Nicotine Replacement Therapy Guidance Document

FINAL – October 29, 2012

Prescribing Nicotine Replacement and Managing Nicotine Withdrawal in Hospitalized Patients

BACKGROUND

An initial interim Nicotine Replacement Therapy (NRT) guidance document was posted in the spring of 2011 to support increased NRT prescribing in response to the City's Outdoor Smoking Bylaw. Since then a committee (Smoking Cessation Medication Expert Advisory Committee) has been meeting to finalize and add further clinical considerations to complete this prescribing resource for hospitalized patients. An updated interim document in January 2012 reflected the input provided and consensus obtained to date regarding general NRT prescribing. Additional clinical considerations have been added regarding relevant specialty areas in this final version. The guidelines in this document will become part of the regional Smoking Cessation Evidence Informed Practice Tool (EIPT) currently under development, which will include information about additional forms of NRT not available on hospital formulary as well as prescription cessation medications bupropion and varenicline. Both this document and the EIPT have been developed for use by all health care providers, including direct care staff, policy makers, educators and administrators.

This document is offered as a resource to assist clinicians in addressing nicotine withdrawal so that patients will have better health outcomes and have minimal urges to smoke outdoors on health care facility grounds in breech of the WRHA Smoke-free Policy and the City of Winnipeg Outdoor Smoking By-law. These guidelines replace both the previous interim guidance documents and the 2004 Nicotine Replacement Therapy algorithm that some of you may recall from the original Smoke-Free Policy implementation.

ASK

All patients over 16 years of age receiving care in Emergency Departments or admitted to hospital should be asked "**have you used tobacco in the past 7 days**" and "**have you used tobacco in the past 6 months**". These questions identify a higher proportion of current or recently quit smokers (and other tobacco users, such as users of spit tobacco) than asking "do you smoke?"

ADVISE AND PRESCRIBE

All patients who have smoked regularly immediately prior to admission should be advised that they should **not smoke during their hospital stay** and **nicotine replacement therapy (NRT) should be routinely prescribed** as soon as possible to manage anticipated nicotine withdrawal unless contraindications exist or declined by the patient. **Abstinence during hospitalization with NRT** for symptom management should routinely be the goal regardless of a patient's interest in smoking cessation at the time of admission.

Patients who have recently quit and were using NRTs or experiencing withdrawal symptoms at the time of admission should also be prescribed NRTs. Patients who initially decline NRT should be frequently assessed for withdrawal symptoms and offered NRTs again if symptoms occur.

Security staff at hospitals will be issuing "Notices of Smoking Ban" (NoSBs) to anyone found smoking in breech of the WRHA Smoke-free Policy and City of Winnipeg Outdoor Smoking Bylaw.

Copies of the NoSBs issued to hospitalized patients will be brought to the patient's care unit, and this should trigger a reassessment of nicotine withdrawal symptoms and re-offer of NRT.

RECOGNIZING WITHDRAWAL

Symptoms of nicotine withdrawal generally start within 2 - 3 hours after the last tobacco use, and peak about 2 - 3 days later. Symptoms may be severe, depending on length and amount of tobacco use. Common symptoms include (1):

- dysphoric or depressed mood
- insomnia
- irritability, frustration, or anger
- anxiety
- difficulty concentrating
- restlessness
- decreased heart rate
- increased appetite or weight gain

SMOKING CESSATION

All patients identified as tobacco users should also be advised to stop tobacco use in the longer term, assessed for their readiness to quit and assisted in their cessation efforts. On discharge, patients can be referred to the Smokers'Helpline, either by patients initiating the call to 1-877-513-5333 or going to the website at www.smokershelpline.ca, or by a faxed referral from the care provider that will trigger a call from the helpline to the patient.

More information on nicotine replacement as well as links to obtain the Smoker's Helpline fax referral form is available on the WRHA website under information for health professionals http://www.wrha.mb.ca/professionals/index.php.

NICOTINE DOSING

The dose of nicotine replacement should be made on the basis of the usual number of cigarettes smoked and titrated to effect. Table 1 below shows general dosing recommendations based on the number of cigarettes typically smoked, however, clinical judgment for individual patients should always be used. Table 2 identifies clinical situations in which NRT use may be contraindicated, or additional risk/benefit considerations may be needed prior to making a prescribing decision. Table 3 provides a summary of common drug interactions.

Once a patient has been established on an adequate NRT dose, this dose should be maintained for a minimum of 4 weeks, followed by a gradual tapering of dose (again titrating for adequate symptom management) until the patient stops using NRT. Some patients, particularly those with persistent and severe mental health diagnoses, may require longer durations of NRT use in order to be successful with stopping smoking.

It should be noted that anyone receiving >21 mg nicotine patch, or patch with gum prn, is being **prescribed NRT "off-label"**. This is becoming the practice norm for most patients who smoke more than 30 cig/day, as the 21 mg patch does not adequately manage nicotine withdrawal for these patients (2, 3).

Historically, NRT was contraindicated if people were also using tobacco (i.e. if person is smoking, should not also use NRT). Health Canada now has approved NRT gum for a "reduce to quit" approach to smoking cessation. The aim is to reduce number of cig/day, and replace some cigarettes with NRT gum. In fact, the risk of harm from cigarette smoking in conjunction with NRT use is minimal/non-existent - patients tend to smoke/use NRT until they feel comfortable (i.e. therapeutic dose), and will stop smoking if they begin to experience symptoms of nicotine toxicity.

Therefore, **concern that a hospitalized patient might smoke against medical advice while using NRT should not be a deterrent from prescribing NRT** (4, 5).

TABLE 1: GENERAL DOSING RECOMMENDATIONS

Cigarettes per day (cpd)	NRT Patch*	NRT Gum*
If patient smokes <10 cpd OR If patient weighs <45 kg	7 mg	2mg one piece q1-2h prn (max: 15 pieces/day) If using as monotherapy: 2mg one piece q1-2h prn (max: 20 pieces/day)
If patient smokes 10 – 20 cpd	14 mg	
If patient smokes 21-30 cpd	21 mg	If using as adjunct to patch: 2mg one piece q1-2h prn (max: 15 pieces/day) If using as monotherapy: 4mg one piece q1-2h prn (max: 20 pieces/day)
If patient smokes 31-40 cpd	28 mg (21 mg + 7 mg patch)	
If patient smokes >40 cpd	42 mg (21 mg patch x2)	

*NOTE: Dosing is based on using patch in combination with gum. The patch provides long-acting nicotine to manage nicotine withdrawal, and the gum is used as an adjunct to address withdrawal symptoms not managed by the patch. If patient requests gum only after understanding rationale for patch, order as per patient preference.

The above dosing pertains to adults. Generally NRT use is avoided with adolescents, and clinical judgment needs to be used with individual adolescent patients.

NRT Gum – Prescribing Considerations (6)

Side Effects - Common side effects include mouth soreness, hiccups, dyspepsia, and jaw ache. These effects are generally mild and transient and often can be alleviated by correcting the patient's chewing technique.

Chewing Technique – Gum should be chewed slowly until a peppery or flavoured taste emerges, then "park" the gum between cheek and gum to facilitate nicotine absorption through the oral (buccal) mucosa. Gum should be slowly and intermittently chewed and parked for about 30 minutes or until taste dissipates.

Absorption – Acidic beverages (eg. coffee, juices, soft drinks) interfere with buccal absorption of nicotine, so eating and drinking anything except water should be avoided for 15 minutes before and during chewing.

Dosing – Patients often do not use enough prn NRT to obtain optimal clinical effects. Instructions to chew the gum on a fixed schedule (one piece q1-2h) may be more beneficial than ad lib use. Consider leaving a small supply of gum at the bedside to ensure patient access to the medication when needed.

*Patients who are recumbent, sedated, dysphagic, and/or obtunded should be evaluated to determine safety of NRT gum (risk of aspiration, not able to use appropriately). Patch alone may be indicated.

Please refer to Table 3 below for common drug interactions with smoking cessation.

NRT Patch – Prescribing Considerations (6)

Location – At the start of each day, the patient should place a new patch on a relatively hairless location, typically between the neck and waist, rotating the site to reduce local skin irritation.

Activities – No restrictions while using the patch.

Dosing – Patch should be applied as soon as the patient wakes on the quit day, and on each subsequent day. With patients who experience sleep disruption, have the patient remove the 24-hour patch prior to bedtime.

Skin Reactions – Up to 50% of patients using the nicotine patch will experience a local skin reaction. These are usually mild and self-limiting, but occasionally worsen with the course of therapy. Local treatment with hydrocortisone cream (1%) or triamcinolone cream (0.5%) and rotating patch sites may ameliorate such local reactions. In fewer than 5% of patients, such reactions require the discontinuation of nicotine patch treatment.

Please refer to Table 3 below for common drug interactions with smoking cessation.

NOTE: NRT inhaler, lozenge, and mist – currently not available on hospital formulary.

CONSIDERATIONS, CAUTIONS AND CONTRAINDICATIONS

Nicotine use is low risk for most healthy adults and the goal of NRT is to remove the exposure to harmful combustion products while withdrawing from nicotine addiction. However, in some health conditions, nicotine itself poses or exacerbates health risks, particularly, cardiovascular. Additionally, NRT use has not been well studied in some patient populations such as adolescents, frail elderly, and pregnant and breastfeeding women. In these situations, additional considerations and cautions should be applied, but in many if not most cases, NRT can and should still be used if that presents less risk than the alternative of continued tobacco use.

There are very few absolute contraindications to the use of NRT. In rare and specific clinical situations nicotine is **strongly contraindicated** through either patient tobacco use or nicotine replacement therapy.

More commonly, **relative contraindications** may occur which should be considered in comparison to the likelihood of continued tobacco use without NRT. If abstinence or cessation is achievable without NRT then that is preferred. However, if continued tobacco use is occurring or very likely to occur, clinical judgment should be used to achieve the lowest feasible nicotine risk. In the past, NRT was too often withheld if there was even minimal concern about nicotine adverse effects. An overly cautious approach to nicotine prescribing can inadvertently result in higher patient nicotine exposure if withdrawal symptoms are self-medicated by continued tobacco use instead of NRT.

Below is a summary of absolute and relative contraindications for NRT. Table 2 provides additional clinical considerations within key service areas. Table 3 summarizes common drug interactions with smoking cessation. **These resources are intended to assist the individual clinical judgment that is needed to achieve the lowest tobacco and nicotine exposure possible for every patient.**

ABSOLUTE CONTRAINDICATIONS

- All free flap patients: NRT and tobacco products must not be used by these patients for at least 2 weeks before and 2 weeks after free flap surgery. For planned procedures involving face and breast, tobacco and NRT use should be avoided 4 weeks before and 4 weeks after surgery. The plastic surgeon managing the patient should decide the timing of NRT. (7-10).

- Patients who, due to the severity of illness and circumstances of care, do not have the option to use tobacco products (ie would not be otherwise exposed to nicotine if not prescribed NRT) and are comfortable without NRT and:
  - are in the immediate (within 2 weeks) post myocardial infarction period (6) or
  - have serious arrhythmias or
  - have unstable angina pectoris (6) or
  - are hemodynamically or electrically unstable (11 -15) or
  - have had orthopedic surgery or a serious fracture(s) (16 -19)

RELATIVE CONTRAINDICATIONS

- Patients who may continue to use tobacco if not prescribed NRT but
  - are in the immediate (within 2 weeks) post myocardial infarction period (6) or
  - have serious arrhythmias or
  - have unstable angina pectoris (6) or
  - are hemodynamically or electrically unstable (11 -15) or
  - have had orthopedic surgery or a serious fracture(s) (16 -19)

Abstinence without NRT is preferred, but NRT may be safer than continued use of tobacco in the above circumstances- **individual clinical judgment required**.

CAUTIONS

- Women who are pregnant or breast feeding

  Abstinence or cessation without NRT is preferred since NRT in pregnant and lactating women has not been well studied. However, NRT is safer than continued use of tobacco in the above circumstances- individual clinical judgment required (20).

- Adolescents

  Although nicotine replacement has been shown to be safe in adolescents, there is little evidence that NRT is effective in promoting long-term abstinence among adolescent smokers (6). Abstinence or cessation without NRT is preferred. For some physically mature youth who are continuing to use tobacco despite attempts to support them to be abstinent or quit without NRT, NRT can be considered.

TABLE 2: NRT USE - CLINICAL CONSIDERATIONS

SERVICE AREA	KEY CLINICAL CONSIDERATIONS
Anesthesia	• General prescribing guidelines can be followed.
Child Health/Adolescent Medicine	• NRT is safe in adolescents but little evidence for long-term cessation. • NRT use has not been studied in children. • Generally NRT use is avoided with adolescents, but clinical judgment needs to be used with individual adolescent patients. • For some physically mature youth who are continuing to use tobacco despite attempts to support them to be abstinent or quit without NRT, NRT can be considered.
Cardiac	• NRT is safe and effective in smokers with stable coronary artery disease. • NRT may be used in hospitalized patients with acute coronary syndromes when necessary, however, NRT should be used with caution among particular cardiovascular patient groups; o those in the immediate (within 2 weeks) post myocardial infarction period, o those with serious arrhythmias and o those with unstable angina pectoris.
Critical Care	• Use in critical care units should be determined on an individual patient basis rather than routinely ordered. • Due to the severity of illness, critical care patients do not generally have the option to use tobacco products against advice, so the risk of NRT is not relative to continued (and higher risk) tobacco use. • Critical care patients often have reduced consciousness due to illness or sedation so may experience less nicotine withdrawal symptoms. • Select subgroups of patients may benefit from NRT, such as those with restlessness refractory to usual management. • NRT use will be considered on the daily goals sheet in situations where NRT may be helpful.
Delirium, Dementia	• Safety of NRT in the setting of delirium or dementia has not been studied. • Nicotine withdrawal may contribute to agitation in delirious or demented patients. In the appropriate setting, consider the cautious use of NRT in agitated, cognitively impaired patients who were recent smokers and who have no other apparent cause of agitation. • Continued smoking significantly limits the choice of Personal Care Home. Advise patients and families about the pros and cons of smoking cessation when paneling for PCH.
Emergency	• For most patients, general prescribing guidelines can be followed. • If differential diagnosis includes conditions associated with

	relative contraindications (e.g. cardiac) the applicable considerations should be followed.
Frail Elderly	• Dose response has not been studied • Depending on life expectancy, long term benefits of smoking cessation (cancer, COPD prevention) may not be relevant. Short term benefits may well make cessation worthwhile (improvement in cardiovascular symptoms and outcomes). • Consider starting NRT at lower doses in frail, low-body-mass elderly. Increase to usual doses if nicotine withdrawal symptoms persist.
General Surgery	• For most patients, general prescribing guidelines can be followed. • If differential diagnosis includes conditions associated with contraindications (such acute MI or serious arrhythmia) the applicable considerations should be followed.
Internal Medicine	• NRT should be routinely offered to all patients who smoke and are admitted to respiratory medicine, internal medicine and coronary care units unless there are specific contraindications. • Patients who are hemodynamically or electrically unstable should have NRT deferred until stabilized and off vasopressors and/or inotropes. • If differential diagnosis includes conditions associated with relative contraindications (eg. cardiac) the applicable considerations should be followed.
Mental Health/Psychiatry (21)	• The use of NRT is safe in the psychiatric population. • Patients can smoke while using NRT. • Combination therapy i.e. patch and gum can be used simultaneously. • If the patient reports nightmares, remove the patch at night. • Mental Health patients often require higher does of NRT due to high levels of smoking. Exceeding the usual maximum dose (i.e. double patching) and duration requires cautious titration upwards and consultation with pharmacy. • Maintenance ($\geq$10 weeks) may have some benefit but must be considered on an individualized basis. • There are several psychotropic drugs whose levels are increased with smoking cessation/abstinence (in particular, Clozapine). More frequent monitoring of serum levels of these medications is advised (22).
Orthopedic Surgery	• Non-nicotine cessation medications and/or cessation counseling should be routinely offered to all orthopedic inpatients who use tobacco. Abstinence or cessation should be attempted without the use of NRT if at all possible. • Nicotine markedly increases complications of fractures, especially non-union.

	• Trauma patients confined to bed do not generally have the option to use tobacco products against advice, so the risk of NRT is not relative to continued (and higher risk) tobacco use. • If orthopedic patients not confined to bed are continuing to use tobacco products, the lesser risk of NRT could be considered with the goal being to achieve the lowest possible exposure to nicotine.
Plastic Surgery	• Given the complexity of plastic surgery and reconstructive procedures, nicotine replacement therapy should always be a deliberate decision by the plastic surgeon as to when it can be safely used. This includes the preoperative phase of care as some authors recommend abstinence from nicotine (both tobacco and NRT use) for at least 4 weeks prior to planned plastic surgical procedures. • All free flap patients must stop smoking before surgery; they are advised that one cigarette may cause flap necrosis. NRT and tobacco products must not be used by these patients for at least 2 weeks before and 2 weeks after free flap surgery. For planned procedures involving face and breast, tobacco and NRT use should be avoided 4 weeks before and 4 weeks after surgery (10). • Smokers who stop smoking for 4 weeks prior to reduction mammoplasty have similar complication rates to non-smokers (23). • Smokers who stop smoking for 3 weeks prior to Head and Neck Reconstructive surgery have similar wound healing to non-smokers (24). • The face lift operation is an excellent model of flap surgery. A face lift patient who smokes is 12.46 X more likely to suffer skin sloughing than a non-smoker (9).
Vascular Surgery	• General prescribing guidelines can be followed • **Note** - particular emphasis on smoking abstinence and/or cessation with vascular patients is warranted due to the detrimental effects of smoking on bypass graft patency rates, AAA growth, and amputation rates compared to non-smokers.
Women's Health (20)	• Pregnant smokers should be encouraged to stop tobacco use without medication. • Nicotine patch and gum have not been studied adequately in pregnant smokers. • Nicotine patch and gum have also not been evaluated in breastfeeding patients. • NRT, especially short-acting NRT (i.e. gum, lozenge, inhaler), is safer than smoking for the pregnant woman and her fetus if she is unable to stop smoking with a behavioural intervention. • A discussion regarding the risks and benefits of any form of nicotine to the developing fetus should be had with the patient. It should be stressed that NRT removes the risk of other highly toxic chemicals from the developing fetus.

TABLE 3: TABLE OF COMMON DRUG INTERACTIONS WITH SMOKING CESSATION

Potential drug interactions with smoking and quitting

(Current as of September 2011)

Many drug interactions have been reported with cigarette smoking.[1-4] Smoking induces drug metabolizing enzymes (primarily CYP1A2) in the liver. As a result, smokers have higher clearance of certain drugs and require higher doses to achieve clinical response. Conversely, when smokers quit smoking, their induced enzyme levels revert to normal. This may result in toxic drug levels in these patients whose drug doses were established while smoking.

Some potential drug interactions associated with cigarette smoking and quitting are depicted below. Although available information was based on case reports and small studies, clinicians should be aware of such potentials and monitor their patients closely for drug efficacy and toxicity.

Drug	Reported effects of smoking	Possible strategies after smoking cessation*
caffeine[1,3]	• ↑ clearance (by 56%)	• Assess total caffeine intake from all sources; ↓ intake by half; monitor for caffeine toxicity (e.g., irritability & insomnia)
clozapine[5,6]	• ↓ plasma concentrations (by 18%)	• Monitor for clozapine toxicity; ↓ dose (by a factor of ~ 1.5) may be required
flecainide[1,4]	• ↑ clearance (by 61%), ↓ trough serum concentrations (by 25%); ↑ dose requirements (by 17%)	• May need to ↓ dose, but no specific recommendation available. Monitor for clinical response
fluvoxamine[1,4,7]	• ↑ clearance (by 24%), ↓ AUC (by 31%), ↓ C_{max} (by 32%), ↓ C_{ss} (by 12-39%)	• Dosage adjustment not routinely recommended; close monitoring for adverse events
insulin[1,3,4] (subcutaneous)	• ↑insulin requirement possible due to nicotine-induced insulin resistance & vasoconstriction (i.e., ↓ absorption)	• Close monitoring of blood glucose, especially for patients prone to hypoglycemia or when tight glucose control is needed
mexiletine[1,4,8]	• ↑ oral clearance (by 25%); ↓ $t_{1/2}$ (by 36%)	• May need to ↓ dose, but no specific recommendation available. Monitor for clinical response. Use caution with older adults
olanzapine[1,3,5]	• ↑ clearance (by 98%),↓ plasma levels (by 12%)	• May need to ↓ dose, but no specific recommendation available. Monitor for excessive adverse effects
propranolol[1,4]	• ↑ clearance (by 77%)	• Blood levels may ↑ but clinical implication is unclear due to wide dosage range; closely monitor for adverse events
theophylline[1,4]	• ↑ clearance (by 58-100%); ↓ $t_{1/2}$ (by 63%); ↑ volume of distribution (by 31%)	• Monitor levels and adjust dose accordingly; ↓ dose (by 25-33%) may be needed to maintain therapeutic drug levels
warfarin[1,4]	• INR prolongation has been reported	• Closely monitor INRs; ↓ dose (by 14-23%) may be needed

* The relationship between the amount of cigarette smoking and the extent of drug interaction is unclear. The information in the table is based on current available literature and should not replace sound clinical judgments. Dosages should be individualized to achieve optimal therapeutic response with minimal toxicities. **Abbreviations**: **AUC** area under concentration-time curve; **C_{max}** peak concentrations; **C_{ss}** steady-state concentrations; **$t_{1/2}$** half-life

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