methadone, opioid, tobacco, nicotine, solvents, hallucinogens, and amphetamines. Results were initially restricted to systematic reviews and randomized control trials/controlled clinical trials. A subsequent search for observational studies was also conducted because there are few RCTs in this field of study. Articles were restricted to human studies published in English. Additional articles were located by hand searching through article reference lists. Searches were updated on a regular basis and incorporated in the guideline up to December 2009. Grey (unpublished) literature was also identified through searching the websites of health technology assessment and health technology assessment-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies.

Values: The quality of evidence was rated using the criteria described in the Report of the Canadian Task Force on the Preventive Health Care. Recommendations for practice were ranked according to the method described in that report (Table 1).

Benefits, harms, and costs: This guideline is intended to increase the knowledge and comfort level of health care providers caring for pregnant women who have substance use disorders. Improved access to health care and assistance with appropriate addiction care leads to reduced health care costs and decreased maternal and neonatal morbidity and mortality.

Recommendations

1. All pregnant women and women of childbearing age should be screened periodically for alcohol, tobacco, and prescription and illicit drug use. (III-A)
2. When testing for substance use is clinically indicated, urine drug screening is the preferred method. (II-2A) Informed consent should be obtained from the woman before maternal drug toxicology testing is ordered. (III-B)
3. Policies and legal requirements with respect to drug testing of newborns may vary by jurisdiction, and caregivers should be familiar with the regulations in their region. (III-A)

4. Health care providers should employ a flexible approach to the care of women who have substance use problems, and they should encourage the use of all available community resources. (II-2B)
5. Women should be counselled about the risks of periconception, antepartum, and postpartum drug use. (III-B)
6. Smoking cessation counselling should be considered as a first-line intervention for pregnant smokers. (I-A) Nicotine replacement therapy and/or pharmacotherapy can be considered if counselling is not successful. (I-A)
7. Methadone maintenance treatment should be standard of care for opioid-dependent women during pregnancy. (II-IA) Other slow-release opioid preparations may be considered if methadone is not available. (II-2B)
8. Opioid detoxification should be reserved for selected women because of the high risk of relapse to opioids. (II-2B)
9. Opiate-dependent women should be informed that neonates exposed to heroin, prescription opioids, methadone, or buprenorphine during pregnancy are monitored closely for symptoms and signs of neonatal withdrawal (neonatal abstinence syndrome). (II-2B) Hospitals providing obstetric care should develop a protocol for assessment and management of neonates exposed to opiates during pregnancy. (III-B)
10. Antenatal planning for intrapartum and postpartum analgesia may be offered for all women in consultation with appropriate health care providers. (III-B)
11. The risks and benefits of breastfeeding should be weighed on an individual basis because methadone maintenance therapy is not a contraindication to breastfeeding. (II-3B)

INTRODUCTION

Substance use during pregnancy is common. In national prevalence surveys, 14% of Canadian women reported using alcohol during their last pregnancy, and 17% reported smoking during pregnancy.^{1,2} The prevalence of illicit drug use among Canadian women of childbearing age is less but not insignificant. In United States population surveys ~5% of pregnant women reported illicit drug use during the preceding month.³ Marijuana remains the most commonly used illegal drug, followed by cocaine. Women report higher rates than men of prescription drug use, including pain relievers (23.1%), opioid analgesics (2.1%), sleeping pills (1.7%), tranquilizers (1.1%), and antidepressants (2.1%).²

The use of alcohol and drugs by pregnant women can result in significant maternal, fetal, and neonatal morbidity.⁴⁻¹⁷ In general, pregnant women with substance use disorders are less likely to seek prenatal care, and they have higher rates of infectious diseases such as HIV, hepatitis, and other sexually transmitted infections.¹⁷⁻¹⁹

There are numerous direct and indirect costs of perinatal substance exposure. In 2002, the overall social cost of substance abuse in Canada, including burden on health care, law enforcement, and loss of productivity due to premature death and ill health, totalled ~\$40 billion.²⁰ Data

ABBREVIATIONS

HCV	hepatitis C virus
MMT	methadone maintenance therapy
NAS	neonatal abstinence syndrome
NRT	nicotine replacement therapy
UDS	urine drug screening

Table 1. Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventive Health Care

Quality of evidence assessment*	Classification of recommendations†
I: Evidence obtained from at least one properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action
II-1: Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action
II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category	D. There is fair evidence to recommend against the clinical preventive action
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	E. There is good evidence to recommend against the clinical preventive action
	L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.¹⁶¹

†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the The Canadian Task Force on Preventive Health Care.¹⁶¹

from American studies have indicated that the increase in cost of neonatal care for infants born to mothers who smoke cigarettes is ~\$700, and the increase in cost for those exposed to cocaine is \$5110 per patient.²¹⁻²³

Because of the prevalence of substance use and its clinical and economic impact, health care providers need to know how to identify and care for the affected patient population. Management of substance use disorders is complicated because of the associated comorbid conditions and psychosocial and socioeconomic factors, such as mental health problems, poor housing, financial stressors, and lack of supports. Canadian physicians have identified a lack of knowledge and training regarding the effects of and treatments for substance use during pregnancy as another barrier to providing care for these patients.²⁴ Perinatal care providers have several opportunities during pregnancy to identify and assist women who have substance use problems. Although most physicians enquire routinely about alcohol, tobacco, and other drug use during pregnancy, many do not use a specific screening tool and are not making referrals to other treatment resources.²⁵⁻²⁸ As motivation to change unhealthy or harmful behaviours is increased during pregnancy, it is an ideal time to intervene with women who have substance use problems.

This guideline provides a unified approach to care for perinatal substance use disorders.

DEFINITIONS

Substance abuse and dependence have well-defined criteria based on the DSM-IV guide (Table 2).²⁹ Substance dependence is characterized by compulsive drug use, loss of control over use, and physical, social, and psychological consequences.³⁰ Physical dependence is characterized by tolerance and withdrawal; however, it is not in itself sufficient to make a diagnosis of substance dependence. Substance withdrawal consists of a combination of drug-specific symptoms and signs that occur within hours to days of stopping drug use (Table 3).

IDENTIFICATION OF SUBSTANCE-RELATED DISORDERS IN PREGNANCY

Screening and Assessment

All pregnant women regardless of socioeconomic status should be asked about past and current alcohol, nicotine, and illicit and prescribed drug use. A high index of suspicion for potential substance use during pregnancy is required in various clinical situations.³¹ There is no optimal screening tool for identifying substance use in pregnancy. Maternal interview using open-ended, non-judgemental questioning is more likely to elicit disclosure of perinatal substance use.^{31,32} Health care providers should develop their own level of comfort and style in asking their patients about this sensitive topic. The T-ACE and TWEAK questionnaires were developed for screening at-risk perinatal alcohol use

(Figure 1).^{33,34} The ALPHA tool incorporates the CAGE questionnaire to screen for maternal recreational drug use, as well as validated questions to identify associated psychosocial risk factors such as family violence or postpartum depression (Appendix).^{35,36} If the woman acknowledges substance use, a more complete assessment is then recommended to determine if there is a history of substance abuse or dependence (Figure 2).

Role of Toxicology Testing

Drug toxicology testing is not recommended for universal screening (i.e., routine testing of all women) because it has numerous limitations (Figure 3), and it should be considered only after a comprehensive assessment if there is a clinical indication.³⁷ If a woman is concerned about providing a sample or is reluctant to do so, clinicians should focus on developing a trusting relationship before suggesting toxicology testing. Vulnerable women may feel threatened if clinicians wish to gather detailed information through drug testing and psychosocial histories.

Urine, hair, and meconium samples are sensitive biological markers of substance use. Urine drug screening can detect only recent substance exposure, while neonatal hair and meconium testing can document intrauterine use because meconium and hair form in the second and third trimester, respectively.³⁸⁻⁴¹ By itself, a single positive test result cannot be used to diagnose substance dependence. Although child protection agencies sometimes request hair analyses, neither hair nor meconium is appropriate for routine clinical use because of the high costs and propensity for false positive results.

UDS has several clinical indications. Evidence shows that the addition of urine drug testing to the structured maternal interview can increase the detection of problematic substance use in pregnancy.^{42,43} Detection can facilitate early intervention, including treatment of maternal and neonatal withdrawal and counselling and referral for long-term outpatient treatment. For example, an unexpected positive UDS result for opioids may prompt an assessment for opioid dependence and observation of the neonate for signs of withdrawal. Ongoing outpatient monitoring with UDS is also used to advocate on behalf of patients with child protection services and to monitor compliance with prescribed medications (e.g., opioids).^{34,38} In addition, it can be performed on maternal request.

Informed consent must be obtained and documented in the medical record before any maternal drug testing is performed (except in life-threatening situations where informed consent is impossible).⁴⁴ If the mother refuses,

Table 2. Definitions of substance-related disorders

Substance use disorder	Definition
Substance dependence	A pattern of substance use, leading to clinically significant impairment or distress, as manifested by ≥ 3 of the following, occurring at any time in the same 12-month period: <ol style="list-style-type: none"> 1. tolerance 2. withdrawal 3. substance taken in larger amounts or over a longer period than was intended 4. persistent desire or unsuccessful efforts to cut down or control substance use 5. a great deal of time spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain-smoking), or recover from its effects 6. important social, occupational, or recreational activities given up or reduced because of substance use 7. continued use despite knowledge of harm
Substance abuse	A pattern of substance use leading to clinically significant impairment or distress, as manifested by ≥ 1 of the following, occurring within a 12-month period: <ol style="list-style-type: none"> 1. recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home 2. recurrent substance use in situations in which it is physically hazardous 3. recurrent substance-related legal problems 4. persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance
Tolerance	Characterized by a need for markedly increased amounts of the substance to achieve desired effect or diminished effect with continued use of the same amount of the substance

this should be documented, and testing should not be performed. Neonatal toxicology testing may be performed without consent of the parent(s) if the person requesting this testing has a legislative right to make decisions for the infant to be tested. However, the mother should be informed that the neonate is being tested.³⁴ Once consent is obtained, any drug toxicology testing to be performed must be ordered by the physician responsible for maternal and/or neonatal care.

Recommendations

1. All pregnant women and women of childbearing age should be screened periodically for alcohol, tobacco, and prescription and illicit drug use. (III-A)

Table 3. Withdrawal syndromes

Substance	Withdrawal symptoms and signs
Nicotine	Irritability, restlessness, anxiety, insomnia, fatigue, poor concentration
Marijuana	Irritability, insomnia, anorexia, anxiety
Opioids	Influenza-like symptoms: myalgias, rhinorrhea, goosebumps, diaphoresis, nausea, vomiting, diarrhea Psychological symptoms: insomnia, anxiety, strong cravings, dysphoria Obstetrical symptoms: abdominal cramping, uterine irritability
Benzodiazepines	Seizures (high dose), anxiety, panic attacks, insomnia, emotional lability
Cocaine/amphetamines	Crash phase: fatigue, increased appetite Withdrawal dysphoria phase: dysphoria, irritability, insomnia, strong cravings
Inhalants	Similar to alcohol withdrawal: tremor, malaise, gastrointestinal symptom

- When testing for substance use is clinically indicated, urine drug screening is the preferred method. (II-2A)
Informed consent should be obtained from the woman before maternal drug toxicology testing is ordered. (III-B)
- Policies and legal requirements with respect to drug testing of newborns may vary by jurisdiction, and caregivers should be familiar with the regulations in their region. (III-A)

COMPONENTS OF OFFICE MANAGEMENT

Obstetrical care providers need to establish rapport with substance-using pregnant women through good communication and a willingness to be flexible in providing prenatal care and ongoing support. These women face a number of barriers to receiving optimal prenatal care (Figure 4).⁴⁵⁻⁴⁸ Flexibility with respect to patient scheduling and understanding late arrivals and missed appointments are key to engaging these women for prenatal care. Women are likely to seek and commit to prenatal care if health care providers are welcoming and non-judgemental, and if they acknowledge the women's courage and persistence in the face of very difficult personal circumstances. Studies have shown that comprehensive care provided at one site is cost-effective and produces better outcomes for both mother and child.^{9,19,49-58}

It is also important to address women's substance use because pregnancy is an ideal time for women to make a change. Harm reduction is defined as a program or policy designed to reduce the drug-related harm without requiring the cessation of drug use.³⁰ The philosophy of care for women with problematic substance use in pregnancy is harm reduction. Components of this philosophy include encouragement of abstinence or reduction of use, safe

use, treatment of withdrawal symptoms, counselling and/or pharmacotherapy. Pregnancy may motivate women to abstain from or reduce drug use, given the potential effects on fetal outcomes.

Pregnant substance-using women are also at increased risk of infectious diseases. Injection drug use remains the most dominant mode of hepatitis C virus acquisition. Approximately, 70% to 80% of HCV-infected patients report a history of current or past injection drug use.⁵⁹ HCV-negative women should be advised about ways to prevent exposure to HCV. Women should be told not to share materials to prepare, inject, or inhale drugs, and that they should not engage in higher risk sexual behaviours (e.g., unprotected sex with multiple sexual partners or unprotected sex with HCV-positive partners). Pregnant HCV-infected women have a 5% chance of transmitting the virus to their infants.⁶⁰ There are no ways to decrease the risk of vertical transmission. Furthermore, mode of delivery and breastfeeding do not affect mother-to-infant transmission. Procedures that promote mixing of maternal and fetal blood, such as use of scalp electrodes, should be avoided, if possible. Serology testing of infants at 12 to 18 months of age is recommended to determine HCV status.

The prevalence of sexually transmitted infections is also higher among pregnant women with a history of substance abuse related to high-risk sexual behaviours.^{61,62} Screening for Chlamydia, gonorrhoea, syphilis, hepatitis, and HIV should be repeated throughout pregnancy if historical factors warrant it.⁶³

There are numerous adverse effects associated with prenatal drug exposure (Table 4). These effects may also be linked to other factors such as inadequate prenatal care, poor social circumstances, and concomitant use of other substances.^{64,65} Therefore, long-term studies are difficult to

Figure 1. T-ACE and TWEAK for problematic alcohol use

<p>T-ACE</p> <p>T How many drinks does it take to make you feel high? (Tolerance)</p> <p>A Have people annoyed you by criticizing your drinking?</p> <p>C Have you felt you ought to cut down on your drinking?</p> <p>E Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover? (Eye-opener)</p> <p>Scoring: T: 2 points if > 3 drinks; A,C,E: 1 point for each yes answer</p> <p>A total of 2 or more points indicates patient is likely to have an alcohol problem.</p> <p>TWEAK</p> <p>T Tolerance</p> <p>W Have friends or relatives complained about your drinking? (Worried)</p> <p>E Eye-opener</p> <p>A Has a friend or family member ever told you about things you said or did while you were drinking that you could not remember? (Amnesia or black-out)</p> <p>K Cut-down</p> <p>Scoring: T: 2 points if > 3 drinks; W, E, A, K: 1 point for each yes answer</p> <p>A total of score of 3 or more points indicates patient is at-risk drinking</p>
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Figure 2. Assessment for substance-related disorders

<p>Complete drug history: name of drug, amount, frequency, duration, route(s), last use, injection drug use, sharing needles/paraphernalia, withdrawal symptoms</p> <p>Stage of change with respect to substance use</p> <ul style="list-style-type: none"> • Consequences of drug use: medical, social, personal • Previous treatment programs, mutual aid groups (e.g., AA) <p>Medical history: HIV, Hepatitis B and C, STIs</p> <ul style="list-style-type: none"> • Chronic medical conditions (e.g., chronic pain), medications <p>Psychiatric history: eating disorders, sexual/physical abuse, mood and anxiety disorders</p> <p>Obstetrical history: cycle regularity, LMP, past obstetrical outcomes and complications</p> <p>Social history: family situation (partner and number of children), custody status, housing situation, legal status (current charges and court dates), finances, nutrition, child protection agency involvement, child safety concerns</p> <p>FIFE: feelings, impressions/ideas, functioning, expectations about pregnancy and drug use</p>

interpret because effects may be due to these confounders and environmental deprivation rather than the drug itself. In addition to routine care, patients should be given counselling regarding the drug-specific fetal, neonatal, and maternal effects of substance use.

Antenatal fetal surveillance should be based on obstetrical indications rather than solely on substance use. Substance use during pregnancy has been associated with obstetrical complications such as preterm labour, placental abruption, and intrauterine growth restriction (Table 4), and these adverse effects may lead to an increased risk of perinatal morbidity and mortality. Therefore, the method and

frequency of antenatal testing will be determined by the presence or absence of these complications.⁶⁶

There are two phases to the management of substance use disorders. The first addresses treatment of withdrawal syndromes. Pregnant women who are dependent on alcohol, opioids, or high-dose benzodiazepines (> 50 mg daily diazepam equivalent) may require medical detoxification under the supervision of a physician (Table 5).³⁰ Women who are in withdrawal from other substances, such as cocaine or marijuana, may also benefit from a supportive admission to a non-medical withdrawal management centre, if available.

Figure 3. Limitations of drug toxicology

- Women can avoid detection of substances in urine samples through simple measures such as abstaining for 1–3 days before testing, drinking lots of water to lower the concentration of the drug in the urine, or substituting samples of another person's urine for their own
- Alcohol is very hard to detect with laboratory testing (blood and urine sampling) because of its short half-life
- The amount of drug in a hair sample correlates with degree of drug use (which is not the case with urine drug testing); however, a positive finding is not diagnostic of addiction
- Hair analysis can have false-positive results due to passive exposure to smoked drugs in environment
- A false positive result can have serious legal and emotional consequences for the mother

Figure 4. Barriers to prenatal care for pregnant substance-using women

- Personal factors: shame, stigma, guilt, lack of family support, substance using male partner, fear of losing children, concomitant psychosocial issues (e.g., transportation, child care)
- Systemic factors: lack of appropriate treatment services for pregnant women, negative attitudes of health care providers

The second phase focuses on relapse prevention by encouraging substance abuse treatment and development of a supportive network. Brief interventions can range from simple physician advice to motivation counselling sessions consisting of goal setting, problem solving with respect to triggers, and information on potential harms. These interventions are effective in reducing alcohol use among pregnant women.^{67,68} Currently, there are no research data on the effectiveness of similar interventions for illicit substance use in pregnancy. However, systematic reviews have shown that outpatient psychotherapy for cannabis dependence is moderately effective at reducing substance use in non-pregnant patients.^{69,70} Therefore, physician counselling may also be of benefit to pregnant women. Pharmacological maintenance options are available for management of nicotine and opioid dependence. Evidence suggests that enhanced treatment programs for opioid dependence that combine methadone maintenance therapy, group psychotherapy, and obstetrical care result in less overall illicit substance use, improved prenatal care, and lower rates of obstetrical complications.^{19,52,71–73} Evaluation of comorbid conditions should include screening for depression, anxiety, and other mental health disorders, domestic violence and abuse, and psychosocial support system. Most women in substance abuse treatment programs report a past history of trauma (including physical and sexual abuse), and approximately 25% have been diagnosed with posttraumatic stress disorder.^{74–76} Partner involvement in prenatal care and addiction treatment is critical to recovery.⁵⁶ A partner's active drug use has been linked to delayed treatment time for women seeking care.^{77,78} Similarly, women with fewer social supports are less likely to seek and to remain in treatment.^{79,80} Appropriate referrals may include counselling to deal with pre-existing trauma and assistance with other social determinants of

health (e.g., food and housing). The cornerstone of care of problematic substance use in pregnant women is harm reduction. Components of this include encouragement of abstinence or reduction of use, safe use, treatment of withdrawal, counselling, and/or pharmacotherapy.

Any health care provider who has a clinical suspicion based on history and/or physical examination that a child is or may be in need of protection because of abuse or neglect must make a report to child protection services.⁸¹ Health care professionals should be aware of province-specific legislation with respect to child welfare and reporting responsibilities. Clinicians are not required to report until birth, because unborn babies do not have any legal rights, but antenatal self-reporting is encouraged to increase maternal self-determination, dignity, and stability and the establishment of a treatment plan. However, if other children present in the home are deemed to be at risk, earlier referral to child protection is indicated to ensure the safety of these children. Health care professionals should advocate on behalf of women involved with child protection agencies and should encourage a positive relationship between mothers and workers. A history of substance dependence is not incompatible with ability to parent.

Recommendations

4. Health care providers should employ a flexible approach to the care of women who have substance use problems, and they should encourage the use of all available community resources. (II-2B)
5. Women should be counselled about the risks of periconception, antepartum, and postpartum drug use. (III-B)

Table 4. Effects of antenatal substance use

Drug	Antenatal complications	Neonatal effects	Long-term effects
Nicotine	<ul style="list-style-type: none"> • SA • PTL, PROM • Placenta previa and placental abruption • IUGR, LBW 	<ul style="list-style-type: none"> • Increased perinatal mortality • SIDS 	<ul style="list-style-type: none"> • Childhood asthma • Behavioural problems • ADHD
Marijuana	<ul style="list-style-type: none"> • Inconsistent effects 	<ul style="list-style-type: none"> • Neurobehavioural effects: decreased self-quieting ability, increased fine tremors and startles, increased hand-to-mouth activity, sleep pattern changes 	<ul style="list-style-type: none"> • Disturbed nocturnal sleep • Behaviour problems: inattention, impulsivity and hyperactivity, delinquency and externalizing problems self-reported depressive and anxiety symptoms
Heroin	<ul style="list-style-type: none"> • Premature labour • IUGR, LBW • Toxemia • Antepartum and postpartum hemorrhage 	<ul style="list-style-type: none"> • Increased perinatal mortality rate 	<ul style="list-style-type: none"> • Increased inattention, hyperactivity and behavioural problems • Difficulty in physical, social, and self-adjustment and learning processes
Methadone		<ul style="list-style-type: none"> • NAS • Strabismus 	
Cocaine	<ul style="list-style-type: none"> • Spontaneous abortion • PROM, PTL • IUGR • Placental abruption 	<ul style="list-style-type: none"> • Congenital anomalies: genitourinary malformations • Transient increase in central and autonomic nervous system symptoms and signs • Lower birth weight, length and head circumference (dose-dependent) 	<ul style="list-style-type: none"> • Expressive language delays
Amphetamines	<ul style="list-style-type: none"> • Maternal hypertension • Fetal demise (at any gestational age) • IUGR 	<ul style="list-style-type: none"> • Congenital anomalies: central nervous system, cardiovascular, oral clefts, limbs • Neurobehavioural effects: decreased arousal, increased stress and poor quality of movement (dose-response relationship) 	<ul style="list-style-type: none"> • Behavioural problems
Hallucinogens (MDMA, LSD)		<ul style="list-style-type: none"> • Congenital anomalies: cardiovascular, MSK defects 	

ADHD: attention-deficit hyperactivity disorder; IUGR: intrauterine growth restriction; LBW: low birth weight; LSD: lysergic acid diethylamide; MDMA: 3,4-methylenedioxymethamphetamine; MSK: medullary sponge kidney; PTL: preterm labour; PROM: premature rupture of membranes; SA: spontaneous abortion; SIDS: sudden infant death syndrome.

NICOTINE DEPENDENCE

Smoking Cessation Counselling

Smoking cessation interventions are effective in reducing the number of women smoking during pregnancy regardless of intensity or provider delivering the intervention.⁸²⁻⁸⁷ Lower rates of preterm delivery and low birth weight infants are additional benefits of smoking cessation interventions. A variety of interventions have been studied ranging from simple advice to cognitive behavioural strategies for quitting smoking. Women also often received pregnancy-specific self-help materials and telephone counselling to support smoking cessation.

These interventions are estimated to be highly cost-effective with savings of US\$3 in health-related costs for every US\$1 spent on smoking cessation for pregnant women.⁸⁸ However, brief interventions are ineffective in preventing postpartum relapse to smoking.⁸⁹

Pharmacotherapy

Controlled trials have failed to demonstrate that nicotine replacement therapy increases smoking cessation rates, although it may reduce the number of cigarettes smoked.^{90,91} NRT (gum, lozenge, or patch), combined with cognitive behavioural therapy, results in higher quit rates during pregnancy than counselling alone.⁹² The safety of NRT is unknown since the link between NRT and congenital anomalies and poor perinatal outcomes is uncertain.^{90,92-96} However, women may be offered NRT if they continue to smoke despite counselling and after an informed discussion regarding the benefits and risks during pregnancy.^{82,83,97,98} Intermittent dosage NRT preparations such as nicotine gum or nasal spray may be preferable to the patch, which gives a continuous dose of nicotine. The lowest effective dose of NRT is advised. If the patch is used, the patient may consider removing it at night. NRT should be discontinued if the woman continues to smoke at the same rate.

Table 5. Management of withdrawal

Substance	Management recommendation
Alcohol	<ul style="list-style-type: none"> • Thiamine 100 mg po od × 3 days, folic acid 5 mg po od • Diazepam 20 mg po q1–2h until minimal symptoms • Use lorazepam 2–4 mg sl/po q2–4h prn during labour • Monitor hydration status and electrolyte levels
High-dose benzodiazepines	<ul style="list-style-type: none"> • Start at 2/3–3/4 of diazepam equivalent dose • Taper by 10% per day
Opioids	<ul style="list-style-type: none"> • Offer symptomatic therapy including gravol for nausea and vomiting, acetaminophen/NSAIDs for myalgias • Consider methadone or buprenorphine initiation • Can use morphine 5–10 mg po q4–6h prn if methadone is not available

NSAIDs: non-steroidal anti-inflammatories

Bupropion and varenicline are effective in non-pregnant populations. There are limited safety data on the use of these medications during pregnancy.^{82,83,97} To date, bupropion has not been associated with malformations during pregnancy.^{83,97,99} Preliminary evidence from a small study suggests that bupropion is effective for smoking cessation during pregnancy.¹⁰⁰ Further research is needed on the safety and efficacy of bupropion and varenicline before they can be recommended for routine use in pregnancy.

Recommendation

6. Smoking cessation counselling should be considered as a first-line intervention for pregnant smokers. (I-A)
Nicotine replacement therapy and/or pharmacotherapy can be considered if counselling is not successful. (I-A)

OPIOID DEPENDENCE

Opioid Detoxification

Opioid detoxification is defined as medication-assisted withdrawal for opioid-dependent patients. There is good evidence that detoxification in the second and third trimesters of pregnancy is not linked to increased adverse perinatal events. Recent studies have failed to show any significant increased rates of obstetrical complications following opioid detoxification.^{91,93,94,101} Regardless, opioid detoxification is not advisable during pregnancy primarily because of the high rate of relapse.^{102–106} Opioid detoxification should be performed only after the first trimester and with informed consent based on a discussion of the potential risks and benefits. Methadone maintenance treatment is associated with longer adherence to treatment and decreased risk of relapse to opioid use; therefore, the standard of care for pregnant opioid-dependent women is opiate substitution therapy.

Methadone Maintenance Treatment

Currently, methadone maintenance treatment is the standard of care for opioid dependence in pregnancy. Methadone is

a full opioid agonist that has an increasing effect with higher doses. There are numerous benefits of methadone use during pregnancy, including improved prenatal care,^{12,107–109} longer gestation,^{50,110} higher birth weight,^{111,112} and increased rates of infants discharged home in the care of their mothers.^{4,12,18,49,101,108,113–118} Although infants of methadone-treated women tend to be smaller (lower birth weight, length, and head circumference) than drug-free controls, studies have shown a catch-up of growth by 12 months of age.^{118,119} Urgent consultation with an addiction medicine specialist should be sought to facilitate rapid access to MMT during pregnancy. Close monitoring of methadone dosing during pregnancy is recommended, especially during the third trimester when methadone metabolism and clearance are increased and dose augmentation is required.^{120,121} Pregnant women should receive the methadone dose that is required for their opioid dependence, because the literature reports inconsistent results regarding the association between maternal methadone dose and severity of neonatal withdrawal. Prenatal discussion with the methadone prescribing physician is recommended to plan for intrapartum methadone dosing.

Any regular, daily antenatal opioid exposure (e.g., morphine, codeine, oxycodone, methadone, or buprenorphine) can produce neonatal withdrawal, also known as neonatal abstinence syndrome. Estimates show that up to 96% of infants display withdrawal symptoms, and a smaller proportion require pharmacotherapy.^{4,68,116,117,120,121} NAS is characterized by respiratory, gastrointestinal, central nervous system, and autonomic symptoms (Table 6). Onset of withdrawal symptoms is dependent on the opiate's half-life; the longer the half-life, the later the onset of withdrawal. Heroin-exposed infants may demonstrate symptoms within 24 hours of birth. In comparison, methadone-maintained infants have a delayed presentation at more than 24 hours, usually within 48 to 72 hours after birth and at up to 4 weeks of age.¹²² The length of monitoring is based on

the specific drug exposure. Treated neonatal withdrawal has not been associated with any long-term complications.

A variety of standards of practice have been documented in Canadian hospitals with variability by region and practitioner. Little research is available to validate current practices. Several scoring scales have been developed for evaluation of NAS and response to therapy. The Finnegan scoring tool (also known as the Finnegan Neonatal Abstinence Scoring System) is the method most commonly used by Canadian hospitals.¹²³ Non-pharmacologic therapy is the standard of care for all opioid-exposed infants.¹²⁴ For a smaller subset of infants, pharmacotherapy may be needed to treat severe symptoms. Opioid agonist medications are the most effective agents for treatment of NAS.^{122,125} Options include morphine, methadone, and diluted tincture of opium (contains small amount of alcohol). Morphine is the most frequently used medication.^{122,123} Phenobarbital may be used as an adjunct to treat infants who are not well-controlled using an opioid alone. One half of Canadian hospitals care for substance-exposed infants in the neonatal care unit or special care nursery. The other half provide care for asymptomatic infants with the mother as part of rooming-in. One retrospective cohort study demonstrated that rooming-in, under the care of supportive nursing and medical staff, was associated with decreased rates and length of morphine treatment, decreased need for admission to an NICU, decreased mean neonatal length of stay in hospital, and increased likelihood of discharge in the custody of the mother.¹²⁶ Additional large-scale prospective studies are required to determine the optimal management of neonatal withdrawal.

Buprenorphine

Buprenorphine represents an alternative opioid replacement treatment. Buprenorphine is a partial agonist with a ceiling effect. It has typical opioid effects with less sedation than methadone and a threshold after which a higher dose has no further effect, thereby reducing the risk of overdose on this medication.¹²⁷ The main rationale for buprenorphine use for treating opioid dependence during pregnancy is reports of reduced incidence and severity of NAS^{128–131}; however, there are limited data regarding the long-term effects of in utero exposure to buprenorphine.^{132,133} Buprenorphine should be prescribed by a physician who has experience with substitution treatment for opioid dependence. The only preparation of buprenorphine readily available in Canada is Suboxone, which is a combination of buprenorphine and naloxone. There is limited information on the safety of this medication in pregnancy; therefore, the use of buprenorphine as a single agent (Subutex) is recommended

Table 6. Neonatal abstinence syndrome

System	Symptoms and signs
Respiratory	Respiratory distress
Central nervous system	Increased tone, tremors, seizure
Gastrointestinal	Poor feeding, vomiting, regurgitation, diarrhea
Autonomic	Sweating

during pregnancy. The availability of buprenorphine during pregnancy is limited through Health Canada's Special Access Program.

OPIOIDS FOR CHRONIC NON-CANCER PAIN

Pregnant women with a history of chronic pain need to be managed according to evidence-based recommendations for chronic non-cancer pain.^{134,135} The goal of therapy is to use the lowest effective dose of scheduled controlled-release opioids.¹³⁴ Most women who use opioids for chronic non-cancer pain are not psychologically dependent on these medications. Risk factors for dependence on prescription opioids include past history of drug dependence and psychiatric comorbid conditions such as posttraumatic stress disorder and eating disorders. Regular opioid use for pain management during pregnancy is associated with neonatal withdrawal.^{136,137} Methadone is the first-line treatment for chronic non-cancer pain and concurrent opioid dependence.

Recommendations

- Methadone maintenance treatment should be standard of care for opioid-dependent women during pregnancy. (II-1A) Other slow-release opioid preparations may be considered if methadone is not available. (II-2B)
- Opioid detoxification should be reserved for selected women because of the high risk of relapse to opioids. (II-2B)
- Opiate-dependent women should be informed that neonates exposed to heroin, prescription opioids, methadone, or buprenorphine during pregnancy are monitored closely for symptoms and signs of neonatal withdrawal (neonatal abstinence syndrome). (II-2B) Hospitals providing obstetric care should develop a protocol for assessment and management of neonates exposed to opiates during pregnancy. (III-B)

PERIPARTUM PAIN MANAGEMENT

Women with substance use disorders, especially those with opioid dependence, face numerous peripartum pain management challenges, including increased pain sensitivity, inadequate analgesia, difficult intravenous access, and anxiety about suffering pain due to their history of addiction.^{138–142} Inappropriate pain management is more likely than provision of opioid analgesics for treatment of acute pain to lead to a relapse. Women on MMT should be continued on the same dose of methadone, although this is ineffective for acute pain management.^{138,142} Opioids have been found to be safe and effective even in opioid-dependent women; however, these women may require higher doses and more frequent analgesics for pain relief.^{138,142,143} Epidural analgesia is an ideal choice for pain management for opioid-dependent women. Agonist-antagonist medications (e.g., butorphanol, nalbuphine, and pentazocine) should not be used in opioid-dependent individuals because of the risk of precipitating acute withdrawal. For more complicated cases (e.g., poor venous access, contraindications to epidural), referral to an anaesthesiologist should be arranged antenatally to discuss, in advance, alternatives for pain management.

Recommendation

10. Antenatal planning for intrapartum and postpartum analgesia may be offered for all women in consultation with appropriate health care providers. (III-B)

MANAGEMENT OF OPIOID OVERDOSE

Education about prevention of opioid overdose should also be provided routinely. This includes advising patients that they could overdose if they suddenly stop or markedly reduce their opioid medication and then resume their usual dose. They are also at risk of overdose if they combine opioids with other sedatives, such as benzodiazepines. They should be warned never to give or sell their opioid medication to anyone else, because others may lack tolerance to opioids. Finally, they should be advised to contact a physician immediately at the first signs of overdose (“nodding off,” slurred speech, drowsiness).

Acute opioid overdose during pregnancy can be managed with respiratory support and the use of naloxone, a short-acting opioid antagonist, as a last resort after an airway has been established. The dose of naloxone should be based on response to treatment and duration of action of ingested opioid. Naloxone may be required on a continuous basis until the effects of the opioid have diminished. Care should be taken to prevent acute withdrawal symptoms, which

can cause fetal distress.¹⁴⁴ On the basis of gestational age and viability, the fetus should be monitored throughout treatment. Similarly, during neonatal resuscitation, naloxone should not be administered to a newborn of an opioid-dependent mother because of the risk of precipitating acute withdrawal and seizures.

POSTPARTUM CARE

Substance-using women require additional supports from health care professionals in the postpartum period. More frequent visits may be required to deal with their complex medical and psychosocial needs. Areas to review include the following:

- Support of breastfeeding, as appropriate (see paragraph below for more details)
- Follow-up of other medical problems such as liver disease and sexually transmitted infections
- Discussion of contraceptive needs
- Surveillance and appropriate referral for treatment of postpartum mood and anxiety disorders
- Assessment of substance use and encouragement to continue attending drug treatment programs
- Support with child protection services involvement
- Assistance with referrals for ongoing primary care and social services

BREASTFEEDING

Although there are numerous benefits of breastfeeding, alcohol and illicit substances that are commonly abused (e.g., marijuana, cocaine, amphetamines) have been detected in breast milk.^{145–148} There have been reports documenting neonatal effects due to breast milk exposure; therefore, the decision to breastfeed should be made on an individual basis after discussing the potential risks and benefits.^{146,147,149,150} Breastfeeding may be delayed after maternal use of any of these agents and any neonatal exposure to any fumes in the environment. Women who are regular substance users should be encouraged to remain abstinent while nursing and counselled regarding the increased risks for neonatal effects.

All opiates have been documented in breast milk in small amounts and are unlikely to be of any clinical significance.^{106,121,151–157} Specifically, the presentation

and treatment of neonatal withdrawal is not affected by exposure to methadone or buprenorphine in breast milk. Therefore, maternal opiate use is considered compatible with breastfeeding.

Codeine should be used with caution by women who are breastfeeding. Neonatal toxicity symptoms and signs such as drowsiness, apnea, and bradycardia have been demonstrated in women who have been prescribed codeine and who have a genetic predisposition to convert codeine to morphine at a faster rate (i.e., CYP2D6 ultrarapid metabolizers).^{158,159} Symptoms and signs worsen after 4 days of codeine use, and alternate pain management should be considered after that time.¹⁶⁰

Recommendation

11. The risks and benefits of breastfeeding should be weighed on an individual basis because methadone maintenance therapy is not a contraindication to breastfeeding. (II-3B)

CONCLUSION

Problematic substance use in pregnancy is prevalent in the Canadian population. Perinatal health care providers can make a significant impact on improving pregnancy outcomes by providing non-judgemental supportive care within a harm reduction model to address substance use issues and social determinants of health. Ongoing education in this area and development of comprehensive care models are essential for the optimal care of patients in these challenging circumstances.

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Appendix

Antenatal Psychosocial Health Assessment (ALPHA)

Addressograph

Antenatal psychosocial problems may be associated with unfavorable postpartum outcomes. The questions on this form are suggested ways of inquiring about psychosocial health. Issues of high concern to the woman, her family or the caregiver usually indicate a need for additional supports or services. When some concerns are identified, follow-up and/or referral should be considered. Additional information can be obtained from the ALPHA Guide. **Please consider the sensitivity of this information before sharing it with other caregivers.*

ANTENATAL FACTORS	CONCERN	COMMENTS / PLAN
FAMILY FACTORS		
Social support (<i>CA, WA, PD</i>) How does your partner/family feel about your pregnancy? Who will be helping you when you go home with your baby?	<input type="checkbox"/> Low <input type="checkbox"/> Some <input type="checkbox"/> High	
Recent stressful life events (<i>CA, WA, PD, PI</i>) What life changes have you experienced this year? What changes are you planning during this pregnancy?	<input type="checkbox"/> Low <input type="checkbox"/> Some <input type="checkbox"/> High	
Couple's relationship (<i>CD, PD, WA, CA</i>) How would you describe your relationship with your partner? What do you think your relationship will be like after the birth?	<input type="checkbox"/> Low <input type="checkbox"/> Some <input type="checkbox"/> High	
MATERNAL FACTORS		
Prenatal care (late onset) (<i>WA</i>) First prenatal visit in third trimester? (check records)	<input type="checkbox"/> Low <input type="checkbox"/> Some <input type="checkbox"/> High	
Prenatal education (refusal or quit) (<i>CA</i>) What are your plans for prenatal classes?	<input type="checkbox"/> Low <input type="checkbox"/> Some <input type="checkbox"/> High	
Feelings toward pregnancy after 20 weeks (<i>CA, WA</i>) How did you feel when you just found out you were pregnant? How do you feel about it now?	<input type="checkbox"/> Low <input type="checkbox"/> Some <input type="checkbox"/> High	
Relationship with parents in childhood (<i>CA</i>) How did you get along with your parents? Did you feel loved by your parents?	<input type="checkbox"/> Low <input type="checkbox"/> Some <input type="checkbox"/> High	
Self esteem (<i>CA, WA</i>) What concerns do you have about becoming/being a mother?	<input type="checkbox"/> Low <input type="checkbox"/> Some <input type="checkbox"/> High	
History of psychiatric/emotional problems (<i>CA, WA, PD</i>) Have you ever had emotional problems? Have you ever seen a psychiatrist or therapist?	<input type="checkbox"/> Low <input type="checkbox"/> Some <input type="checkbox"/> High	
Depression in this pregnancy (<i>PD</i>) How has your mood been during this pregnancy?	<input type="checkbox"/> Low <input type="checkbox"/> Some <input type="checkbox"/> High	

ASSOCIATED POSTPARTUM OUTCOMES

The antenatal factors in the left column have been shown to be associated with the postpartum outcomes listed below. ***Bold, Italics*** indicates *good* evidence of association. Regular text indicates fair evidence of association.

CA – Child Abuse CD – Couple Dysfunction PI – Physical Illness

PD – Postpartum Depression WA – Woman Abuse

ANTENATAL FACTORS	CONCERN	COMMENTS / PLAN
SUBSTANCE USE		
Alcohol/drug abuse (WA, CA) (1 drink=1½ oz liquor, 12 oz beer, 5 oz wine) How many drinks of alcohol do you have per week? Are there times when you drink more than that? Do you or your partner use recreational drugs? Do you or your partner have a problem with alcohol or drugs? Consider CAGE (Cut down, Annoyed, Guilty, Eye opener)	<input type="checkbox"/> Low <input type="checkbox"/> Some <input type="checkbox"/> High	
FAMILY VIOLENCE		
Woman or partner experienced or witnessed abuse (physical, emotional, sexual) (CA, WA) What was your parents' relationship like? Did your father ever scare or hurt your mother? Did your parents ever scare or hurt you? Were you ever sexually abused as a child?	<input type="checkbox"/> Low <input type="checkbox"/> Some <input type="checkbox"/> High	
Current or past woman abuse (WA, CA, PD) How do you and your partner solve arguments? Do you ever feel frightened by what your partner says or does? Have you ever been hit/pushed/slapped by a partner? Has your partner ever humiliated you or psychologically abused you in other ways? Have you ever been forced to have sex against your will?	<input type="checkbox"/> Low <input type="checkbox"/> Some <input type="checkbox"/> High	
Previous child abuse by woman or partner (CA) Do you/your partner have children not living with you? If so, why? Have you ever had involvement with a child protection agency (ie. Children's Aid Society)?	<input type="checkbox"/> Low <input type="checkbox"/> Some <input type="checkbox"/> High	
Child discipline (CA) How were you disciplined as a child? How do you think you will discipline your child? How do you deal with your kids at home when they misbehave?	<input type="checkbox"/> Low <input type="checkbox"/> Some <input type="checkbox"/> High	

FOLLOW UP PLAN

- | | | |
|---|--|---|
| <input type="checkbox"/> Supportive counselling by provider | <input type="checkbox"/> Homecare | <input type="checkbox"/> Legal advice |
| <input type="checkbox"/> Additional prenatal appointments | <input type="checkbox"/> Parenting classes / parents' support group | <input type="checkbox"/> Children's Aid Society |
| <input type="checkbox"/> Additional postpartum appointments | <input type="checkbox"/> Addiction treatment programs | <input type="checkbox"/> Other: _____ |
| <input type="checkbox"/> Additional well baby visits | <input type="checkbox"/> Smoking cessation resources | <input type="checkbox"/> Other: _____ |
| <input type="checkbox"/> Public Health referral | <input type="checkbox"/> Social Worker | <input type="checkbox"/> Other: _____ |
| <input type="checkbox"/> Prenatal education services | <input type="checkbox"/> Psychologist / Psychiatrist | <input type="checkbox"/> Other: _____ |
| <input type="checkbox"/> Nutritionist | <input type="checkbox"/> Psychotherapist / marital / family therapist | |
| <input type="checkbox"/> Community resources / mothers' group | <input type="checkbox"/> Assaulted women's helpline / shelter / counseling | |

COMMENTS:

Date Completed _____

Signature _____