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This article reviews the literature to compare differential outcomes among men and women after smoking cessation, assess barriers they may face during cessation and provide recommendations to address gender-specific challenges in smoking cessation interventions. There is some evidence that women achieve lower abstinence rates than men after a quit attempt with nicotine replacement therapy, as well as without pharmacotherapy, and several underlying mechanisms were discussed to account for these findings. These include: (a) women have specific genetic variants that affect pharmacokinetics and pharmacodynamics of the medication, (b) hormonal influences increase nicotine metabolism and withdrawal symptoms, (c) women are more responsive to nonpharmacological aspects of smoking than men, (d) women are more vulnerable to depression and negative mood than men, (e) weight concerns are greater barriers for women than for men, and (g) women receive less effective social support than men during a quit attempt. Gender-specific counselling that accounts for these factors and addresses the different needs of men and women may be a promising approach to improve long-term abstinence rates. However, more research is required to identify gender-related underlying mechanisms of differential smoking cessation outcomes, develop tailored interventions that account for gender differences and study the implementation and outcomes of gender-responsive treatment approaches.

Keywords: smoking, nicotine dependence, gender, treatment, review

Tobacco use remains the most important single modifiable risk factor for morbidity and mortality (US Department of Health and Human Services, 2004) and smoking cessation has major and immediate health benefits for people of all ages and at all stages in the smoking career (US Department of Health and Human Services, 1990). However, even with intensive interventions that combined behavioural treatment with pharmacotherapy, long-term abstinence rates have remained between 20–35% (Alterman, Gariti, & Mulvaney, 2001; Batra et al., 2010). Such findings of persistently low abstinence rates indicate the need for developing new and more effective tobacco cessation programs.

Recent studies have investigated smoker subgroups and individual differences in smoking in order to adapt the interventions to their specific needs (Ranney, Melvin, Lux, McClain, & Lohr, 2006). In this context, gender is regarded an important variable influencing smoking behaviour (US Department of Health and Human Services, 2001). The consideration of differences between men and women in tobacco-related studies is based on the assumption that they are associated with differences in other clinically relevant factors such as smoking motivation, response to treatment and reasons for relapse. Hence, the application of questionnaires, pharmacotherapy dosages and counselling strategies based on this information may improve both diagnostic accuracy and treatment outcome. The objectives of this article are to review the evidence of gender differences in smoking behaviour and cessation and to discuss implications for counselling and treatment.

Gender Differences in the Efficacy of Pharmacotherapy for Smoking Cessation

The seven FDA-approved first-line medications for the treatment of tobacco dependence are nicotine gum,
nicotine inhaler, nicotine lozenge, nicotine nasal spray, nicotine patch, bupropion and varenicline. The Cochrane Tobacco Addiction Group concluded that all forms of nicotine replacement therapy (NRT) increase the chances of quitting from 4% (gum) to 10% (nasal spray) and that the intensity of additional support is not essential for the success of NRT (Stead, Perera, Bullen, Mant, & Lancaster, 2008). However, there is inconsistent evidence as to whether NRT is equally effective in women as in men. Three meta-analyses have given special attention to this question. Munafo and colleagues (2004) evaluated 11 studies on the efficacy of nicotine patch and found that men and women were equally likely to quit when using the patch. More recently, Perkins and Scott (2008) reanalysed the data of this meta-analysis including three additional studies that reported gender differences in abstinence rates. They found that the increase in smoking cessation due to the nicotine versus placebo patch was only about half as large in women as in men, and concluded that women gain significantly less long-term benefit than men from using the nicotine patch. A third meta-analysis on different kinds of nicotine replacement products arrived at similar conclusions. Although NRT was more effective than placebo at any follow-up for men, the benefits for women were evident only at the 3- and 6-month but not at the 12-month follow-up. At the 6-month follow-up, NRT was more effective than placebo only in conjunction with high-intensity nonpharmacological support, but not with low support. After 12 months, NRT was not found to be superior to placebo in women, regardless of counselling intensity (Cepeda-Benito, Reynoso, & Erath, 2004). However, the results need be interpreted with some caution. On the one hand, most clinical studies had sample sizes that were probably too small to detect gender differences. Additionally, only very few studies showed superior outcomes for women compared to men, which appears to support the assumption that women have more difficulties in smoking cessation (Perkins, 2001). On the other hand, it is important to note that almost no study addressed smoking of cigars and pipes, which are used largely by men (U.S. Department of Health and Human Services, 2001). Furthermore, the majority of published studies did not present cessation results disaggregated by gender. For example, Cepeda-Benito et al. (2004) identified 83 articles that met their inclusion criteria, but only seven studies reported abstinence rates for both NRT and placebo groups separately for men and women. Upon request, they obtained unpublished data for 14 studies. Finally, their analyses included data from 21 studies, which represented only 25% of the initial sample. Similar experiences were reported by Munafo et al. (2004). It remains unclear whether gender differences were not investigated in other studies, or whether the results did not reach statistical significance and therefore were not presented. Publication bias may have resulted in an overrepresentation of studies that found gender differences in meta-analyses. Despite inconsistent findings, several researchers have suggested that women face unique barriers during cessation and require special attention and targeted intervention strategies (Perkins, 2001; Reynoso, Susabda, & Cepeda-Benito, 2005; Schnoll, Patterson, & Terman, 2007).

To date no gender differences in the efficacy of non-nicotinic smoking cessation medication were reported. In a meta-analysis examining the efficacy of the antidepressant bupropion, this drug was found to be equally efficacious for men and women in aiding cessation (Scharf & Shiffman, 2004). Varenicline, a selective α4β2 nicotinic acetylcholine receptor partial agonist, was FDA approved as a pharmacotherapy for tobacco dependence in 2006. Gender differences were explored in one clinical trial that showed this medication was as efficacious in women as in men (Gonzales et al., 2006). However, lower abstinence rates for women have been reported for studies without any assistance (Osler, Prescott, Godtfredsen, Heia, & Schnohr, 1999; Ward, Klesges, Zbikowski, Bliss, & Garvey, 1997).

**Gender-Related Factors Affecting Smoking Behaviour and Cessation**

One potentially promising approach to improving abstinence rates is the use of treatment matching, where different smokers receive different treatments depending on individual vulnerabilities to treatment failure or relapse, and adapted to individual needs (Smith et al., 2001). Several biological and psychosocial factors have been posited to explain possible gender differences in smoking cessation studies and to be targets for treatment-matching strategies. Specifically, it has been assumed that (a) genetic differences may lead to gender-specific responses to NRT, (b) hormonal influences may affect nicotine metabolism and withdrawal symptoms, (c) women may be more responsive to the nonpharmacological aspects of smoking than men, (d) women may be more vulnerable to depression and negative affective states than men, (e) weight concerns related to smoking cessation may be greater in women than in men and (f) social support and social interactions are more important for women than for men during cessation.

**Genetic Factors**

Specific genes are associated with nicotine metabolism, risk of smoking initiation, nicotine dependence and tobacco cessation (Ho & Tyndale, 2007). The results of individual genetic studies indicated that NRT may have less beneficial effects in females because they have specific genetic variations that influence the pharmacokinetics and pharmacodynamics of nicotine products (Schnoll & Patterson, 2009). Smoking and exposure to nicotine leads to a release of neurotransmitters in the brain — especially dopamine, which is critical for the acute reinforcing effects of nicotine (Benowitz, 2009). Differences in smoking cessation may be related to the...
dopamine d2 receptor (DRD2) gene. A specific variation in DRD2, namely the TaqI A1, is associated with a reduced number of dopamine-binding sites in the brain. In females the effectiveness of NRT may be related to this genotype. A placebo-controlled study on the efficacy of the nicotine patch showed a significant genotype-sex interaction related to treatment outcome: specifically, females with at least one A1 form of the DRD2 gene (and accordingly, less dopamine-binding sites in the brain) had greater benefit from the active patch compared to females with the more common homozygous A2 form of the DRD2. No significant association between genotype and treatment outcome was found for males (Yudkin et al., 2004).

Other studies found genotype effects on smoking abstinence related to catechol-O-methyl-transferase (COMT), an enzyme that metabolises and inactivates dopamine in the brain. Different variants of the gene that encodes this enzyme are associated with different levels of metabolic activity. There is a common variation of the COMT gene that results in an enzyme with low-metabolism activity. This low-metabolism activity form is associated with a considerable reduction of the dopamine degradation and increased dopamine levels in the brain (Lachman et al., 1996). Colilla and colleagues (2005) examined quit rates in female participants of a population-based case-control study and an NRT intervention study. In the case-control study, females with the low-activity form of the COMT enzyme were significantly more likely to be ex-smokers than current smokers. In the intervention study, the low-activity form of the COMT was associated with smoking cessation among females, independent of the type of NRT. The probability of smoking cessation increased significantly with each allele (corresponding to lower COMT activity and higher dopamine concentrations). There was no significant association between the COMT genotype and smoking cessation in male participants of the intervention study.

Tobacco-related studies on differences in genetics between men and women are, however, in their infancy stage. Only few studies have been published to address these questions, many of which were underpowered and many findings have not been replicated. So far, these results cannot be used to individualise treatment for nicotine dependence based on sex and genotype. To further our understanding of the role of genes and sex in smoking cessation and response to medications, more research with larger study samples is needed to replicate the findings (Scholl & Patterson, 2009).

**Hormonal Factors**

It has also been assumed that differences in sex hormones or menstrual phase related factors may account for potential sex differences in smoking. For example, nicotine and cotinine metabolism is substantially increased during pregnancy (Dempsey, Jacob, & Benowitz, 2002). Furthermore, in adolescents (Berlin, Gasior, & Moolchan, 2007) as well as in adults (Benowitz, Lessov-Schlaggar, Swan, & Jacob, 2006), nicotine metabolism is substantially higher in females using hormonal contraception compared to males, and also compared to females not using hormonal contraception. It has been suggested that oestrogenic hormones accelerate nicotine metabolism and that females may need higher doses of NRT than males in order to benefit to the same extent (Benowitz et al., 2006).

Furthermore, levels of sex hormones alternate during the menstrual cycle and, in many females, these fluctuations result in negative affective states such as depression and irritability that are similar to tobacco withdrawal symptoms. Accordingly, smoking behaviour and withdrawal symptoms may alternate across the menstrual phases, possibly peaking during the premenstrual phase. The evidence suggests that females who attempt to quit smoking experience heavier withdrawal during the luteal (premenstrual) phase (Carpenter, Upadhyaya, L Rowe, Saladin, & Brady, 2006).

The current menstrual phase may be considered when scheduling a quit date, especially for females who are affected by severe premenstrual discomfort. There is some evidence that a quit attempt during the follicular phase might be more successful than during the luteal phase (Carpenter, Saladin, Leinbach, L Rowe, & Upadhyaya, 2008; Franklin et al., 2008). NRT has been found to diminish craving and affective symptoms in females, particularly in the luteal phase (Allen, Hatsukami, Christianson, & Brown, 2000). In case NRT does not relieve withdrawal symptoms in individual women, counsellors should take into account that this may be the result of an accelerated nicotine metabolism and consider increasing the nicotine dose.

**Pharmacological Versus Nonpharmacological Smoking Motives**

In addition to biological variables, how psychosocial factors affect men and women differently have been discussed. For example, it has been hypothesised that men smoke mainly for nicotine reinforcement, while women may be more responsive to nonpharmacological aspects of smoking such as the hand-to-mouth-movement; the smell, taste and inhaling of the smoke; or social interactions; and are therefore at higher risk for relapse due to the exposure to conditioned smoking cues (Perkins, Donny, & Caggiula, 1999). This assumption was supported by laboratory studies, where women were less likely than men to accurately differentiate nicotinic from placebo nasal spray, and they self-administered nicotine replacement products to a lesser extent compared to men (Perkins, 1996). They also reported more pleasurable effects after smoking a cigarette in comparison to receiving the same amount of nicotine via nasal spray, while there were no such differences in men. In contrast,
Smokers are more likely to have a history of depression than nonsmokers (Klingsøyr, Nygård, Sorensen, & Sandanger, 2006; Murphy et al., 2003) and this association may be stronger for women (Husky, Mazure, Paliwal, & McKee, 2008). Furthermore, depressive disorders are more prevalent in women than in men (Strine et al., 2008). Screening for depressive disorders should therefore be included in the diagnostic process after initiating smoking cessation counselling. If a client has a history of depression or indicates using smoking to cope with negative emotions, the counselling program should include teaching depression-specific components (Wilhelm, Wedgwood, Niven, & Kay-Lambkin, 2006) such as mood and stress management and techniques to interrupt ruminative thinking, especially for individuals who do not benefit from brief smoking cessation interventions (Smith et al., 2001). The discussion of alternative behaviours to smoking should focus on pleasant and rewarding activities that increase the ex-smoker's quality of life. Bupropion may be considered for pharmacotherapy. Furthermore, to prevent and manage tobacco relapses and depressive episodes after smoking cessation, counselling and support could be provided over a period of several months, including cognitive–behavioural relapse-prevention and -management strategies for both smoking and depression when indicated. Smokers who have clinically relevant depression or other mental health disorder should be referred to psychiatric and/or psychotherapeutic services.

**Weight Concerns**

Concerns about weight gain have often been considered as a barrier to smoking cessation that is more relevant for women. Indeed, women reported greater weight control expectancies attached to smoking (Reig-Ferrcr & Cepeda-Benito, 2007), expressed more weight concerns regarding a quit attempt (Clark et al., 2006) and tended to gain more weight after quitting than men (Plega, Trotano, Pamuk, Kuczmarski, & Campbell, 1995). Nicotine replacement therapy (bupropion, fluoxetine) limited post-cessation weight gain at the end of treatment, but this effect was not maintained in the long term (Parsons, Shraim, Inglis, Aveyard, & Hajek, 2009).

Nonpharmacological interventions — mostly designed for women specifically — used two different strategies to address weight concerns and weight gain: cognitive approaches aimed at reducing weight and body image concerns by reevaluating maladaptive beliefs about the ideal shape and the importance of low weight showed some promising results (Perkins, Marcus, et al., 2001). In contrast, behavioural exercise- or diet-based programs aimed at preventing weight gain. Two recent reviews of weight gain prevention strategies for patients who were quitting smoking concluded that such interventions have neither beneficial nor adverse effects on tobacco abstinence, and limited weight gain in the short

Negative Mood and Depression

It has also been suggested that women more often than men use cigarettes to cope with negative emotions and are more vulnerable to develop negative affective states and depressive disorders during a quit attempt. This assumption was supported by studies where women scored higher than men on negative-affect-reduction smoking scales (Reig-Ferrcr & Cepeda-Benito, 2007; Ward et al., 1997), and were less confident in their ability to refrain from smoking when experiencing negative emotions (Etter, Prokhorov, & Ferneger, 2002). During abstinence, women also reported greater increases than men in negative affective states, withdrawal-related distress and smoking urges to relieve distress (Leventhal et al., 2007). A smoking cessation intervention study showed that women with a history of major depression were less likely to be abstinent than women without depression history, while a history of depression did not predict abstinence for men (Hall et al., 1998).
term but not in the long term (Parsons et al., 2009; Spring et al., 2009). However, besides promoting abstinence, smoking cessation interventions aim at facilitating and encouraging a healthy lifestyle including balanced diet and regular exercise, therefore, both the cognitive and the behavioural approach may be combined during smoking cessation counselling. If clients use eating and smoking to cope with negative emotions, the counselling program should also include mood management strategies.

Social Support
Finally, the importance and the role of smoking for social relations and relationship behaviour may be stronger for women than for men. In a longitudinal study, nonsmoking wives were more likely to resume/initiate smoking when they were married to smokers than to nonsmokers, while wives' smoking status did not predict husbands' initiation of smoking (Homish & Leonard, 2005). In a smoking cessation intervention study, individuals with a smoking partner were more likely to relapse than individuals without a smoking partner and this effect was more pronounced in women than in men (Manchón Walsh et al., 2007). Men and women may also have different needs in terms of social support for a smoking cessation attempt. In a study where support persons of prospective quitters were included in the intervention, men who received social support had higher abstinence rates compared to men without social support at any follow up. Although support was also initially effective for women, it had no effect on mid- and long-term abstinence (Carlson, Goodey, Bennett, Taenzer, & Koopmans, 2002). Furthermore, for male smokers greater influence from spouse/partner was associated with greater reduction in daily smoking. In contrast, for women the greater the partner influence, the less they reduced their smoking (Westmaas, Wild, & Ferrence, 2002). It has been suggested that such differences in outcome might simply reflect more effective support provided to male smokers by their wives compared with the support given to female smokers by their husbands (Perkins, 2001).

Smoking behaviour among family members, friends and colleagues should be assessed in the initial counselling phase in order to identify factors and situations that may impede cessation or increase the risk for relapse. Smokers should be encouraged to seek support from ex- or non-smoking friends, who share their experiences, discuss helpful strategies and problems related to smoking cessation and express confidence in the person's ability to quit. In addition, practising and expanding social skills during the counselling sessions may be particularly helpful for women. In case that she has a partner who smokes, has a lot of arguments about smoking with her partner or feels pressured by her partner, a woman may benefit from developing strategies to relieve tension associated with the quit attempt and to represent her own interests without affecting the relationship. However, smoking is often embedded in the social and family context over many years, and may play an important and stabilising role for couple and family dynamics by facilitating intimacy, communication and emotional regulation (Doherty & Whitehead, 1986). A smoking cessation attempt by one or both partners and the accompanying change or loss of shared rituals may threaten the stability of the relationship (Nyborg & Nevid, 1986). Therefore, smoking cessation counsellors may consider initiating a discussion about the positive aspects of smoking in the relationship, and help the couple to establish new shared rituals and to develop strategies to cope with relapses in a way that it does not threaten the relationship or the partner's abstinence (Rohrbaugh et al., 2001).

Conclusion
This article reviews the literature to compare men and women in smoking cessation behaviours, and provides recommendations to address gender-specific challenges in smoking cessation interventions. In summary, two meta-analyses found that women achieved lower abstinence rates than men when using NRT; and genetic, hormonal, psychological and social factors have been discussed to account for these outcomes.

It is important to note that many studies did not find gender differences after smoking cessation (e.g., Croghan et al., 2009; Gritz et al., 1998; Killen, Fortmann, Varady, & Kraemer, 2002; McGrady & Pederson, 2002). Similarly, gender differences in smoking motives and many of the characteristics of tobacco dependence could not be conclusively confirmed (Wetter, Fiore, et al., 1999; Wetter, Kenford, et al., 1999). In view of the current state of research, the scientific treatment guidelines recommend the same intervention strategies for men and women (Fiore et al., 2008), mainly due to the limited research with respect to gender differences in clinical outcome studies (Piper, Fox, Welsch, Fiore, & Baker, 2001). However, the number of studies that evaluated smoking cessation programs designed for one gender is increasing. More research and clinical work is required to appropriately tailor treatments for tobacco dependence, account for gender differences and study the implementation and outcomes of gender-responsive treatment approaches.

Our findings suggest that NRT combined with counselling that accounts for gender-specific factors such as hormonal influences, smoking motivation, negative mood, weight concerns and social/partnership needs may be a promising approach to improve long-term abstinence rates. However, the findings do not suggest that counsellors should only focus on psychological/emotional aspects of tobacco dependence in women and on physical aspects in men (and conversely overlook essential psycho-
logical needs in men and nicotine-related needs in women). Rather, counsellors should systematically assess smoking behaviour and the characteristic of tobacco dependence in each individual who presents for tobacco dependence counselling and to carefully tailor the intervention to individual needs.

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