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No. 349-Substance Use in Pregnancy

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Key Words: Pregnancy, substance-related disorders, substance use, neonatal abstinence syndrome

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Abstract

Objectives: 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 the 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: Updates in the literature were retrieved through searches of Medline, PubMed, and The Cochrane Library published from 1996 to 2016 using the following key words: pregnancy, electronic cigarettes, tobacco use cessation products, buprenorphine, and methadone. Results were initially restricted to systematic reviews and RCTs/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.

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

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 lead to reduced health care costs and decreased maternal and neonatal morbidity and mortality.

Recommendations

1. All pregnant women and women of child-bearing age should be asked periodically about alcohol, tobacco, 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).

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[a]	Classification of recommendations[b]
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 the 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.
	I. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making.

Taken from: Task Force on Preventive Health Care. New grades for recommendations from the Canadian Task Force on Preventive Health Care. CMAJ 2003;169:207e8.

[a]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.

[b]Recommendations included in these guidelines have been adapted from the Classification of recommendations criteria described in the Canadian Task Force on Preventive Health Care.

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 and harm reduction approach to the care of pregnant women who use alcohol, tobacco, or drugs. Pregnant women at risk for problematic substance use should be offered brief interventions and referral to community resources for further psychosocial interventions (II-2B).
5. Women should be counselled about the risks of periconception, antepartum, and postpartum substance use (III-B).
6. Health care providers should offer smoking cessation interventions to all pregnant smokers. Psychosocial interventions should be considered first-line (I-A). Nicotine replacement therapy and/or pharmacotherapy can be considered if counselling is not successful (I-A).
7. The standard of care for the management of opioid use disorders during pregnancy is opioid agonist treatment with methadone or buprenorphine. Other sustained-release opioid preparations are also an option if methadone or buprenorphine is not available (I-A).
8. Opioid detoxification should be reserved for selected women because of the high risk of relapse to opioids (II-2B).
9. Opioid-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 opioids during pregnancy (III-B).
10. Women who become pregnant while on methadone should continue on methadone maintenance therapy and should not switch to buprenorphine due to the risk of opioid withdrawal (I-A).
11. Women who become pregnant while on buprenorphine/naloxone should be switched to buprenorphine monoproduct. Combination product should be continued until the monoproduct becomes available. Women taking buprenorphine should only switch to methadone if the buprenorphine monoproduct is not accessible and/or the woman feels that she is not responding to the current treatment (II-1A).
12. Health care providers should advise pregnant women to abstain from or reduce cannabis use during pregnancy to prevent negative long-term cognitive and behaviour outcomes for exposed children (II-1A).
13. Antenatal planning for intrapartum and postpartum analgesia may be offered for all women in consultation with appropriate health care providers (III-B).
14. Pregnant women on opioid agonist treatment should be encouraged to breastfeed regardless of the maternal dose, in the absence of an absolute contraindication (II-2B). Women with active substance use should be encouraged to discontinue alcohol or other drug use while breastfeeding, and the risks and benefits of breastfeeding versus breast milk exposure to substances should be discussed (II-2B).

ABBREVIATIONS

ATOD	alcohol, tobacco, and other drugs
BI	brief intervention
HCV	hepatitis C virus
HIV	human immunodeficiency virus
MMT	methadone maintenance therapy
NAS	neonatal abstinence syndrome
NRT	nicotine replacement therapy
OAT	opioid agonist treatment
RCT	randomized controlled trial
UDS	urine drug screening
WHO	World Health Organization

INTRODUCTION

National population surveys continue to demonstrate that a significant proportion of women report using ATOD during pregnancy. The prevalence of opioid and cannabis use is estimated at 1% and 2% of the pregnant population, respectively.[1] ATOD can have short- and long-term negative medical and social consequences for both the mother and infant. Comprehensive care for perinatal substance use consists of obstetrical and addiction services and has been associated with improved maternal and neonatal outcomes.

A standardized approach to identify and manage substance use disorders consists of screening, followed by BIs and referral to an addiction treatment program.[2] 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 barriers to providing care for these patients.[3] Perinatal care providers have several opportunities during pregnancy to identify and assist women who have substance use problems. Although most physicians inquire routinely about use of ATOD during pregnancy, many do not use a specific screening tool and do not make referrals to other treatment resources.[4–7] Because motivation to change harmful behaviours is increased during pregnancy, it is an ideal time to intervene with women who have substance use problems.

This updated guideline provides a comprehensive review of a unified approach to care for perinatal substance use disorders. These recommendations were made according to the ranking of the Canadian Task Force on Preventive Health Care (Table 1). BIs remain the standard of care for managing substance use disorders for all pregnant women. More recent evidence relating to nicotine and opioid use disorders has affected the medical management of these disorders during pregnancy. Management recommendations have been revised to incorporate this new evidence.

DEFINITIONS

Since the publication of the 5th edition of the *Diagnostic and Statistical Manual of Mental Disorders*, the terms *substance abuse* and *substance dependence* have been eliminated and replaced with a new term called *substance use disorder*.[8] Based on the *Diagnostic and Statistical Manual of Mental Disorders*, a substance use disorder is defined as a cluster of cognitive, behavioural, and psychological symptoms indicating that the woman continues to use despite significant substance-related problems. Table 2 presents the diagnostic criteria indicating an abnormal pattern of behaviours secondary to substance use. The spectrum of substance use disorder is based on the number of criteria endorsed by the patient. The severity ranges from mild to severe.

IDENTIFICATION OF SUBSTANCE-RELATED DISORDERS IN PREGNANCY

Maternal Interview

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.[9] Maternal interview using open-ended, non-judgemental questioning is more likely to elicit disclosure of perinatal substance use.[9,10] Health care providers should develop their own level of

Table 2. Definition of substance use disorder[8]

Definition	Maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by two or more of the criteria within a 12-month period: 1. Taking substance in larger amounts or for longer than intended 2. Wanting to cut down or quit but not being able to decrease or discontinue use 3. Spending a great deal of time obtaining, using, or recovering from effects of substance 4. Craving or a strong desire to use 5. Repeatedly unable to fulfill major role obligations at work, school, or home 6. Continued use despite persistent or recurring social or interpersonal problems caused or made worse by substance 7. Stopping or reducing important social, occupational, or recreational activities 8. Recurrent use in physically hazardous situations 9. Continued use despite acknowledgment of persistent or recurrent physical or psychological problems related to substance use 10. Tolerance as defined by either a need for markedly increased amounts to achieve desired effect or markedly diminished effect with continued use of the same amount 11. Withdrawal manifesting as a characteristic syndrome with reduced concentration of substance after prolonged heavy use
Severity	Mild: 2–3 criteria Moderate: 4–5 criteria Severe: ≥6 criteria

comfort and style in asking their patients about this sensitive topic.

There is no optimal screening tool for identifying substance use in pregnancy; however, there are a few validated questionnaires targeting prenatal populations. The T-ACE questionnaire was developed for screening for at-risk perinatal alcohol use (Figure 1).[11] The ALPHA tool incorporates the CAGE questionnaire to screen for maternal alcohol or recreational drug use and includes validated questions to identify associated psychosocial risk factors such as family violence or postpartum depression (Appendix).[12,13] If the woman acknowledges substance use, a more complete assessment is required to determine whether there is a history of a substance use disorder (Figure 2).

Role of Drug Toxicology

Drug toxicology testing is not recommended for universal screening (i.e., routine testing of all women) because it has numerous limitations (Figure 3), and thus, it should only be considered as confirmatory testing after a comprehensive assessment if there is a clinical indication.[14] 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.

Maternal urine and hair and fetal urine, hair, and meconium samples are sensitive biological markers of substance use. UDS can detect only recent substance exposure, whereas neonatal hair and meconium testing can document intrauterine use because meconium and neonatal hair form in the second and third trimesters, respectively.[15–18] By itself, a single positive test result cannot be used to diagnose a substance use disorder. Although child protection agencies sometimes request hair analyses, neither hair nor meconium testing is appropriate for routine clinical use because of the high costs, delayed results, and propensity for false positive results.

Figure 1. T-ACE for problematic alcohol use.

T-ACE

T How many drinks does it take to make you feel high? (Tolerance)

A Have people annoyed you by criticizing your drinking? (Annoyance)

C Have you felt you ought to cut down on your drinking? (Cut down)

E Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover? (Eye-opener)

Scoring

T: 2 points if > 2 drinks; A, C, E: 1 point for each yes answer.

A total score of 2 or more points indicates prenatal risk drinking.

Figure 2. Assessment for substance-related disorders.

Complete drug history: name of drug, amount, frequency, duration, route(s), last use, injection drug use, sharing needles/paraphernalia, withdrawal symptoms

Stage of change with respect to substance use

- Consequences of drug use: medical, social, personal
- Previous treatment programs, mutual aid groups (e.g., Alcoholics Anonymous)

Medical history: HIV, hepatitis B and C, sexually transmitted infections

- Chronic medical conditions (e.g., chronic pain), medications, septic thrombophlebitis, endocarditis, septic arthritis

Psychiatric history: eating disorders, sexual/physical abuse, mood and anxiety disorders

Obstetrical history: cycle regularity, LMP (last menstrual period), past obstetrical outcomes and complications

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, expectations about pregnancy and drug use

UDS has several clinical indications. Evidence shows that the addition of urine drug testing to the structured maternal inquiry about substance use can increase the detection of problematic substance use in pregnancy.[19,20] Identification can facilitate early intervention, including treatment of maternal and neonatal withdrawal, counselling, and referral for long-term outpatient treatment. 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).[15,18] Demonstration and documentation of compliance with either abstinence or MMT may be of use for a woman with respect to retaining custody of her child.

Informed consent needs to be obtained and documented in the medical record before any maternal or neonatal drug testing is performed (except in life-threatening situations for which informed consent is impossible).[21] If the mother refuses, this should be documented, and testing should not be performed. Once consent is obtained, any drug toxicology testing to be performed must be ordered by the physician responsible for maternal and/or neonatal care.

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.
- A false positive result can have serious legal and emotional consequences for the mother.

Recommendations

1. All pregnant women and women of child-bearing age should be asked periodically about alcohol, tobacco, 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).

Components of office management

Maternity 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).[22–25] Flexibility with respect to patient scheduling and understanding late arrivals and missed appointments are critical to engaging these women for prenatal care. Women are likely to seek and commit to prenatal care if health care providers are welcoming and nonjudgemental 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.[26–36]

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

It is also important to address a woman's substance use because pregnancy is an ideal time for women to make a change. The philosophy of care for women with problematic substance use in pregnancy is harm reduction. *Harm reduction* is defined as a program or policy designed to reduce drug-related harm without requiring the cessation of drug use.[37] Pregnancy may motivate women to abstain from or reduce drug use, given the potential effects on fetal outcomes.

Comorbid Conditions

Pregnant substance-using women are at increased risk for numerous infectious diseases. Injection drug use remains the most dominant mode of HCV acquisition. Approximately, 70% to 80% of HCV-infected patients report a history of current or past injection drug use.[38] HCV-negative women should be advised about ways to prevent exposure to HCV. Women should be advised 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.[39] There are no ways at present 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.

HIV may also be transmitted by similar risk behaviours such as sharing drug equipment for injection drug use and/or unprotected sex.

The prevalence of sexually transmitted infections is also higher among pregnant women with a history of substance abuse related to high-risk sexual behaviours.[40,41] Screening for chlamydia, gonorrhea, syphilis, hepatitis, and HIV should be repeated throughout pregnancy if indicated by clinical history, such as continued substance use or multiple sexual partners.[42]

Most women in substance abuse treatment programs report a history of trauma (including physical and sexual abuse), and approximately 25% have been diagnosed with post traumatic stress disorder.[43–45] Partner involvement in prenatal care and addiction treatment can have a positive

impact on recovery.[31] Conversely, a partner's active drug use has been linked to delayed treatment time for women seeking care.[46,47] Similarly, women with fewer social supports are less likely to seek and remain in treatment.[48,49] Appropriate referrals may include counselling to deal with pre-existing trauma and assistance with other social determinants of health (e.g., food and housing).

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.[50] 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.

Therefore, based on the complex needs of substance-using women, evaluation of comorbid conditions should include screening for infectious diseases; depression, anxiety, and other mental health disorders; domestic violence and abuse; and psychosocial supports.

Obstetrical and Neonatal Risks

There are numerous adverse effects associated with antenatal drug exposure (Table 3). These effects may also be linked to other factors such as inadequate prenatal care, poor social circumstances, and concomitant use of other substances.[51,52] Therefore, long-term studies are difficult to 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 informed about 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 3), 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.[53]

MANAGEMENT OF SUBSTANCE USE DISORDERS DURING PREGNANCY

There are two phases to the management of substance use disorders. The first priority should be addressing treatment of withdrawal syndromes. Substance withdrawal consists of drug-specific symptoms and signs that occur within hours to days of stopping use (listed in Table 4). 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).[37] 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 service, if available, for relapse prevention and counselling.

The second phase focuses on maintenance by encouraging substance abuse treatment and development of a supportive network. BIs by health care providers may be of benefit to pregnant women.[54,55] Pharmacological maintenance options are also available for management of nicotine and opioid dependence. Evidence suggests that enhanced treatment programs for opioid dependence that combine MMT, group psychotherapy, and obstetrical care result in less overall illicit substance use, improved prenatal care, and lower rates of obstetrical complications.[27,30,56–58]

Brief Interventions

BIs consist of simple advice or short counselling/educational sessions (5–20 minutes) provided as part of routine clinical care. Multiple sessions and an established relationship are more effective than a single intervention. These sessions consist of goal setting, problem solving with respect to triggers for use, and information on potential harms. Several studies have documented the effectiveness of BIs in reducing alcohol use among pregnant women.[54,55] However, there are no research data on the effectiveness of BIs targeted at pregnant women with illicit substance use. Systematic reviews have shown that outpatient counselling for cannabis dependence was moderately effective in reducing substance use in non-pregnant individuals.[59,60] Despite a small body of evidence for prenatal populations, WHO strongly endorses BIs for all pregnant women due to the potential benefit in terms of ceasing or reducing use.[61] Therefore, health care providers should advise all substance-using pregnant women to abstain from or reduce perinatal substance use. If a BI is not effective, consultation with a physician with expertise in addiction medicine and/or referral to community resources for more intense psychosocial interventions should be considered.

Comprehensive Care

Women with substance use disorders have unique and complex needs, including increased prevalence of mental

Table 3. Effects of antenatal substance use

Drug	Antenatal complications	Neonatal effects	Long-term effects
Nicotine	• SA • PTL, PROM • Placenta previa and placental abruption • IUGR, LBW	• Increased perinatal mortality • SIDS	• Childhood asthma • Behavioural problems • ADHD
Marijuana	• Inconsistent effects	• Neurobehavioural effects: decreased self-quieting ability; increased fine tremors, startles, and hand-to-mouth activity; sleep pattern changes	• Disturbed nocturnal sleep • Behaviour problems: inattention, impulsivity and hyperactivity, delinquency, externalizing problems, self-reported depressive and anxiety symptoms
Heroin/prescription opioids	• Premature labour • IUGR, LBW • Toxemia • Antepartum and postpartum hemorrhage	• Increased perinatal mortality rate	• Increased inattention, hyperactivity, and behavioural problems • Difficulty in physical, social, and self-adjustment and learning processes
Methadone		• NAS • Strabismus	
Cocaine	• SA • PROM, PTL • IUGR • Placental abruption	• Congenital anomalies: genitourinary malformations • Transient increase in central and autonomic nervous system symptoms and signs • Lower birth weight, length, and head circumference (dose-dependent)	• Behavioural problems
Hallucinogens (MDMA, LSD)		Congenital anomalies: cardiovascular, MSK defects	

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

health and eating disorders, past and current abuse and trauma, and poor social supports and parenting capacity. Therefore, pregnant substance-using women require comprehensive services including medical and obstetrical care, addiction counselling, and psychosocial supports to reduce negative outcomes for both mother and child.[62,63]

Table 4. 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 symptoms

Table 5. Management of withdrawal

Substance	Management recommendation
Alcohol	• Thiamine 100 mg po od × 3 days, folic acid 5 mg po od • Diazepam 20 mg po q1–2 h until minimal symptoms • Lorazepam 2–4 mg sl/po q2–4 h prn during labour • Monitor hydration status and electrolyte levels
High-dose benzodiazepines	• Start at $^{2}/_{3}$ to $^{3}/_{4}$ of diazepam equivalent dose • Taper by 10% per day
Opioids	• Offer symptomatic therapy including dimenhydrinate (Gravol) for nausea and vomiting, acetaminophen/non-steroidal anti-inflammatory for myalgias • Consider methadone or buprenorphine initiation • Can use morphine 5–10 mg po q4–6 h prn if methadone or buprenorphine is not available

po: by mouth; od: once daily; q: every; sl: sublingual; prn: as needed.

Numerous studies have documented that comprehensive care reduced maternal substance use, improved access to prenatal care, and resulted in higher rates of neonatal discharge home in the care of their mothers.[62,64,65]

Comprehensive care of the substance-using pregnant woman should also encourage collaboration and communication between all treating providers to plan for a supportive environment during labour, delivery, and the postpartum period.[66] Maternity care providers should be aware of local resources and encourage women to engage in community supports for both pregnancy and postpartum counselling/support and to facilitate the transition into the parenting role.

Recommendations

4. Health care providers should employ a flexible and harm reduction approach to the care of pregnant women who use alcohol, tobacco, or drugs. Pregnant women at risk for problematic substance use should be offered brief interventions and referral to community resources for further psychosocial interventions (II-2B).
5. Women should be counselled about the risks of periconception, antepartum, and postpartum substance use (III-B).

NICOTINE USE DISORDER

Smoking Cessation Counselling

Smoking cessation counselling has documented effectiveness in terms of reducing the number of women smoking cigarettes during pregnancy regardless of intensity or provider delivering the intervention.[67–74] Lower rates of preterm delivery and low-birth-weight infants are additional benefits of smoking cessation interventions. Several 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.[75] However, BIs have not been shown to be effective in preventing postpartum relapse to smoking.[76]

Therefore, health care providers should routinely educate women about the possible risks of tobacco exposure and advise all women to quit or reduce cigarette smoking during pregnancy and the postpartum period. Health care providers should direct women who require more intense interventions with reducing or quitting smoking to local counselling resources or provincial smokers' helplines for telephone or online support.

Pharmacotherapy

Controlled trials have failed to demonstrate that NRT increases smoking cessation rates, although it may reduce the number of cigarettes smoked.[73,77] NRT (gum, lozenge, or patch), combined with cognitive behavioural therapy, results in higher quit rates during pregnancy than does counselling alone.[74] The safety of NRT is unknown because the link between NRT and congenital anomalies and poor perinatal outcomes is unclear.[74,77–81] 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.[67,68,82,83] 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.

Bupropion and varenicline have been studied and found to be effective in non-pregnant populations. However, there are limited safety data on the use of bupropion during pregnancy.[67,68,82] To date, bupropion has not been associated with malformations during pregnancy.[68,82,84] In addition, preliminary evidence from 1 small study suggests that bupropion is effective for smoking cessation during pregnancy.[85] Additional research is needed on the safety and efficacy of bupropion and varenicline before they can be recommended for routine use in pregnancy.

Electronic Cigarettes

Electronic cigarettes or e-cigarettes are hand-held, battery-operated devices that heat up and vaporize a liquid to an aerosol. The use of e-cigarettes is frequently called vaping. The e-liquid may contain propylene glycol, glycerin, flavorings, additives, and contaminants and may also have variable amounts of nicotine. At present, there are no observational or randomized studies addressing the safety and efficacy of e-cigarettes during pregnancy. Possible harms include the risks of in utero exposure to nicotine and other contaminants on the fetus and the mother. Due to the lack of evidence, a recommendation regarding the use of e-cigarettes cannot be made. Pregnant women should be cautioned about using e-cigarettes until further research is conducted on the safety and efficacy of e-cigarette use during pregnancy.

Recommendation

6. Health care providers should offer smoking cessation interventions to all pregnant smokers. Psychosocial interventions should be considered first-line (I-A).

Nicotine replacement therapy and/or pharmacotherapy can be considered if counselling is not successful (I-A).

OPIOID USE DISORDERS

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.[73,78,79,86] Regardless, opioid detoxification is not recommended during pregnancy primarily because of the high rate of relapse.[87–91] If opioid detoxification is attempted during pregnancy, it is preferable to start only after the first trimester and after a discussion of the potential risks and benefits. MMT is associated with longer adherence to treatment and decreased risk of relapse to opioid use; therefore, the pregnant opioid-dependent women are encouraged to initiate opiate substitution therapy rather than attempt opioid detoxification.

OAT

The standard of care for the management of opioid use disorder during pregnancy is OAT with either methadone, buprenorphine, or other sustained-release preparations, if the first two options are not available. Several studies have been conducted to compare the effectiveness of methadone and buprenorphine to determine the optimal medication to improve both maternal and neonatal outcomes, especially the risk of NAS.

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,[75,92–94] longer gestation,[29,95] higher birth weight,[96,97] and increased rates of infants discharged home in the care of their mothers.[28,75,86,93,98–105] Although infants of methadone-treated women tend to be smaller (lower birth weight, length, and head circumference) than drug-free control infants, studies have shown a catch-up of growth by 12 months of age.[105,106]

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.[107] The main rationale for buprenorphine use for treating opioid dependence during pregnancy is reports of reduced incidence and severity of NAS[108–111]; however, there are limited data regarding the long-term effects of in utero exposure to buprenorphine.[112] 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 during pregnancy. Buprenorphine is available during pregnancy through Health Canada's Special Access Program.

Comparison of Opioid Agonist Treatments: Methadone Versus Buprenorphine

Evidence regarding the management of opioid use disorders stems from an RCT and systematic reviews. The landmark Maternal Opioid Treatment: Human Experimental Research study was a double-blind, double-dummy RCT comparing methadone and buprenorphine for use in pregnant women with opioid use disorders.[113] Based on study findings, there was no statistical significant difference in the peak NAS score or percentage of neonates requiring NAS treatment; however, there were significant differences in the total amount of morphine needed for treatment of NAS and length of neonatal hospital stay. Neonates exposed to buprenorphine needed 89% less morphine and spent 43% less time in the hospital and 58% less time in the hospital for NAS pharmacotherapy compared with neonates exposed to methadone. No other significant findings were shown in secondary outcomes. Both groups had an average of ~9 prenatal visits and 10% to 15% of women tested positive for drugs at delivery. Treatment retention was higher among the methadone maintained group. Overall, this study provided promising evidence for the use of buprenorphine as an alternative to methadone during pregnancy.

A recent Cochrane intervention review also evaluated the effectiveness of different maintenance treatment pharmacotherapy agents, including methadone, buprenorphine, and morphine.[114] This systematic review included only four studies consisting of 271 pregnant opioid-dependent women and assessed maternal, obstetrical, and neonatal outcomes. Multiple analyses failed to show any significant differences among the agents for any outcomes to make any specific recommendations. The number of women included was too small to make definitive conclusions regarding the most effective OAT.

Furthermore, another published systematic review included a pooled meta-analysis of prenatal exposure to buprenorphine maintenance treatment versus MMT on neonatal outcomes.[115] The final meta-analyses were based

on 12 studies and included a population of 515 buprenorphine maintenance treatment–exposed and 855 MMT-exposed neonates. After adjusting for possible confounders, there were no significant differences in NAS treatment, total amount of morphine used for NAS treatment, and preterm birth.

MMT remains the standard of care for opioid use disorders in pregnant women. Recent findings provide evidence for the use of buprenorphine for the management of opioid use disorders during pregnancy after a discussion about benefits and risks. Geographic variations in the availability of OATs will determine which agent will be used for pregnant women.

Urgent consultation with an addiction medicine specialist should be sought to facilitate rapid access to OAT during pregnancy. Close monitoring of OAT dosing during pregnancy is recommended, especially during the third trimester when methadone and buprenorphine have increased metabolism and clearance rates and dose augmentation may be required.[116–118]

Pregnant women should receive the methadone dose that is required to alleviate withdrawal symptoms and cravings because there is no association between maternal methadone dose and severity of neonatal withdrawal.[119] Prenatal discussion with the methadone or buprenorphine prescribing physician is recommended to plan for intrapartum and postpartum dosing.

Buprenorphine/Naloxone Versus Buprenorphine Monoproduct Formulation

A search of the literature resulted in 3 published retrospective cohort studies evaluating the use of buprenorphine/naloxone in pregnancy for the treatment of opioid use disorders.[120–122] A total of 71 pregnant women were maintained on buprenorphine/naloxone throughout their pregnancies. Neonates were born at term with normal birth parameters and no congenital anomalies. Rates of NAS were comparable to buprenorphine. Overall, there were no significant differences in maternal or neonatal outcomes compared with methadone or buprenorphine monoproduct. These preliminary findings are not sufficient to recommend the routine use of the combined formulation during pregnancy, and a larger study to evaluate buprenorphine/naloxone as an alternative treatment for opioid use disorders during pregnancy is required.

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.[123] The goal of therapy is to use the lowest effective dose of scheduled controlled-release opioids.[123] 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 substance use disorder 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.[124,125]

IDENTIFICATION AND MANAGEMENT OF NAS

Any regular, daily antenatal opioid exposure (e.g., morphine, codeine, oxycodone, methadone, or buprenorphine) can produce neonatal withdrawal, also known as NAS. Estimates show that up to 96% of infants display withdrawal symptoms, and a smaller proportion requires pharmacotherapy.[55,98,103,104,116,117] NAS is characterized by respiratory, gastrointestinal, central nervous system, and autonomic symptoms (Table 6). 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 48–72 hours after birth and at up to 4 weeks of age.[126] The length of monitoring is based on the specific opioid's half-life.

The Finnegan scoring tool (also known as the Finnegan Neonatal Abstinence Scoring System) is the most commonly used tool for assessment of NAS.[127] Non-pharmacological therapy is the standard of care for all opioid-exposed infants.[128] For a smaller subset of infants, pharmacotherapy may be needed to treat severe symptoms and usually consists of opioids such as morphine or methadone.[126,129] Canadian hospitals care for substance-exposed infants in different settings such as the neonatal care unit or special care nursery or by rooming-in depending on geographical resources and expertise. 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 mean neonatal length of stay in the hospital, and an increased likelihood of discharge in the custody of the mother.[130] Additional large-scale prospective studies are required to determine the optimal management of neonatal withdrawal. Treated neonatal withdrawal has not been associated with any long-term complications.

Recommendations

7. The standard of care for the management of opioid use disorders during pregnancy is opioid agonist treatment with methadone or buprenorphine. Other sustained-release opioid preparations are also an

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

option if methadone or buprenorphine is not available (I-A).

8. Opioid detoxification should be reserved for selected women because of the high risk of relapse to opioids (II-2B).
9. Opioid-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 opioids during pregnancy (III-B).
10. Women who become pregnant while on methadone should continue on methadone maintenance therapy and should not switch to buprenorphine due to the risk of opioid withdrawal (I-A).
11. Women who become pregnant while on buprenorphine/naloxone should be switched to buprenorphine monoproduct. Combination product should be continued until the monoproduct becomes available. Women taking buprenorphine should only switch to methadone if the buprenorphine monoproduct is not accessible and/or the woman feels that she is not responding to the current treatment (II-1A).

CANNABIS USE DISORDER

Women of reproductive age need to be aware of the short- and long-term impacts of cannabis use during pregnancy. Evidence from 3 prospective longitudinal cohort studies demonstrated that prenatal cannabis is associated with both neurocognitive and behavioural deficits for exposed children.[131] Younger children aged 3 to 4 exhibited deficits in several domains, including memory, verbal, and perceptual skills and verbal and visual reasoning. Older children and adolescents experienced deficits in executive functioning.[131] Behavioural problems included aggressiveness and hyperactivity, impulsivity, and inattention.[131] Because these neurocognitive and behavioural effects may be dose dependent, pregnant women should be advised to reduce or abstain from cannabis use during pregnancy.[132]

Recommendation

12. Health care providers should advise pregnant women to abstain from or reduce cannabis use during pregnancy to prevent negative long-term cognitive and behaviour outcomes for exposed children (II-1A).

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 experiencing pain due to their history of addiction.[133–137] Inappropriate pain management is more likely to lead to a relapse than is provision of required opioid analgesics for treatment of acute pain. Women on OAT should be continued on the same dose of methadone or buprenorphine, although this is ineffective for acute pain management.[133,137] 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.[133,137,138] 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 intrapartum and postpartum pain management and to develop a multimodal analgesia plan.

Recommendation

13. 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 an overdose is possible if they suddenly stop or markedly reduce their opioid use and then resume at 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, individuals should be advised to access emergency care 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 the ingested opioid. Naloxone may be required on a repeated and continuous basis until the effects of the opioid have diminished. Care should be taken to prevent acute withdrawal symptoms, which can cause fetal distress.[139] 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 frequents 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 the following section 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

Alcohol and illicit substances (e.g., marijuana, cocaine, and amphetamines) have been detected in breast milk.[140–143] Furthermore, there have been reports documenting negative neonatal effects due to breast milk exposure, and therefore, the decision to breastfeed should be made on an individual basis after discussing the potential risks and benefits.[141,142,144,145] Breastfeeding may be delayed after maternal use of any of these agents and any neonatal exposure to any fumes in the environment to reduce exposure to substances in breast milk. Women who are regular substance users should be encouraged to remain abstinent while nursing and counselled regarding the increased risks for neonatal effects.

All opioids have been documented in breast milk in small amounts but are unlikely to be of any clinical significance.[91,117,146–152] Therefore, maternal opiate use is considered compatible with breastfeeding, and women who are stable on OAT and not actively using other substances should be encouraged to breastfeed. However, the rate of breastfeeding initiation among women on OAT remains low, between 20% and 75%, and is reduced further by 6–12 weeks postpartum.[153–155]

Evidence is emerging that breastfeeding may reduce NAS severity and length of pharmacological treatment.[153,154] The beneficial effects of breastfeeding may be due to the low concentration of methadone in breast milk and/or the act of breastfeeding, including the small frequent feeds, close physical contact, and maternal response to infant.[154] Because the benefits of breastfeeding outweigh the risks, methadone is compatible with breastfeeding regardless of maternal methadone dose.

Preliminary results have found that buprenorphine use during lactation resulted in low concentrations of buprenorphine and its metabolites in breast milk; however, this was not associated with reduced severity of NAS or treatment rates for NAS, indicating that buprenorphine in breast milk did not suppress NAS.[154–156] However, given the limited literature, women need to consider the risks and benefits of breastfeeding versus buprenorphine exposure during lactation.

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).[157,158] Symptoms and signs worsen after 4 days of codeine use, and alternative pain management should be considered after that time.[157]

Recommendation

14. Pregnant women on opioid agonist treatment should be encouraged to breastfeed regardless of the maternal dose, in the absence of an absolute contraindication (II-2B). Women with active

substance use should be encouraged to discontinue alcohol or other drug use while breastfeeding, and the risks and benefits of breastfeeding versus breast milk exposure to substances should be discussed (II-2B).

CONCLUSION

Problematic substance use in pregnancy is prevalent in the Canadian population. The use of ATOD continues to be widespread in Canada and is a cause of significant medical and social consequence for both the mother and infant. Perinatal health care providers can make a significant impact on improving maternal and neonatal outcomes by providing non-judgemental supportive care and BIs to assist with reducing or discontinuing substance use and by assisting pregnant women with ATOD to access obstetrical and addiction care. 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

FROM THE TASK FORCE ON PREVENTIVE HEALTH CARE. NEW GRADES FOR RECOMMENDATIONS FROM THE CANADIAN TASK FORCE ON PREVENTIVE HEALTH CARE. CMAJ 2003;169:207–8.

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 (CA, WA, PD)

How does your partner/family feel about your pregnancy? Who will be helping you when you go home with your baby? Low Some High

Recent stressful life events (CA, WA, PD, PI) What life changes have you experienced this year?

What changes are you planning during this pregnancy?

Low Some High

Couple's relationship (CD, PD, WA, CA)

How would you describe your relationship with your partner? What do you think your relationship will be like after the birth? Low Some High

MATERNAL FACTORS

Prenatal care (late onset) (WA)

First prenatal visit in third trimester? (check records) Low Some High

Prenatal education (refusal or quit) (CA)

What are your plans for prenatal classes? Low Some High

Feelings toward pregnancy after 20 weeks (CA, WA)

How did you feel when you just found out you were pregnant? How do you feel about it now? Low Some High

Relationship with parents in childhood (CA) How did you get along with your parents? Did you feel loved by your parents? Low Some High

Self esteem (CA, WA)

What concerns do you have about becoming/being a mother?

Low Some High

History of psychiatric/emotional problems (CA, WA, PD)

Have you ever had emotional problems?

Have you ever seen a psychiatrist or therapist? Low Some High

Depression in this pregnancy (PD)

How has your mood been during this pregnancy? Low Some 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

SUBSTANCE USE

Alcohol/drug abuse (WA, CA) (1 drink=11/2 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) Low Some 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? Low Some 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?

Low Some 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)?

Low Some 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?

Low Some High

FOLLOW UP PLAN

- ☐ Supportive counselling by provider
- ☐ Additional prenatal appointments
- ☐ Additional postpartum appointments
- ☐ Additional well baby visits
- ☐ Public Health referral
- ☐ Prenatal education services
- ☐ Nutritionist
- ☐ Community resources / mothers' group
- ☐ Homecare
- ☐ Parenting classes / parents' support group
- ☐ Addiction treatment programs
- ☐ Smoking cessation resources
- ☐ Social Worker

- ☐ Psychologist / Psychiatrist
- ☐ Psychotherapist / marital / family therapist
- ☐ Assaulted women's helpline / shelter / counseling
- ☐ Legal advice
- ☐ Children's Aid Society
- ☐ Other:
- ☐ Other:
- ☐ Other:
- ☐ Other:

COMMENTS:

Date Completed Signature