

Women who smoke

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A review of the evidence

Background

Women who smoke are at significantly greater risk of developing a smoking related disease than men. They are also at risk of pregnancy related complications due to smoking and have more difficulty quitting. There are important gender differences in smoking behaviour that have implications for the quitting process. Advice to female smokers should take these factors into account and support should be tailored to their needs.

Objective

This article presents a summary of the evidence and a range of gender specific strategies that general practitioners can use to optimise the support they give to female smokers.

Discussion

Women may need more intensive behavioural and pharmacological support when quitting. Particular emphasis should be placed on addressing stress, social support, smoking cues and concerns about weight gain. Nicotine replacement therapy is less effective in women. However, it is still useful if used in adequate doses and can be used in pregnancy if the woman is unlikely to quit without it. Varenicline and bupropion are not approved in pregnancy or in lactation.

Keywords: smoking; women; health promotion

There is an increasing awareness of the special risks and needs of women who smoke. Women are at significantly greater risk of developing a smoking related disease than men, as well as being susceptible to gender specific health issues and pregnancy complications.1 Women also have more difficulty quitting smoking than men and may need extra support and advice to help them guit.^{2,3} In spite of this, women are less likely than men to be asked by their general practitioner about smoking or to be advised to quit.4 Even in pregnancy, GP intervention rates are well below recommended levels.5

Smoking rates are lower in Australian women than men: 17.7% of women and 21.1% of men smoke cigarettes daily.⁶ In the indigenous

population, 49% of women smoke daily compared to 51% of men.⁷ Women also smoke fewer cigarettes; 13 cigarettes per day on average compared to 14.5 per day for men.⁶

However, women are less likely than men to quit successfully, whether quitting on their own, with counselling or by using nicotine replacement therapy (NRT).² In one large study of 6600 smokers, women were 16% less likely to have quit than men at 13 years follow up.³

Nicotine in women

Premenopausal women metabolise nicotine faster than men and postmenopausal women, and have significantly lower blood nicotine levels for the same cigarette intake.⁸ Women on the combined oral contraceptive pill (COCP) metabolise nicotine faster still, and the rate accelerates even further in pregnancy.^{8,9} Nicotine withdrawal symptoms are equally severe in men and women,¹⁰ and, in women, greater during the luteal phase.¹¹

Smoking in men is strongly reinforced by the psychoactive effects of nicotine. Women are more influenced by non-nicotine factors such as a desire to reduce negative mood, to facilitate social interaction and to prevent weight gain. Women also smoke more in response to cues or triggers, such as being with friends who smoke or when under stress.^{2,10,12}

Health effects

Women are at significantly greater overall risk from the health effects of smoking than men. A meta-analysis of 19 studies found that women had a 35% increased overall risk compared to men for a range of serious smoking related diseases such as stroke, acute myocardial infarction and cancers. In heavier smokers the additional risk for women was substantially greater. Female smokers also have a 60% increased risk of coronary heart disease compared to men who smoke, ¹³ and in women taking COCP, smoking

is associated with a 10-fold increased risk of coronary heart disease. 13 This risk increases with age and cigarettes smoked per day and is regarded as a contraindication for women over 35 years of age who smoke 15 or more cigarettes per day. 14 Gender specific health issues experienced by women are outlined in Table 1.

Smoking in pregnancy and lactation

Although most Australian women are aware of the substantial health risks to themselves and their fetus, 14.8% of nonindigenous women and 51.8% of indigenous women reported smoking during pregnancy. 15 Only 7% of nonindigenous women and 3% of indigenous women are able to quit smoking in the first half of pregnancy. 16

Nicotine and carbon monoxide cross the placenta freely and reach high concentrations in the fetus, reducing placental blood flow and creating fetal hypoxia and growth restriction.¹⁷ Smoking in pregnancy approximately doubles the risk of stillbirth, spontaneous miscarriage and preterm delivery.17

Nicotine is a neurotoxin to the developing brain and causes cognitive, emotional and behavioural problems. 18 Children born to mothers who smoke in pregnancy also have reduced lung function and an increased risk of respiratory illness and SIDS. 19 Exposure to heavy smoking in utero also increases the risk of nicotine dependence in adulthood.20

Nicotine from smoking passes into breast milk. However, infant exposure to nicotine is estimated to be about 50 times less than maternal exposure

and is unlikely to be harmful.²¹ Smoking may reduce milk production.²²

Weight gain

Weight gain is a major concern for many women who smoke. Fifty percent of female smokers say that concerns about weight gain discourage them from trying to quit.²³ On average, women gain more weight than men after guitting smoking, with 60% of the extra weight gained in the first year.²⁴ Women are also more prone to extreme weight gain; 19.1% of women gain 20% or more of their baseline weight compared to 7.6% of men.²⁴ Weight gain during or after smoking cessation increases the risk of relapse.²³

Management

Optimising quit attempts

Smoking cessation support in general practice should follow Australian guidelines, which are based on assessing the smoker's readiness to change and the 5As: Ask, Assess, Advise, Assist and Arrange. 25, 26 However, guidelines need to be adapted to the special needs of women (Table 2).

- In view of their lower success rates, women may need more intensive interventions to improve their chance of quitting successfully^{2,27}
- In premenopausal women, quitting in the follicular phase may minimise withdrawal symptoms. 11,28 Quit rates may be higher at this time with NRT,29,30 although a recent trial found better results from quitting in the luteal phase with bupropion31

- If cigarettes are being used to self medicate anxiety and dysphoric mood, these disorders need to be addressed. Alternative strategies commonly used in general practice include problem solving, cognitive behaviour therapy, meditation, relaxation techniques, exercise and medication
- Women are more affected by smoking cues than men. Cues include social interaction, drinking coffee and alcohol, stress, and the end of a meal. Discuss coping strategies for relevant triggers and high risk situations and find alternative behaviours for when they occur²⁸
- Social support for women such as group meetings, smoking mentors and peer support may increase the chance of quitting32
- Encourage a smoking partner to quit, especially in pregnancy, as this can improve quit rates.33

Managing weight gain

Two recent reviews of weight gain prevention strategies for patients who were quitting smoking concluded that interventions are of borderline clinical benefit and are not justified on current evidence. 24,25 There was mixed evidence for exercise in reducing weight gain.²⁵ Giving general advice about reducing kilojoules was not shown to be effective in controlling weight or in achieving abstinence and is not recommended.25

Nicotine replacement therapy, bupropion and probably varenicline reduce weight gain while being used, but this effect is not maintained at 12 months after quitting.24

A pragmatic solution is to advise women to eat sensibly, exercise regularly and to accept some weight gain. Explain that one in four guitters will lose weight or stay the same³⁴ and that the health benefits of quitting are almost always greater than the health effects of the extra weight.

The role of medication in quitting

The Smoking cessation guidelines for Australian general practice^{25, 26} advise pharmacotherapy for all motivated smokers who are nicotine dependent. NRT is less effective in women than men. A meta-analysis found that the increase in quitting due to the nicotine patch versus placebo was only about half as large in women as in men at 6 months (4.6% vs. 9.3%).2

Table 1. Gender specific health issues	
Condition	Effect of smoking
Cervical cancer	RR: 1.83 ⁴³
Mucinous ovarian cancer	RR: 2.10 ⁴⁴
(16% of total ovarian cancers)	
Breast cancer	44% increased risk in slow 'NAT 2 gene acetylators' (50–60% of Caucasians) ⁴⁵
Endometrial cancer	Reduced by 25% in postmenopausal women who smoke^{46}
Infertility in women	OR: 1.6
	2 month delay in conception ⁴⁷
Assisted reproduction	OR: 0.54 ⁴⁸
Dysmenorrhoea	OR: 1.37 ⁴⁹
Menopause	1–4 years earlier ⁵⁰
RR = relative risk; OR = odds ratio	

Table 2. Smoking cessation guidelines for Australian general practice (adapted for women*)

Ask

Ask all patients and document in medical record (women are less likely to be asked*)

- Do you smoke? If yes, how many, previous quit attempts?
- · Have you ever smoked?

Assess

Readiness to change

- · How do you feel about your smoking?
- Are you ready to guit now?

Nicotine dependence

- How soon after you wake do you have your first cigarette?
- Did you have cravings or withdrawal symptoms in previous guit attempts?
- How many cigarettes do you smoke per day? (Smoking within 30 minutes of waking, withdrawal symptoms in previous guit attempts and smoking >15 cigarettes per day are indicators of nicotine dependence)

Barriers to quitting

• Weight gain, * social pressure, * stress, * withdrawal symptoms, fear of failure

Advise

Advise all smokers to quit in a clear but nonconfrontational way (eg. the best thing you can do for your health is to quit smoking)

Assist

Not ready smokers

• Discuss health issues; offer written information; invite to return when ready

Unsure smokers

- Discuss health issues; explore barriers to quitting; offer written information
- Do brief motivational interviewing

Ready to quit (women may need more intensive intervention*)

- Set a guit date (avoid the luteal phase*) or gradually cut down if preferred
- Discuss weight gain concerns and give simple dietary and exercise advice*
- Assess for anxiety and depression and offer assistance*
- Develop coping strategies for smoking cues such as social interaction, stress and alcohol*
- Advise social support*
- Encourage partner to quit*
- Pharmacotherapy if nicotine dependent:
 - nicotine replacement therapy. Optimise with adequate dose. precessation nicotine patch, combination therapy*
 - varenicline or bupropion if not pregnant*
- Consider referral to Quitline 13 78 48

Arrange

Follow up within 7 days

- · Give encouragement; review progress, problems and medication; give relapse prevention advice
- Negotiate further follow up visits

Adapted from Zwar N, Richmond R, Borland R, Stillman S, Cunningham M, Litt J. Smoking cessation guidelines for Australian general practice. Canberra: Commonwealth Department of Health and Ageing, 2004

*Factors of special importance to women

Another meta-analysis of all nicotine replacement therapies (gum, patch, inhaler and spray) found they were equally effective in women and men in the short term but were significantly less effective in women at long term follow up. However, they did reduce withdrawal symptoms effectively in women. 10 This gender difference in response to NRT may be partly due to genetic differences.34

Nicotine replacement therapy is still worth considering for smoking cessation in women due to its safety, accessibility over-the-counter, ease of use and low cost. Nicotine patches are now available on a Pharmaceutical Benefits Scheme (Authority required), reducing the cost even further.

Because of the faster metabolism of nicotine in premenopausal women, larger doses of NRT may be required, especially in women taking COCP. 8 All commercially available forms of NRT increase chances of successful smoking cessation. There is some evidence that precessation nicotine patches and combination therapy (nicotine patch with gum, lozenge or inhaler) are the most effective forms of NRT.35

Varenicline³⁶ and bupropion³⁷ appear to be equally effective in women and men, although absolute quit rates are higher with varenicline at 1 year (RR: 1.52).38

Quitting during pregnancy and lactation

In pregnancy, smoking cessation interventions are modestly effective. Interventions reduce smoking by only 6% compared to control groups but do improve health outcomes.39

Quitting without any medication is preferred. However, NRT should be considered if the woman is unable to guit without it, although NRT has not yet been demonstrated to be effective in pregnancy in clinical trials.^{25,34} Nevertheless, it is likely to be beneficial given the strength of data in nonpregnant smokers.40

Nicotine replacement therapy product information advises using intermittent dosing products such as gum or lozenges in pregnancy as they are likely to deliver a smaller daily dose of nicotine. However, because of the accelerated metabolism of nicotine in pregnancy, higher than standard doses are likely to be needed to control withdrawal symptoms and cravings. 9 In practice, the minimum effective dose that controls

symptoms should be used.²¹ Expert consensus is that NRT is safer than smoking in pregnancy. 41 Of women who do quit in pregnancy up to 80% will relapse within 1 year of birth. If a pregnant woman is unable to guit, cigarette reduction has been correlated with increased birth weight. A reduction to less than eight cigarettes per day may minimise harm.42

Product information also advises intermittent dosing NRT products during lactation to minimise risk to the infant. However, nicotine concentrations in the infant from NRT are low and unlikely to be harmful. NRT is considerably less hazardous to both mother and child than exposure to cigarette smoke.21

Bupropion and varenicline are not approved in pregnancy or lactation.

Summary of important points

- Women have more difficulty quitting and need more intensive support.
- · Particular emphasis should be placed on addressing stress and mood disorders, social support and smoking cues in women.
- · Weight gain prevention strategies are not supported by evidence.
- NRT is less effective in women but still has a useful role. Precessation nicotine patch and combination therapies are most effective.
- NRT should be considered in pregnancy if the woman is unable to quit without it.
- Varenicline and bupropion are equally effective in women and men but are not approved in pregnancy.

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Conflict of interest: Dr Mendelsohn has received honoraria for teaching, consulting and travel from Pfizer and GlaxoSmithKline. He is on Pfizer's Champix Advisory Board and has served on GlaxoSmithKline's Nicotine Replacement Therapy Expert Panel. Both companies have sponsored articles in Your Health newsletter, of which Dr Mendelsohn is editor.

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References

- Mucha L, Stephenson J, Morandi N, Dirani R. Meta-analysis of disease risk associated with smoking, by gender and intensity of smoking. Gend Med 2006;3:279-91.
- Perkins KA, Scott J. Sex differences in long-term smoking cessation rates due to nicotine patch. Nic Tob Res 2008;10:1245-51.
- Hyland A. Li Q. Bauer JE. Giovino GA. Steger C. Cummings KM. Predictors of cessation in a cohort of current and former smokers followed over 13 years. Nic Tob Res 2004;6(Suppl):63-9.
- Young JM, Ward JE. Influence of physician and patient gender on provision of smoking cessation advice in general practice. Tob Control 1998;7:360-3.
- Pullon S, Webster M, McLeod D, Benn C, Morgan S. Smoking cessation and nicotine replacement therapy in current primary maternity care. Aust Fam Physician 2004;33:94-6.
- Australian Institute of Health and Welfare 2008. 2007 National Drug Strategy Household Survey: first results. Drug Statistics Series number 20. Cat. No. PHE 98. Available at www.aihw.gov.au.
- Australian Bureau of Statistics. National Aboriginal and Torres Strait Islander Health Survey 2004-05, ABS Cat. no. 4715.0. Canberra: ABS, 2006.
- Benowitz NL, Sessov-Schlagger CN, Swan GE, Jacob 3rd P. Female sex and oral contraceptive use accelerate nicotine metabolism. Clin Pharmacol Ther 2006:79:480-8.
- Dempsey D, Jacob P 3rd, Benowitz NL. Accelerated metabolism of nicotine and cotinine in pregnant smokers. J Pharmacol Exp Ther 2002:301:594-98.
- 10. Cepeda-Benito A. Revnoso JT, Erath S. Metaanalysis of the efficacy of nicotine replacement therapy for smoking cessation: differences between men and women. J Cons Clin Psych 2004:72:701-22
- 11. Carpenter MJ. Upadhyaya HP. LaRowe SD. Saladin ME, Brady KT. Menstrual cycle phase effects on nicotine withdrawal and cigarette cravings: a review. Nic Tob Res 2006;8:627-38.
- 12. Berlin I, Singleton EG, Pedarriosse A, et al. The Modified Reasons for Smoking Scale: factorial structure, gender effects and relationship with nicotine dependence and smoking cessation in French smokers. Addiction 2003;98:1575-83.
- 13. Tan YY, Gast GM, van der Schouw YT, Gender differences in risk factors for coronary heart disease. Maturitas 2010;65:149-60.
- 14. World Health Organization. Medical eligibility criteria for contraceptive use. 4th edn. 2009. Available at http://whglibdoc.who.int/publications/2010/9789241563888_eng.pdf [Accessed 7 February 2011].
- 15. Laws P, Sullivan EA. Australia's mothers and babies 2007. Perinatal Statistics Series no. 23. Cat. No. PER 48. Sydney: AIHW National Perinatal Statistics Unit. Available at www.aihw.gov.au/ publications/per/per-48-10972/per-48-10972.pdf.
- Wills R, Coory M. Effect of smoking among indigenous and non-indigenous mothers on preterm birth and full-term low birthweight. Med J Aust 2008;189:490-4.

- 17. Einarson A. Riordan S. Smoking in pregnancy and lactation: a review of risks and cessation strategies. Eur J Clin Pharmacol 2009;65:325-30.
- 18. Rogers JM. Tobacco and pregnancy. Reproductive Toxicology 2009:28:152-60.
- 19. Carlson KH, Carlson KC. Respiratory effects of tobacco smoking on infants and young children. Paediatr Respir Rev 2008:9:11-9.
- 20. Buka SL, Shenassa ED, Niaura R, Elevated risk of tobacco dependence among offspring of mothers who smoked during pregnancy: a 30-year prospective study. Am J Psychiatry 2003:160:1978-84.
- 21. Dempsey D, Benowitz N. Risks and benefits of nicotine to aid smoking cessation in pregnancy. Drug Safety 2001:24:277-322.
- 22. Amir LH. Maternal smoking and reduced duration of breastfeeding: a review of possible mechanisms. Early Hum Dev 2001;61:45-67.
- 23. Spring B. Howe D. Berendsen M. et al. Behavioral intervention to promote smoking cessation and prevent weight gain: a systematic review and meta-analysis. Addiction 2009;104:1472-86.
- 24. Parsons AC, Shraim M, Inglis J, Aveyard P, Hajek P. Interventions for preventing weight gain after smoking cessation. Cochrane Database Syst Rev 2009, Issue 1. Art. No.: CD006219. DOI: 10.1002/14651858.CD006219.pub2.
- Zwar N, Richmond R, Borland R, Stillman S, Cunningham M, Litt J. Smoking cessation guidelines for Australian general practice. Canberra: Commonwealth Department of Health and Ageing, 2004. Available at www.racgp.org.au/ guidelines/smokingcessation.
- 26. Zwar N, Richmond R, Borland R, Peters M, Stillman S, Litt J, Bell J. Smoking cessation pharmacotherapy: an update for health professionals. South Melbourne: The Royal Australian College of General Practitioners, 2007.
- 27. Steinberg MB, Akincigil A, Delnevo CD, Crystal S, Carson JL. Gender and age disparities for smoking cessation treatment. Am J Prev Med 2006:30:405-12.
- 28. Perkins KA. Smoking cessation in women. Special considerations. CNS Drugs 2001;15:391-411.
- 29. Carpenter MJ, Saladin ME, Leinback AS, Larowe SD, Upadhyaya HP. Menstrual phase effects of smoking cessation: a pilot feasability study. J Women's Health 2008;17:293-301.
- 30. Franklin TR, Ehrman R, Lynch KG, Harper D, Sciortino N, O'Brien CP. Menstrual cycle phase at quit date predicts smoking status in an NRT treatment trial: a retrospective analysis. J Womens Health 2008;17:287-92.
- 31. Mazure CM, Toll B, McKee SA, Wu R, O'Malley SS. Menstrual cycle phase at quit date and smoking abstinence at 6 weeks in an open label trial of bupropion. Drug Alcohol Depend 2010. doi:10.1016/j.drugalcdep.2010.07.024.
- Stewart MJ, Kushner KE, Greaves L, Letourneau N, Spitzer D, Boscoe M. Impacts of a support intervention for low-income women who smoke. Soc Sci Med 2010. doi:10.1016/j.socscimed.2010.08.023.
- 33. Gage JD, Everett KD, Bullock L. A review of research literature addressing male partners and smoking during pregnancy. J Obstet Gynecol Neonatal Nurs 2007;36:574-80.

- Schnoll RA. Sex heterogeneity in pharmacogenetic smoking cessation clinical trials. Drug and Alcohol Dependence 2009:S94

 –99.
- Stead LF, Perera R, Bullen C, Mant D, Lancaster T.
 Nicotine replacement for smoking cessation. Cochrane Database Syst Rev 2008, Issue 1. Art. No.:CD000146. DOI: 10.1002/14651858.CD000146.pub3.
- Gonzales D, Rennard S I, Nides M, et al. Varenicline, an a4b2 nicotinic acetylcholine receptor partial agonist, vs. sustained-release bupropion and placebo for smoking cessation. JAMA 2006;296:47–55.
- Scharf D, Shiffman S. Are there gender differences in smoking cessation, with and without bupropion? Pooled and meta-analyses of clinical trials of bupropion SR. Addiction 2004;99:1462

 –69.
- Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. Cochrane Database Syst Rev 2008, Issue 3. Art. No.: CD006103. DOI: 10.1002/14651858.CD006103.pub3.
- Lumley J, Chamberlain C, Dowswell T, Oliver S, Oakley L, Watson L. Interventions for promoting smoking cessation during pregnancy. Cochrane Database Syst Rev 2009, Issue 3. Art. No.: CD001055. DOI: 10.1002/14651858.CD001055. pub3.
- Oncken CA, Kranzler HR. What do we know about the role of pharmacotherapy for smoking cessation before and during pregnancy? Nic Tob Res 2009;11:1265–73.
- Zwar N, Bell J, Peters M, Christie M, Mendelsohn C. Nicotine and nicotine replacement therapy – the facts. Australian Pharmacist 2006:25:969–73.
- England LJ, Kendrick JS, Wilson HG, et al. Effects of smoking reduction during pregnancy on birth weight of term infants. Am J Epidemiol 2001;154:694

 –701.
- Gandini S, Botteri E, Iodice S, et al. Tobacco smoking and cancer: a meta-analysis. Int J Cancer 2008;122:155

 –64.
- 44. Jordan SJ, Whiteman DC, Purdie DM, Green AC, Webb PM. Does smoking increase risk of ovarian cancer? A systematic review. Gynecol Oncol 2006;103:1122–9.
- Ambrosone CB, Kropp S, Yang J, Yao S, Shields PG, Chang-Claude J. Cigarette smoking, n-acetyltransferase 2 genotypes, and breast cancer risk: pooled analysis and meta-analysis. Cancer Epidemiol Biomarkers Prev 2008;1:15–26.
- Zhou B, Yang L, Sun Q, et al. Cigarette smoking and the risk of endometrial cancer: a meta-analysis. Am J Med 2008;121:501–8.
- Augood C, Duckitt K, Templeton AA. Smoking and female infertility: a systematic review and meta-analysis. Hum Reprod 1998;13:1532–9.
- Waylen AL, Metwally M, Jones GL, Wilkinson AJ, Ledger WL. Effects of cigarette smoking upon clinical outcomes of assisted reproduction: a meta-analysis. Hum Reprod Update 2009;15:31–44.
- Latthe P, Mignini L, Gray R, Hills R, Khan K. Factors predisposing women to chronic pelvic pain: systematic review. BMJ 2006:332:749–55.
- Practice Committee of the American Society for Reproductive Medicine. Smoking and infertility. Fertil Steril 2006;86(Suppl 1):S172–7.

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