Supporting smoking cessation during pregnancy - nicotine replacement therapy (NRT)

General practice version

Key messages

- Non-pharmacological interventions such as multi-session behavioural intervention (for example, as delivered by Quitline) are recommended as first-line therapy.
- Nicotine replacement therapy (NRT) in conjunction with behavioural intervention may be considered in women unable to achieve abstinence using non-pharmacological interventions alone.
- NRT can be introduced early in pregnancy to maximise health benefits from smoking cessation. NRT use should be regularly reviewed by a medical practitioner (general practitioner (GP) or obstetric care provider) as often as practicable.
- NRT should be used at the most effective dose for the shortest duration possible to minimise foetal exposure to nicotine.

In this document

Purpose

The purpose of this guideline is to provide women who smoke with effective, evidence-informed treatments including nicotine replacement therapy (NRT) to support tobacco smoking cessation during pregnancy.

Target audience

This guideline applies to clinicians who are supporting pregnant women who smoke to quit. The content is intended to be relevant to those clinicians working in health services as well as the primary care setting.

Definitions

CO – carbon monoxide

Faster-acting NRT includes lozenge, mini lozenge, gum, inhalator and mouth spray

GORD – Gastroesophageal reflux disease

HSI – Heaviness of Smoking Index

NICU - neonatal intensive care unit

NRT – nicotine replacement therapy

PBS – Pharmaceutical Benefits Scheme

PKU – phenylketonuria

Background

Tobacco smoking during pregnancy has been associated with an increased risk of obstetric complications, adverse birth outcomes and infant mortality (1, 2).

The benefits of smoking cessation during pregnancy include reduced rates of low birth weight, preterm birth and neonatal intensive care unit (NICU) admission (3).

Women should be encouraged to stop smoking as early as possible using effective, evidence-informed treatments.

Ask, Advise, Help

The 'Ask, Advise, Help' model is an approach that promotes cessation and aims to connect people who smoke to best practice tobacco dependence treatment (such as multi-session behavioural intervention) (Appendix 1).

'Ask' – Asking about smoking status

At every antenatal appointment and during any hospital admission, ask all women about their tobacco smoking status and document this in the medical record.

Smoking status:

- Currently smokes
- Quit because of pregnancy (spontaneously quit/recently quit); document quit date
- Previously smoked; document quit date
- Never smoked

Offer carbon monoxide (CO) monitoring to all pregnant women if available. CO monitors are used to measure the amount of CO on a person's breath, and provide a motivational visual aid to encourage cessation and measure progress.

'Advise' – Advising women of the most effective way to quit and why quitting is important

Provide advice to all pregnant women who are currently smoking and those who have quit because of pregnancy, in a clear, strong, personalised and non-judgemental way. This may include:

- The importance of quitting completely, not just cutting down
- Benefits of quitting for woman and baby, personalised to the woman's unique clinical situation where possible
- The most effective way to quit using evidenced-informed interventions (i.e. behavioural intervention ± NRT)
- The importance of remaining abstinent, especially in women who have recently quit (recognising that these women are at higher risk of relapse)

If a woman declares she is not ready to quit smoking:

- Explore barriers to quitting
- Discuss the importance of reviewing and monitoring smoking status at every visit

'Help' – Helping women stop smoking

Non-pharmacological interventions such as multi-session behavioural intervention (for example, as delivered by Quitlines) are recommended as first-line therapy.

Offer all women who are currently smoking and those who have quit because of pregnancy a referral to Quitline (13 7848) for multi-session behavioural intervention.

Refer women with cardiovascular disease, mental illness or diabetes, and/or those who are taking concurrent medicines to a medical practitioner (*see – Assessment prior to smoking cessation*).

NRT may be considered in women unable to achieve abstinence using non-pharmacological interventions alone or in those with moderate to high nicotine dependence. The risks and benefits of NRT should be discussed with the woman prior to initiation. Risk-benefit discussions should be delivered in the context of nicotine use compared to continued smoking, rather than nicotine use alone.

Table 1: Risks and benefits of using NRT compared to tobacco smoking

Risks	Benefits
• Long term effects are unknown. • Adverse effects from NRT are possible. • Nicotine may be associated with potential risk of low birth weight, preterm birth, stillbirth, and/or cognitive impairment (1, 2, 4-6). However, findings from studies evaluating NRT during pregnancy did not corroborate these claims (7).	• NRT generally delivers lower levels of nicotine compared to tobacco smoking (8-10). • NRT provides a 'clean' source of nicotine, thus minimising the exposure to other harmful chemicals of tobacco smoke. • NRT use has been shown to increase smoking cessation rates by 43% (7). • Infants born to women who quit using NRT had better developmental outcomes at two years of age, compared to those born to women who did not quit (11).

Engage the woman's partner and other close family members who currently smoke and offer referral to Quitline.

Document the discussion in the woman's medical record and provide ongoing follow up care and support at all subsequent appointments.

Assessment prior to smoking cessation

Review underlying medical conditions

Relevant underlying medical conditions should be taken into consideration when a woman stops smoking and prior to the commencement of NRT. Consult a medical practitioner if the woman has any of the following:

Table 2: Relevant underlying medical conditions, concerns and recommendations.

Underlying medical condition	Concerns and recommendations
Mental illness	• Nicotine withdrawal symptoms (such as depressed mood, irritability and anxiety) can be mistaken for symptoms of mental illness. • Refer to a mental health professional for further advice.
Cardiovascular disease	• Smoking tobacco is known to contribute to adverse cardiovascular events, including acute coronary syndrome, myocardial infarction, stroke, angina, or congestive heart failure. • Anecdotal reports of adverse cardiac and vascular consequences resulting from the use of NRT have led to cautious use or avoidance in pregnant women. However, this is not supported by the current evidence. • NRT use in women with underlying cardiovascular disease is not associated with an increased risk of adverse cardiovascular events (12-14). However, it should be used under medical supervision (15).
Diabetes mellitus or gestational diabetes mellitus	• Nicotine may decrease insulin absorption, secondary to peripheral vasoconstriction (16). • Monitor blood sugar levels during and post-NRT. Insulin dose adjustment may be required. • Consider use of sugar free faster-acting NRT.
Generalised skin disease	• NRT patch may not be suitable in women with pruritus secondary to conditions such as obstetric cholestasis and pruritic urticarial papules and plaques of pregnancy. • Consider use of faster-acting NRT.
Nausea and vomiting, including hyperemesis and gastroesophageal reflux disease (GORD)	• Faster-acting NRT may exacerbate nausea and vomiting. • Swallowing nicotine can exacerbate symptoms of oesophagitis and gastric or peptic ulcer disease. • Ensure correct use of faster-acting NRT.

Other considerations

There are other considerations for some medical conditions/scenarios. Certain NRT formulations will not be suitable for some women, and an alternative should be considered.

Table 3. Additional considerations that may require alternative formulations of NRT.

Consideration	Recommendation
Phenylketonuria (PKU)	Avoid faster-acting NRT containing aspartame in women with PKU.
Dentures or complicated dental work	Avoid the use of nicotine gum as it may stick to and damage the dentures or dental work. Consider an alternative NRT formulation.
Asthma	Use NRT inhalator with caution as it may irritate the throat and cause coughing. Consider an alternative NRT formulation.

Review concurrent medicines use

Review concurrent medicines use when a woman stops smoking and prior to the commencement of NRT. Consult a medical practitioner if the woman is currently taking any medicines listed in Appendix 2.

General considerations:

- When a woman quits or significantly cuts down on smoking, the dose of certain medicines may need to be adjusted.
- Chemicals in tobacco smoke accelerate the metabolism of certain medicines by inducing the cytochrome P450 (CYP) 1A2 (17) and uridine 5'-diphosphate glucuronosyltransferases (18).
- Nicotine may counter the pharmacological actions of certain medicines via stimulation of the sympathetic nervous system (16).

Review history of previous quit attempts and withdrawal symptoms

Women who experience withdrawal symptoms during previous quit attempts are likely to experience them again.

Withdrawal from nicotine can be an uncomfortable experience, particularly within the first 24 hours when symptoms are most severe.

Symptoms of nicotine withdrawal can include:

- Restlessness, anxiety, irritability, emotional lability, frustration, anger
- Depression
- Inability to concentrate
- Insomnia
- Increased appetite, weight gain
- Headaches

Treatment

Assessing nicotine dependence

Nicotine dependence in women who smoke cigarettes can be assessed using the Heaviness of Smoking Index (HSI) (Table 4) (19).

Table 4: The Heaviness of Smoking Index (HSI)

Question	Answer	Score
How many cigarettes do you smoke each day?	10 or fewer	0
	11 to 20	1
	21 to 30	2
	31 or more	3
How soon after waking do you smoke your first cigarette?	After 60 minutes	0
	31 to 60 minutes	1
	6 to 30 minutes	2
	Within 5 minutes	3
	Total Score	

Treatment recommendations:

Treatment recommendations are based on HSI, taking into consideration previous quit attempts.

Pregnant women who have relapsed in the past or who experience cravings using one form of NRT alone may consider combination NRT (i.e. NRT patch and faster-acting NRT) under medical supervision.

Table 5: Treatment recommendation based on the level of nicotine dependence

HSI Score (level of dependence)	**0 to 2 (Low nicotine dependence)**	**3 to 4 (Moderate nicotine dependence)**	**5 to 6 (High nicotine dependence)**
Treatment recommendation	Multi-session behavioural intervention (Quitline) alone	Multi-session behavioural intervention (Quitline) ± faster-acting NRT Use the highest strength faster-acting NRT initially	Multi-session behavioural intervention (Quitline) + NRT patch ± faster-acting NRT
	If cravings or withdrawal symptoms are not controlled, consult a medical practitioner and consider:		
	The addition of faster-acting NRT	The addition of a NRT patch	Maximising the dose of NRT patch and faster-acting NRT

NRT can be introduced early in pregnancy.

NRT should be used at the most effective dose for the shortest duration possible to minimise foetal exposure to nicotine. To prevent relapse, do not stop NRT until the woman is able to resist trigger situations. NRT may then be ceased abruptly at the end of treatment.

NRT use should be regularly reviewed by a medical practitioner (general practitioner (GP) or obstetric care provider) as often as practicable.

If women are tempted to smoke after stopping NRT, encourage use of behavioural intervention through Quitline to help manage cravings. Consider reinitiating or resuming previous dose of NRT if necessary.

Behavioural intervention (Quitline)

Behavioural intervention has been shown to be effective in supporting pregnant women to stop smoking (3).

Quitline delivers phone-based multi-session behavioural interventions to people who smoke, including pregnant women.

Quitline counsellors use a range of behaviour change techniques to support people to make and sustain a quit attempt (including setting a quit date) and adjust to a smoke-free life.

Quitline counsellors encourage people to use smoking cessation pharmacotherapies if clinically appropriate, and in consultation with a health professional.

Pregnant women can be referred to Quitline either via fax (1800 931 739) or an online referral form (visit www.quit.org.au).

Nicotine replacement therapy (NRT) formulations

Faster-acting NRT

Faster-acting formulations of NRT such as lozenge, gum or inhalator that allow intermittent dosing are recommended for women with lower levels of nicotine dependence, or women who have been successful in cutting down on smoking but have not been able to quit.

Faster-acting NRT may be useful when strong cigarette cravings occur (20).

Women should keep a diary to identify smoking triggers and to determine daily NRT use. This information is useful to inform and optimise smoking cessation strategies.

Eating and drinking, especially acidic beverages (e.g. coffee or soft drinks), should be avoided 15 minutes before and during the use of faster-acting NRT as reduced salivary pH may interfere with nicotine absorption through the oral mucosa (21).

The mouth spray contains a small amount of alcohol and is not considered first line therapy in pregnancy.

Table 6: Faster-acting NRT

NRT formulation	Strengths	Recommended dose	Directions for use
Lozenge	2mg 4mg	One lozenge every 1 to 2 hours (up to 15 lozenges per 24 hours Maximum of 12 (2mg) lozenges per 24 hours when used in combination with an NRT patch	• Allow the lozenge to slowly dissolve in the mouth (may take up to 30 minutes) • Move the lozenge from one side of the mouth to the other from time to time • The lozenge should not be chewed or swallowed whole • Lozenge containing aspartame is not suitable for women with PKU
Mini lozenge	1.5mg 4mg	One mini lozenge every 1 to 2 hours (up to 20 (1.5mg) mini lozenges or 15 (4mg) mini lozenges per 24 hours). Maximum of 12 (1.5mg) mini lozenges per 24 hours when used in combination with an NRT patch	
Gum	2mg 4mg	One piece of gum every 1 to 2 hours (up to 20 (2mg) gums or 10 (4mg) gums per 24 hours). Maximum of 12 (2mg) gums per 24 hours when used in combination with an NRT patch	• Slowly chew the gum (about ten times) until there is a tingling or bitter taste, then place it between gum and cheek. When the strong taste or tingling has subsided, chew again • Repeat until the strong taste fades or it no longer causes tingling (can be up to 30 minutes) • The gum may not be suitable for women with dentures or complicated dental work • Gum containing aspartame is not suitable for women with PKU
Inhalator	15mg	The contents of one cartridge to be inhaled as required (up to six cartridges per 24 hours)	• Take short and shallow inhalations • Avoid deep inhalation as it may cause coughing and/or throat irritation • Nicotine in the inhalator is absorbed buccally • About eight to ten inhalator puffs substitute for one cigarette puff (i.e. if a cigarette is smoked in eight puffs, 64 to 80 puffs of the inhalator is required) • Each cartridge substitutes for seven cigarettes, after which a new cartridge should be used • Cartridges should be regularly changed • The inhalator should be used with caution in those with asthma and chronic throat conditions
Mouth spray	1mg	One to two sprays every 30 to 60 minutes	This NRT formulation contains small amounts of alcohol (less than 100mg per spray), and

NRT formulation	Strengths	Recommended dose	Directions for use
		(up to 4 sprays per hour and up to 64 sprays per 24 hours) Maximum of two sprays per hour (up to 32 sprays per 24 hours) when used in combination with an NRT patch	therefore is not considered first line in pregnancy. • Prime the pump before initial use, or if it has not been used for several days • Spray into the inside of the cheek or under the tongue; do not inhale whilst spraying • Avoid swallowing for a few seconds to allow the nicotine to be absorbed

NRT patches

The NRT patch provides a steady dose of nicotine throughout the day. However, it may not be effective for the relief of breakthrough cravings (22). Intermittent use of faster-acting NRT may be required to relieve cravings and manage withdrawal symptoms.

There is no evidence that weaning with lower strength patches at the end of treatment offers any benefit over abrupt cessation (23).

Remove nicotine patch at bedtime to minimise adverse effects and foetal exposure to nicotine.

Table 7: NRT patches

NRT formulations	Strengths	Recommended dose	Directions for use
Patch (16 hours)	25mg 15mg 10mg	One patch daily Consider the 21mg/24hr or 15mg/16hr patch in women with high nicotine dependence (7)	• The patch should be applied on waking in the morning and removed at bedtime • Apply the patch to dry, clean, hairless area(s) on the upper body or arm • Rotate sites of application
Patch (24 hours)	21mg 14mg 7mg		

Adverse effects

NRT is generally safe and well tolerated. However, minor adverse effects may occur. Correct use of all NRT formulations is paramount, as many adverse effects may be due to poor technique.

Table 8: NRT formulations and common adverse effects

NRT formulation	**Common adverse effects**
Patch	Skin irritation and erythema
Gum, lozenge, and mini lozenge	Nausea, vomiting, indigestion, and hiccups
Inhalator and mouth spray	Mouth or throat irritation, cough, nausea, vomiting, indigestion, and hiccups

References

1. National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health. The health consequences of smoking-50 years of progress: a report of the surgeon general. Atlanta (GA): Centers for Disease Control and Prevention (US); 2014.
2. Scollo M, Winstanley M. Tobacco in Australia: facts and issues. Melbourne: Cancer Council Victoria; 2019.
3. Chamberlain C, O'Mara-Eves A, Porter J, Coleman T, Perlen SM, Thomas J, et al. Psychosocial interventions for supporting women to stop smoking in pregnancy. Cochrane Database of Systematic Reviews. 2017;2:CD001055.
4. National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health. How tobacco smoke causes disease: the biology and behavioral basis for smoking-attributable disease: a report of the surgeon general. Atlanta (GA): Centers for Disease Control and Prevention (US); 2010.
5. Bruin JE, Gerstein HC, Holloway AC. Long-term consequences of fetal and neonatal nicotine exposure: a critical review. Toxicological Sciences. 2010;116(2):364-74.
6. Wickström R. Effects of nicotine during pregnancy: human and experimental evidence. Current Neuropharmacology. 2007;5(3):213-22.
7. Coleman T, Chamberlain C, Davey MA, Cooper SE, Leonardi-Bee J. Pharmacological interventions for promoting smoking cessation during pregnancy. Cochrane Database of Systematic Reviews. 2015(12):CD010078.
8. Fant RV, Owen LL, Henningfield JE. Nicotine replacement therapy. Primary Care: Clinics in Office Practice. 1999;26(3):633-52.
9. Ogburn PL, Jr., Hurt RD, Croghan IT, Schroeder DR, Ramin KD, Offord KP, et al. Nicotine patch use in pregnant smokers: nicotine and cotinine levels and fetal effects. American Journal of Obstetrics & Gynecology. 1999;181(3):736-43.
10. Oncken CA, Hatsukami DK, Lupo VR, Lando HA, Gibeau LM, Hansen RJ. Effects of short-term use of nicotine gum in pregnant smokers. Clinical pharmacology and therapeutics. 1996;59(6):654-61.
11. Cooper S, Taggar J, Lewis S, Marlow N, Dickinson A, Whitemore R, et al. Effect of nicotine patches in pregnancy on infant and maternal outcomes at 2 years: follow-up from the randomised, double-blind, placebo-controlled SNAP trial. The Lancet Respiratory Medicine. 2014;2(9):728-37.
12. Joseph AM, Norman SM, Ferry LH, Prochazka AV, Westman EC, Steele BG, et al. The safety of transdermal nicotine as an aid to smoking cessation in patients with cardiac disease. The New England journal of medicine. 1996;335(24):1792-8.
13. Hubbard R, Lewis S, Smith C, Godfrey C, Smeeth L, Farrington P, et al. Use of nicotine replacement therapy and the risk of acute myocardial infarction, stroke, and death. Tobacco Control. 2005;14(6):416-21.
14. Woolf KJ, Zabad MN, Post JM, McNitt S, Williams GC, Bisognano JD. Effect of nicotine replacement therapy on cardiovascular outcomes after acute coronary syndromes. The American journal of cardiology. 2012;110(7):968-70.
15. The Royal Australian College of General Practitioners. Supporting smoking cessation: a guide for health professionals. East Melbourne, Vic: RACGP; 2019.
16. Zevin S, Benowitz NL. Drug interactions with tobacco smoking. An update. Clinical pharmacokinetics. 1999;36(6):425-38.
17. Zhou SF, Yang LP, Zhou ZW, Liu YH, Chan E. Insights into the substrate specificity, inhibitors, regulation, and polymorphisms and the clinical impact of human cytochrome P450 1A2. The American Association of Pharmaceutical Scientists Journal. 2009;11(3):481-94.
18. Villard PH, Herber R, Seree EM, Attolini L, Magdalou J, Lacarelle B. Effect of cigarette smoke on UDP-glucuronosyltransferase activity and cytochrome P450 content in liver, lung and kidney microsomes in mice. Pharmacology & toxicology. 1998;82(2):74-9.
19. Borland R, Yong HH, O'Connor RJ, Hyland A, Thompson ME. The reliability and predictive validity of the Heaviness of Smoking Index and its two components: findings from the International Tobacco Control Four Country study. Nicotine & Tobacco Research. 2010;12 Suppl(Suppl 1):S45-S50.
20. Australian Medicines Handbook [Online]. Adelaide: Australian Medcines Handbook Pty Ltd; 2019.

21. Henningfield JE, Radzius A, Cooper TM, Clayton RR. Drinking Coffee and Carbonated Beverages Blocks Absorption of Nicotine From Nicotine Polacrilex Gum. The Journal of the American Medical Association. 1990;264(12):1560-4.
22. Ferguson SG, Shiffman S. The relevance and treatment of cue-induced cravings in tobacco dependence. Journal of Substance Abuse Treatment. 2009;36(3):235-43.
23. Stead LF, Perera R, Bullen C, Mant D, Hartmann-Boyce J, Cahill K, et al. Nicotine replacement therapy for smoking cessation. Cochrane Database of Systematic Reviews. 2012;11:CD000146.
24. Desai HD, Seabolt J, Jann MW. Smoking in patients receiving psychotropic medications: a pharmacokinetic perspective. CNS Drugs. 2001;15(6):469-94.
25. Oliveira P, Ribeiro J, Donato H, Madeira N. Smoking and antidepressants pharmacokinetics: a systematic review. Annals of General Psychiatry. 2017;16:17.
26. Faber MS, Fuhr U. Time response of cytochrome P450 1A2 activity on cessation of heavy smoking. Clinical pharmacology and therapeutics. 2004;76(2):178-84.
27. Wahawisan J, Kolluru S, Nguyen T, Molina C, Speake J. Methadone toxicity due to smoking cessation-a case report on the drug-drug interaction involving cytochrome P450 isoeznyme 1A2. Annals of Pharmacotherapy. 2011; 45(6):e34
28. Claire R, Chamberlain C, Davey M, Cooper SE, Berlin I, Leonardi-Bee J, et al. Pharmacological interventions for promoting smoking cessation during pregnancy. Cochrane Database of Systematic Reviews. 2020;CD010078

Further reading

For further information on smoking cessation, including in pregnancy, refer to the Royal Australian College of General Practitioners' *Supporting smoking cessation: A guide for health professionals*. Available at: https://www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines/supporting-smoking-cessation

Quit has developed practical videos demonstrating how to use each type of NRT formulation. Visit quit.org.au.

Appendices

Appendix 1: Summary of the smoking cessation pathway - 'Ask, Advise, Help' model

<table>
<tr><td>Ask</td><td>

Ask all women about their tobacco smoking status and document in the medical record

"Do you currently smoke?"
- Currently smokes
- Quit because of pregnancy (spontaneously quit/recently quit) – Congratulate and continue pathway
- Previously smoked – Congratulate and encourage them to remain abstinent.
- Never smoked

Offer CO monitoring to all pregnant women if available.

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<tr><td>Advise</td><td>

Advise all pregnant women, who are currently smoking and those who have quit because of pregnancy, in a clear, strong, personalised and non-judgemental way.

Provide information about:
- The importance of quitting completely, not just cutting down
- Benefits of quitting for the woman and her baby
- The most effective way to quit using evidenced-based interventions
- The importance of remaining abstinent, especially in women who have recently quit (recognising that these women are at higher risk of relapse)

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<tr><td>Help</td><td>

Helping women quit smoking through evidence-based smoking cessation interventions

- Refer women with underlying medical conditions or those who are taking concurrent medicines to a medical practitioner
- Assess level of nicotine dependence using the Heaviness of Smoking Index (HSI) in women who smoke cigarettes
- Offer all pregnant women who smoke or those who quit because of the pregnancy referral to Quitline for behavioural intervention
- Initiate NRT if clinically appropriate and after the risk-benefits have been explained to the women; dose according to the nicotine dependence level

<table>
<tr><th>Low nicotine dependence (HSI score 0 to 2)</th><th>Moderate nicotine dependence (HSI score 3 to 4)</th><th>High nicotine dependence (HSI score 5 to 6)</th></tr>
<tr><td>Behavioural intervention alone</td><td>Behavioural intervention ± faster-acting NRT

Use the highest strength faster-acting NRT initially</td><td>Behavioural intervention + NRT patch ± faster-acting NRT</td></tr>
<tr><td colspan="3">If cravings or withdrawal symptoms are not controlled, consult a medical practitioner and consider:</td></tr>
<tr><td>The addition of faster-acting NRT</td><td>The addition of a NRT patch</td><td>Maximising the dose of NRT patch and faster-acting NRT</td></tr>
</table>

NRT should be used at the most effective dose for the shortest duration possible.
- Follow up and document progress in medical record
- Reassess CO at follow up appointments, if available

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	• Offer the woman's partner a referral to Quitline, if they currently smoke

Appendix 2: Examples of clinically significant drug interactions with cigarette smoking (16, 24-27).

The information presented is adapted from the references and is not exhaustive. Please refer to a pharmacist for further information or other drug interaction resources.

Medicine	Effects of cigarette smoking	Recommendation post-smoking cessation
Benzodiazepine	Reduced sedation mediated by nicotine stimulation of central nervous system	Monitor for clinical effectiveness and adverse effects. Consider dose reduction if clinically indicated
Beta blockers (Increased clearance has been reported with propranolol)	Decreased blood pressure and heart rate control mediated by nicotine activation of sympathetic nervous system	Monitor for clinical effectiveness and adverse effects. Consider dose reduction if clinically indicated
Caffeine	Increased clearance, decreased plasma concentration	Reduce caffeine intake by 50%
Chlorpromazine	Decreased AUC and plasma concentration	Monitor clinical effectiveness and adverse effects. Consider dose reduction if clinically indicated
Clozapine	Increased clearance, decreased plasma concentration	Consider dose reduction and monitor trough plasma concentrations, clinical effectiveness, and adverse effects
Duloxetine	Increased clearance, decreased plasma concentration	Monitor for clinical effectiveness and adverse effects. Consider dose reduction if clinically indicated
Flecainide	Increased clearance, decreased plasma concentration	Monitor for clinical effectiveness and adverse effects. Consider dose reduction if clinically indicated
Fluvoxamine	Increased clearance, decreased plasma concentration	Monitor for clinical effectiveness and adverse effects. Consider dose reduction if clinically indicated
Haloperidol	Increased clearance, decreased plasma concentration	Monitor for clinical effectiveness and adverse effects. Consider dose reduction if clinically indicated
Insulin	Decreased subcutaneous absorption secondary to nicotine mediated peripheral vasoconstriction. Smoking may also increase insulin resistance	Monitor blood glucose level and adjust insulin dose as required. Ensure the woman is alert for signs of hypoglycaemia
Methadone	Increased clearance, decreased plasma concentration	Monitor for signs and symptoms of opioid toxicity. Consider dose adjustment if clinically indicated
Mirtazapine	Increased clearance, decreased plasma concentration	Monitor for clinical effectiveness and adverse effects. Consider dose reduction if clinically indicated
Olanzapine	Increased clearance, decreased plasma concentration	Monitor clinical effectiveness and adverse effects. Consider dose reduction if clinically indicated

Theophylline	Increased clearance, decreased half-life	Consider dose reduction and monitor trough plasma concentrations, clinical effectiveness, and adverse effects
Tricyclic antidepressants (amitriptyline, clomipramine, and imipramine)	Increased clearance, decreased plasma concentration	Monitor for clinical effectiveness and adverse effects. Consider dose reduction if clinically indicated
Warfarin	Increased clearance, decreased plasma concentration; no measurable effect on prothrombin time	Monitor INR and adjust dose accordingly

Document title	Supporting smoking cessation during pregnancy - nicotine replacement therapy (NRT)
Date	February 2020
Lead Author	Yuan Loke (Pharmacist, The Women's)
Contributing authors	Emma Dean (Senior Clinical Advisor, Quit) Wirawan Jeong (Pharmacist, The Women's) Dr Jasmine Just (Clinical Communications and Advocacy Coordinator, Quit) Hao Vo-Tran (Pharmacist, The Women's)
Reviewers	Professor Mark Umstad (Clinical Director of Maternity Services, The Women's) Jenny Ryan (Director of Maternity Services, The Women's)

Appendix 3: General Pharmaceutical Benefit Scheme (PBS) prescribing schedule for NRT

Eligibility for PBS subsidised NRT

- Patients who are ready to stop smoking can access up to 12 weeks of PBS subsidised NRT per year (24 weeks for an Aboriginal or Torres Strait Islander person).
- Patients must or be about to undertake behavioural intervention for smoking cessation at the commencement of the PBS subsidised NRT.
- PBS subsidised NRT brands include:
  - 21mg/24hr patch (Nicotinell® Step 1, Nicabate® P)
  - 14mg/24hr patch (Nicotinell® Step 2)
  - 7mg/24hr patch (Nicotinell® Step 3)
  - 25mg/16hr patch (Nicorette® 16hr Invispatch)
  - 4mg or 2mg lozenge (Nicotinell®)
  - 4mg or 2mg chewing gum (Nicotinell®)
- Only one PBS subsidised therapy for nicotine dependence at a time can be prescribed.
- For more information, refer to http://www.pbs.gov.au/pbs/search?term=nicotine.