



## **Smoking Cessation Pharmacotherapy: Special Populations Pearls**

### **Cardiovascular Disease**

Smoking cessation in patients with established cardiovascular disease (CVD) has been shown to reduce the risk of recurrent heart attack<sup>1</sup> and stroke<sup>2</sup>. It also reduces the progression and improves symptoms of heart failure<sup>3</sup> and peripheral arterial disease<sup>4</sup>. With the possible exception of varenicline, the first line smoking cessation agents appear to be safe for patients with stable CVD.<sup>5,6</sup> Information on the safety of these agents in patients with unstable CVD is limited.

<b><i>Smoking Cessation Pharmacotherapy in Patients with Cardiovascular Disease</i></b>	
<b>NRT</b> (Nicotine Replacement Therapy)	(i) Considered safe for patients with stable cardiovascular disease. <sup>7</sup> (ii) Use with caution if patients have coronary heart disease, serious arrhythmias or vasospastic diseases such as Buerger's disease or Prinzmetal's angina. <sup>7</sup> (iii) Monographs contraindicate use if life-threatening arrhythmias, severe or worsening angina pectoris, recent stroke, and for 2 weeks following myocardial infarction. <sup>5,7</sup> However, a recently published retrospective study (2012) suggests that NRT use after acute coronary syndrome does not increase the risk of cardiovascular events. <sup>(1)</sup>
<b>Bupropion</b>	(i) Safe and effective in patients with stable cardiovascular disease. <sup>6</sup> (ii) Safety in unstable heart disease and immediately after a myocardial infarction is unknown. <sup>8</sup> Use with caution. (ii) Combination with NRT has been associated with a trend towards increased blood pressure, especially in patients with pre-existing hypertension. Blood pressure should be monitored when combination is used. <sup>9</sup>
<b>Varenicline</b>	(i) Conflicting data on safety in patients with stable cardiovascular disease. <sup>10,11</sup> There may be a small increase in risk of cardiovascular adverse events (2% versus 1%). <sup>12</sup> Health Canada and the FDA are currently reviewing this issue. (ii) Known benefits of varenicline in smoking cessation must be weighed against this potential risk in smokers with CVD. <sup>13</sup> Expert opinion favors benefit <sup>(2)</sup> but caution is advised until more evidence is available <sup>(3)</sup> . (iii) Advise patients to monitor for and report new or worsening symptoms of CVD while taking varenicline. <sup>13</sup>

The second line smoking cessation agents, clonidine and nortriptyline, should be used cautiously in patients with CVD. Clonidine lowers blood pressure and heart rate.<sup>14</sup> Tricyclic antidepressants as a class have been associated with cardiac arrhythmias.<sup>15</sup> Both agents are contraindicated in the two week period immediately after a myocardial infarction and in patients with heart failure.<sup>14,15</sup>

(1) Woolf K, Zabad M, Post J et al. Effect of nicotine replacement therapy on cardiovascular outcomes after acute coronary syndromes. *Am J Cardiol* 2012;110:968–970.

(2) The Medical Letter on Drugs and Therapeutics • August 22, 2011 (Issue 1371) p. 65

(3) Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. *Cochrane Database of Systematic Reviews* 2012, Issue 4. Art. No.: CD006103. DOI: 10.1002/14651858.CD006103.pub6.

**Mental Health Population:**

Smoking is problematic in mental health patients due to its potential to reduce the efficacy of antipsychotic medications.<sup>16,17</sup> Smoking is associated with increased CYP1A1/ 1A2 and 2E1 activity<sup>2,3</sup>. Upon smoking cessation, substrates of these enzymes (e.g., theophylline, clozapine, caffeine, fluvoxamine, haloperidol, olanzapine, lorazepam, alprazolam, diazepam etc.) might have reduced clearance and dose adjustments may be necessary.<sup>16,17,18</sup> Upon smoking cessation, enzyme induction will abate quickly so there is potential for a period of dangerously high blood levels if dosage adjustments are not made.<sup>16,17</sup>

<b><i>Smoking Cessation Pharmacotherapy in Mental Health Population:</i></b>	
<b>NRT</b>	(i) Lack of evidence for efficacy in patients with schizophrenia. <sup>(4)</sup> Monograph recommended NRT doses may not control withdrawal symptoms in heavy smokers with <i>schizophrenia</i> . <sup>16</sup> (ii) Nicotine patch can be used for steady state replacement and nicotine gum or lozenges can be used to manage acute urges to smoke (monitor regularly) AND/OR sustained release bupropion (monitor regularly) <sup>20</sup>
<b>Bupropion</b>	(i) In cases of mild, untreated depression clinicians view bupropion as a good choice as it can treat both depression and smoking; however, it has not been determined to be superior to other agents in patients with clinical <i>depression</i> or <i>bipolar disorder</i> <sup>21</sup> (ii) Avoid in <i>bipolar</i> patients as antidepressant use may trigger mania <sup>21</sup> (iii) In a recent meta-analysis (2012), bupropion was the only pharmacological treatment to show benefit in reducing the number of cigarettes smoked and increasing complete smoking cessation in patients with schizophrenia. <sup>(4)</sup>
<b>Varenicline</b>	(i) Avoid if patient has a history of suicidal ideation/current unstable psychiatric status <sup>6,7</sup> (ii) May consider using with caution and careful monitoring if other methods have failed. <sup>21-23,(5)</sup> (iii) Instruct patients to stop taking immediately and contact physician if they experience, (or others observe) new/worsened psychiatric symptoms; in many post-marketing reports, there can be resolution of symptoms upon discontinuation – but in some cases symptoms persisted <sup>23</sup>

Smoking cessation pharmacotherapy works to curb symptoms of nicotine withdrawal; however mental health patients may experience an exacerbation in psychiatric symptoms. Nicotine withdrawal symptoms can mimic or aggravate anxiety disorders so it is imperative to monitor and treat symptoms accordingly.<sup>24</sup>

(4) Tsoi DT, Porwal M, Webster AC. Interventions for smoking cessation and reduction in individuals with schizophrenia. *Cochrane Database of Systematic Reviews* 2010, Issue 6. Art. No.: CD007253. DOI: 10.1002/14651858.CD007253.pub2.

(5) Rigotti N. Strategies to Help a Smoker Who Is Struggling to Quit *JAMA*. 2012;308(15):1573-1580.

**Pregnant & Breastfeeding Women:**

Adverse outcomes in pregnancy can result due to cigarette smoking such as: spontaneous pregnancy loss, placental abruption, preterm premature rupture of membranes, preterm labor and delivery, low birth weight, and ectopic pregnancy. As for the post-partum period of lactation, smoking is associated with a decreased likelihood and duration of breast feeding.<sup>25</sup> Additionally, there is an increased risk of sudden infant death syndrome (SIDS) in newborns due to second-hand smoke exposure in the home.<sup>26</sup> Therefore, facilitation of smoking cessation for pregnancy and breastfeeding is an intervention that should be maintained throughout completion of the breastfeeding phase.

Specific to pregnancy, the Clinical Practice Guidelines for Treating Tobacco Use and Dependence (United States Department of Health and Human Services) offer a framework of practice that is readily applicable and easy to adopt as pharmacists.<sup>24</sup>

(i) **Offer psychosocial intervention.** Non-pharmacological therapy is first line treatment in pregnancy and lactation. Women who smoke five cigarettes or fewer per day should be advised to quit smoking by using behavioral support.<sup>27</sup>

(ii) **Offer intervention throughout pregnancy.** Quitting early in pregnancy is most beneficial, albeit quitting at any point within the pregnancy still has value. Reduction in number of cigarettes smoked alone does not improve fetal health outcomes whereas sustained abstinence does.<sup>28</sup>

(iii) **Offer pharmacotherapy.** Consider when a pregnant woman is: (a) otherwise unable to quit via non-pharmacological therapy (b) when the likelihood of quitting, with its potential benefits, outweighs the risks of the pharmacotherapy and potential continued smoking.<sup>24</sup>

<b><i>Smoking Cessation Pharmacotherapy in Pregnant/Breastfeeding Women:</i></b>	
<b>NRT</b>	<p>(i) Although considered the pharmacologic therapy of choice if nonpharmacological measure fail, there is no clear evidence that NRT is efficacious in smoking cessation in pregnant women.<sup>(6)</sup> Use should be <i>evaluated case by case</i>.*</p> <p>(ii) Nicotine crosses the placenta but fetal exposure is less with NRT than with moderate to heavy smoking.<sup>(7)</sup> If transdermal patch is used, recommend removing at night, tapering as directed and discontinuing after 8 to 10 weeks.<sup>(8)</sup></p> <p>(iii) NRT may pass into breast milk.<sup>29</sup> Rapid release/as needed forms, such as nicotine gum or lozenges are preferred for breastfeeding women.<sup>25,27</sup> These products will produce variable peaks similar to smoking; therefore breastfeeding mothers should be advised to refrain from breastfeeding 2-3 hours after using the gum or lozenge product. Co-ordinate dose to suit the smoker's needs</p> <p>(iv) Nicotine patch is shown to have no significant influence on the milk intake by the infant; the patch provides a sustained and lower nicotine plasma level<sup>30</sup></p> <p>(v) A nicotine inhaler will produce plasma levels too low to affect a breastfeeding infant<sup>30</sup></p>
<b>Bupropion</b>	<p>(i) Recommendations vary amongst health professionals; limited data on the safety of bupropion in human pregnancies; may pass into breast milk although plasma levels in breastfed infants are undetectable<sup>23-32**</sup></p> <p>(ii) No nicotine exposure to the fetus in pregnancy and patient may experience less withdrawal symptoms such as weight gain and cravings<sup>28</sup></p> <p>(iii) <i>Zyban</i><sup>®</sup> post marketing reports suggest some neonates exposed to bupropion SR, SSRIs, or other new antidepressants during the 3<sup>rd</sup> trimester have developed complications involving hospitalization; if a pregnant woman is treated with bupropion SR, consider tapering in the third trimester<sup>27,29</sup></p>

<b>Varenicline</b>	(i) Varenicline has not been studied in pregnancy or lactation <sup>28,29,31</sup> (ii) Should not be used until animal and human data are collected <sup>26,27,31</sup> (iii) Varenicline may pass into breast milk. Due to long half-life and kinetics it is not advisable to use <sup>30</sup>
--------------------	---

\* Be aware that NRT manufacturers/CPS state that any form of nicotine administration is contraindicated in pregnant and breastfeeding women<sup>6</sup>. According to international guidelines and the Motherisk Program, there are benefits to the mother and the fetus if NRT results in smoking cessation<sup>24,31,32</sup>

\*\*According to a 2005 statement from the American College of Obstetricians and Gynecologists (ACOG), bupropion may be considered during pregnancy and lactation when nonpharmacologic therapies fail<sup>8</sup>. However, bupropion use in pregnancy is not recommended by the Motherisk Program until more efficacy and safety data are available<sup>29,31</sup>.

(6) Coleman T, Cooper S, Thornton J et al. A Randomized Trial of Nicotine-Replacement Therapy Patches in Pregnancy N Engl J Med 2012;366:808-18.

(7) Clark S, Naka R. Pharmacotherapeutic Management of Nicotine Dependence in Pregnancy. Obstet Gynecol Clin N Am 38 (2011) 297–311.

(8) Briggs G, Freeman R, Yaffe S. Nicotine replacement therapy monograph. Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk, 9th Ed., 2011. Lippincott Williams & Wilkins Philadelphia.

**Adolescents:**

Teenagers who begin smoking in their adolescent years are likely to continue smoking as adults; therefore management of early nicotine dependence is key. Behavioral and motivational interventions should always be employed.<sup>32</sup> The majority of smoking cessation studies focus on the adult population. The only therapies that have been evaluated in adolescents include the nicotine patch, nicotine gum and bupropion. In general, studies demonstrate that these interventions can lead to a decrease in the number of cigarettes smoked daily, but abstinence rates overall were low.<sup>33</sup>

<b><i>Smoking Cessation Pharmacotherapy in Adolescents:</i></b>	
<b>NRT</b>	(i) 1 <sup>st</sup> line pharmacotherapy in adolescents; patch or gum have demonstrated safety (ii) Low starting doses for patient <45kg OR smokes less than ½ pack a day <sup>33</sup>
<b>Bupropion</b>	(i) Can try as 2 <sup>nd</sup> line agent; lower abstinence rates and rapid relapse upon d/c <sup>27,33</sup>
<b>Varenicline</b>	(i) Not recommended; lack of evidence and safety concerns raised in adult post-marketing reports <sup>24,27,34, 35</sup>

**Hospital Based Populations:**

The hospital environment provides smokers a chance to be in a smoke free setting. Often the reason for admission serves as an eye-opener to the dangers of smoking and can motivate smoking cessation.<sup>21</sup> Being removed from the smoking cues associated with home life affords the patient an occasion to actively pursue a quit attempt. Data to date supports offering hospital-based interventions to all smokers.<sup>36</sup> For the preoperative hospital population, evidence shows that smoking cessation interventions may decrease postoperative morbidity. Generally, if interventions were implemented 4 to 8 weeks prior to the surgery (NRT and weekly counseling) this would be more likely to result in long-term smoking cessation.<sup>37</sup>

<b><i>Smoking Cessation Pharmacotherapy in Hospital Based Populations:</i></b>	
<b>NRT</b>	(i) Useful to curb nicotine withdrawal symptoms in smokers forced to abstain from smoking temporarily while in hospital <sup>16</sup>

	(ii) <b>Use with caution in following patients:</b> $\leq 2$ weeks post myocardial infarction, patients with arrhythmias of concern, and patients with serious or deteriorating angina pectoris <sup>27</sup> (iii) Habitrol (patch) most studied; effective; ideal for bed-ridden patients <sup>35</sup> (iv) Adding NRT to intensive counseling begun during hospitalization increases cessation rates over counseling alone. <sup>(9)</sup>
<b>Bupropion</b>	(i) Limited evidence to support use of bupropion in hospital setting
<b>Varenicline</b>	(i) The efficacy of starting varenicline in the hospital setting has not been studied <sup>35</sup>

(9) Rigotti NA, Clair C, Munafò MR, Stead LF. Interventions for smoking cessation in hospitalised patients. *Cochrane Database of Systematic Reviews* 2012, Issue 5. Art. No.: CD001837. DOI: 10.1002/14651858.CD001837.pub3.

#### **Aboriginal People:**

In respect to the rest of the Canadian population, the smoking rate within the Aboriginal community is more than double for adults and youth.<sup>38-40</sup> This is particularly worrisome because smoking is a chief source of morbidity and mortality for this population.<sup>38</sup> Limited evidence suggests that cessation strategies tailored to aboriginal peoples' culture and traditions may be successful.<sup>(10)</sup> Within Saskatchewan, the TAR program (Tobacco Addiction Recovery) is a culturally relevant tobacco cessation program developed specifically for Aboriginal communities.<sup>16</sup> It is important to convey that smoking isn't the only type of tobacco that causes health problems. Smokeless tobacco, including chewing tobacco and snuff, contain many of the same harmful and addictive substances as cigarettes, pipes and cigars.<sup>16,40</sup>

It has been noted that lack of awareness of coverage options is associated with less compliance to use drug therapy available for smoking cessation.<sup>38</sup> Therefore, as a healthcare practitioner, it is helpful to discuss applicable drug coverage available to Aboriginal patients as that can help motivate cessation. ***Under FNIHB the following drugs are covered for approximately 3 months of therapy per year: varenicline, bupropion, nicotine gum, lozenges, patch and inhaler.***<sup>40</sup>

(10) Carson KV, Brinn MP, Peters M, et al. Interventions for smoking cessation in Indigenous populations. *Cochrane Database of Systematic Reviews* 2012, Issue 1. Art.No.: CD009046. DOI: 10.1002/14651858.CD009046.pub2.

#### **Effects of Smoking/Quitting on Medications:**

##### **Pharmacokinetic drug interactions:**

Polycyclic aromatic hydrocarbons (PAH's) are in the tar of tobacco smoke and they can interfere with medications by increasing the metabolism of certain drugs, thereby leading to diminished pharmacologic response.<sup>16</sup> PAHs are potent inducers of the hepatic CYP P-450 isoenzymes 1A1/1A2, and 2E1. CYP1A2 accounts for 15% of the total cytochromes present in the liver and there can be significant individual variation in its metabolic activity.<sup>41</sup> After a person quits smoking, an important consideration is how quickly the induction of CYP1A2 dissipates.<sup>18</sup> Upon cessation of smoking, with or without NRT, there may be reduced clearance of medications that are metabolized by this isoenzyme.<sup>28</sup> Theophylline, clozapine, olanzapine, clomipramine, imipramine, and fluvoxamine are examples of drugs that are metabolized by CYP 1A2. The degree of the interaction may vary depending on the importance of CYP 1A2 for clearance and the range of the therapeutic window for the involved drugs.<sup>18,27,41</sup> Caffeine levels can increase 2- to 3-fold after patients *stop* smoking. The irritability and insomnia that patients think is due to nicotine withdrawal may be from caffeine toxicity.<sup>27</sup>

##### **Pharmacodynamic drug interactions:**

A clinically significant interaction can occur with smoking and *combined hormonal contraceptives*. Oral contraceptive use itself can increase the risk of cardiovascular adverse effects and smoking increases the risk of arterial events associated with oral contraceptives.<sup>18</sup> The efficacy of *inhaled or oral corticosteroids* can be reduced in those individuals who smoke.<sup>18,42</sup> Insulin dependent diabetics may experience decreased

subcutaneous absorption of insulin, leading to greater dosing requirements. This connection has a dose-response relationship which can be noted between the number of cigarettes smoked and degree of insulin sensitivity.<sup>43,44</sup>

### General management guidelines:

- i. For most drugs the clinician can monitor for an increase in adverse effects of the affected medication post smoking cessation. ***Dose adjustments should be guided by monitoring the clinical status of the patient***<sup>19</sup>
- ii. For narrow therapeutic index drugs, decrease dose of affected drugs by 10% for each day for 4 days after quitting.<sup>17</sup> Monitoring serum drug level (if accessible) is also an option, before stopping smoking, and up to two weeks post smoking cessation.
- iii. If the patient lapses and begins smoking again then adjustment needs to be again considered as sub therapeutic drug levels may result.<sup>16,17</sup>
- iv. Pharmacotherapy coverage can positively influence likelihood of use and success rates.<sup>45</sup>
- v. For the general population, cost analysis studies demonstrate bupropion and varenicline are more cost-effective than NRT.<sup>45</sup>
- vi. Since smoking can affect drug levels, it is useful to note smoking status on patient profiles.

Prepared by Gurpreet Nijjar, BSP (SDIS) June 2011. Updated by Karen Jensen MSc, BSP (SDIS) October 2012  
Reviewed by Janice Burgess, BSP (PACT); Shannon Appel, BSP (PACT)

### References:

1. Suskin N, Sheth T, Negassa A, Yusuf S. Relationship of current and past smoking to mortality and morbidity in patients with left ventricular dysfunction. *J Am Coll Cardiol* 2001;37:1677–1682.
2. Goldenberg I, Jonas M, Tenenbaum A, et al. Current smoking, smoking cessation, and the risk of sudden cardiac death in patients with coronary artery disease. *Arch Intern Med* 2003;163:2301.
3. Rea T, Heckbert S, Kaplan R, et al. Smoking status and risk for recurrent coronary events after myocardial infarction. *Ann Intern Med* 2002;137:494.
4. Kawachi I, Colditz G, Stampfer M, et al. Smoking cessation and decreased risk of stroke in women. *JAMA* 1993;269:232.
5. Ratchford E, Black J. Approach to smoking cessation in the patient with vascular disease. *Curr Treat Options Cardiovasc Med*. 2011;13:91-102.
6. Tonstad S, Farsang C, Klaene G, et al.: Bupropion SR for smoking cessation in smokers with cardiovascular disease: a multicentre, randomised study. *Eur Heart J* 2003;24:946–955.
7. Working Group for the Study of Transdermal Nicotine in Patients With Coronary Artery Disease. Nicotine replacement therapy for patients with coronary artery disease. *Arch Intern Med* 1994;154:989-995.
8. Joseph AM, Norman SM, Ferry LH, et al. The safety of transdermal nicotine as an aid to smoking cessation in patients with cardiac disease. *N Engl J Med* 1996;335:1792-1798.
9. Controlled Trial of Sustained-Release Bupropion, a Nicotine Patch, or Both for Smoking Cessation *New Engl J Med* 1999;340:685-691
10. Rigotti N, Pipe A, Benowitz N, et al. Efficacy and safety of varenicline for smoking cessation in patients with cardiovascular disease: a randomized trial. *Circulation* 2010;121:221-9.
11. Singh S, Loke Y, Spangler J, Furberg C. Risk of serious adverse cardiovascular events associated with varenicline: a systematic review and meta-analysis. *CMAJ* 2011;183: 1359-66.
12. Health Canada. Health Canada reviewing stop-smoking drug Champix (varenicline tartrate) and potential risk of heart problems in patients with heart disease. Available at [http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2011/2011\\_84-eng.php](http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2011/2011_84-eng.php). Accessed November 2011.
13. FDA Drug Safety Communication: Chantix (varenicline) may increase the risk of certain cardiovascular adverse events in patients with cardiovascular disease. Available at <http://www.fda.gov/Drugs/DrugSafety/ucm259161.htm>. Accessed November 2011.
14. e-CPS [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2011]. Catapres [product monograph]. Available from: <http://www.e-cps.ca>. Also available in paper copy from the publisher. Accessed November 2011.
15. e-CPS [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2011]. Nortriptyline [CPhA monograph]. Available from: <http://www.e-cps.ca>. Also available in paper copy from the publisher. Accessed November 2011.
16. 2010 PACT Workshop. Janice Burgess. March 25, 2010.
17. Management of Tobacco Addiction in Individuals with Mental Illness – April 2009. Ron Pohar, BScPharm. Accessed May 4, 2011. Available from: <http://pharma-com.sitepreview.ca/lessons/cccep-849-0109.pdf>. Accessed May 5, 2011.
18. Drug Interactions with Smoking . *American Journal of Health-System Pharmacy*. 2007;64(18):1917-1921. © 2007 American Society of Health-System Pharmacists. Available at: <http://www.medscape.com/viewarticle/562754>. Accessed May 4, 2011.
19. Brennan K. Which medicines need dose adjustment when a patient stops smoking? *Medicines Q&A* 136.3. UK Medicines Information: London; 2010. Available from: <http://www.nelm.nhs.uk/en/NeLM-Area/Evidence/Medicines-Q--A/Which-medicines-need-dose-adjustment-when-a-patient-stops-smoking2/>. Accessed May 12, 2011.
20. Hitsman B, Moss TG, Montoya ID, George TP. Treatment of tobacco dependence in mental health and addictive disorders. *Can J Psychiatry*. 2009 Jun;54(6):368-78. [PMID: 19527557].

21. Rennard S, Rigotti N, Daughton S. Management of Smoking Cessation in Adults. In UpToDate® online. Available by subscription at [www.uptodate.com](http://www.uptodate.com). Accessed May 12, 2011.
22. Health Canada Media Room: Advisories, Warnings and Recalls. Important Safety Information for Healthcare Professionals - CHAMPIX (varenicline tartrate). June 13, 2008. [http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2008/champix\\_hpc-cps-eng.php](http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2008/champix_hpc-cps-eng.php). Accessed May 11, 2011.
23. Pfizer Communication. April 8, 2011.
24. Fiore MC, Jaen CR, Baker TB, et al. *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service. May 2008. [Accessed April 28, 2011]. Available from: [http://www.surgeongeneral.gov/tobacco/treating\\_tobacco\\_use08.pdf](http://www.surgeongeneral.gov/tobacco/treating_tobacco_use08.pdf)
25. Rodriguez-Thompson D. Smoking and Pregnancy In UpToDate® online. Available by subscription at [www.uptodate.com](http://www.uptodate.com). Accessed May 12, 2011.
26. Ontario Medical Association Position Paper. 2008. Rethinking Stop Smoking Medications: Treatment Myths and Medical Realities. Available from: <https://www.oma.org/Resources/Documents/e2008RethinkingStop-SmokingMedications.pdf>. Accessed May 4, 2010.
27. Article; Canadian Pharmacist's Letter; January 2011; Vol: 27
28. Lumley J, Chamberlain C, Dowswell T, Oliver S, Oakley L, Watson L. Interventions for promoting smoking cessation during pregnancy. *Cochrane Database of Systematic Reviews* 2009, Issue 3. Art. No.: CD001055.
29. e-CPS [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2011]. Champix [product monograph]. Available from: <http://www.e-cps.ca>. Also available in paper copy from the publisher. Accessed May 2011.
30. Various monographs. Medications and Mothers' Milk. Thomas Hale. 2010. 14<sup>th</sup> Edition.
31. Motherisk. Smoking During Pregnancy Versus No Smoking and Using Nicotine Replacement Therapies (NRT). Adrienne Einarson, Assistant Director, Motherisk Program. 2006. A Critical Review of "Smoking Habits, Nicotine Use, and Congenital Malformations." *Morales-Suarez-Varela MM, Bille C, Christensen K, Olsen J Obstet Gynecol*. 2006 Jan; 107(1):51-57. Available from: [http://www.motherisk.org/JFAS\\_documents/JFAS\\_6003\\_e4.pdf](http://www.motherisk.org/JFAS_documents/JFAS_6003_e4.pdf). Accessed May 4, 2010.
32. American College of Obstetricians and Gynecologists Committee on Health Care for Underdeserved Women. ACOG committee opinion. Number 316, October 2005. Smoking cessation during pregnancy. *Obstet Gynecol* 2005;106:883-8.
33. Grimshaw G, Stanton A. Tobacco cessation interventions in young people. *Cochrane Database Syst Rev* 2006; (4): CD003289.
34. Rosen J, Sockrider M. Management of Smoking Cessation in Adolescents. In UpToDate® online. Available by subscription at [www.uptodate.com](http://www.uptodate.com). Accessed May 12, 2011.
35. Institute for Clinical Systems Improvement. Health care guidelines: tobacco use prevention and cessation for adults and mature adolescents. June 2004. [http://www.icsi.org/tobacco\\_use\\_prevention\\_and\\_cessation\\_for\\_adults/tobacco\\_use\\_prevention\\_and\\_cessation\\_for\\_adults\\_and\\_mature\\_adolescents\\_2510.html](http://www.icsi.org/tobacco_use_prevention_and_cessation_for_adults/tobacco_use_prevention_and_cessation_for_adults_and_mature_adolescents_2510.html). Accessed May 15, 2011
36. Rigotti N, Munafo MR, Stead LF. Interventions for smoking cessation in hospitalised patients. *Cochrane Database of Systematic Reviews* 2007, Issue 3. Art. No.: CD001837.
37. Thomsen T, Villebro N, Møller AM. Interventions for preoperative smoking cessation. *Cochrane Database of Systematic Reviews* 2010, Issue 7. Art. No.: CD002294.
38. [Wardman D](#), [Quantz D](#), [Tootoosis J](#), [Khan N](#). 2007 May;9(5):607-11. [Nicotine Tob Res](#). Tobacco Cessation Drug Therapy Among Canada's Aboriginal People. [PMID: 17454717]
39. Elton-Marshall T, Leatherdale ST, Burkhalter R. Tobacco, alcohol and illicit drug use among Aboriginal youth living off-reserve: results from the Youth Smoking Survey. [CMAJ](#). 2011 May 9. [Epub ahead of print]. [PMID: 21555383]
40. CAN-ADAPTT. Aboriginal Course. Available from: <http://www.canadaptt.net/English/Guideline/Aboriginal%20Peoples/Tools%20and%20Resources.aspx>.
41. Tscheng D. New drug: Nicorette Inhaler (Nicotine Inhalation System). Canadian Pharmacist's Letter 2004; 20(9):200917.
42. RESPTrec. Asthma Management Module. April 14<sup>th</sup> – April 17<sup>th</sup>, 2011.
43. [Borissova AM](#), [Tankova T](#), [Kirilov G](#), [Dakovska L](#), [Krivoshiev S](#). The effect of smoking on peripheral insulin sensitivity and plasma endothelin level. [Diabetes Metab](#). 2004 Apr;30(2):147-52. [PMID: 15223986]
44. [Justin J. Sherman](#) MCS, PharmD. The Impact of Smoking and Quitting Smoking on Patients With Diabetes. *Diabetes Spectrum*. October 2005 vol. 18 no. 4 202-208. Available from: <http://spectrum.diabetesjournals.org/content/18/4/202.full>. Accessed June 9, 2011.
45. Canadian Agency for Drugs and Technologies in Health (CADTH). Pharmacologic-based Strategies for Smoking Cessation. Report in Brief. September 2010. Available from: <http://www.cadth.ca/index.php/en/publication/2666>. Accessed June 9, 2011.