



Smokers with mental illness

Breaking down the myths

COLIN MENDELSON MB BS(Hons); MARK E. MONTEBELLO MB BS, FRANZCP, FACHAM

Key points

- People with mental illness have a smoking prevalence twice that of people without mental illness.
- Smokers with mental illness are more likely to die from tobacco-related disease than from mental illness.
- Smokers with mental illness are at least as motivated to quit as those without mental illness and can quit successfully, generally without any exacerbation of their mental health condition.
- The same evidence-based therapies for quitting used in the general population are recommended for smokers with mental illness, with some special considerations in choice of pharmacotherapy.
- Patients should be monitored for side effects of psychotropic medications when quitting as dosages may need to be adjusted.

Smokers with mental illness are motivated to stop smoking and can quit successfully, usually without any exacerbation of their mental illness. GPs should be proactive in helping these patients to quit.

People with mental illness make up an increasing proportion of the smoking population. Although smoking rates in Australia have declined significantly in recent years, the prevalence of smoking in patients with mental illness remains high and is twice that of people without mental illness.¹⁻³

Nearly one in two Australian adults have a mental health disorder at some time in their lives.¹ Patients with mental illness have poorer health and a shorter life expectancy than the rest of the population, and smoking is a major contributor to this health gap.^{4,5} Smoking also has a substantial financial impact. Smokers with schizophrenia may spend up to 30% of their limited income on cigarettes, sacrificing a healthier diet, social activities or medication in order to smoke.⁶

Smokers with mental illness are less likely to be offered professional help to quit,⁷ in part because of the many myths and misconceptions about smoking in this population (Table 1⁹⁻²⁰).⁸

For example, many health professionals mistakenly believe people with mental illness are not interested or are unable to quit, or that quitting will worsen their mental illness.⁸ However, smokers with mental illness are often highly motivated to quit,^{9,10} and GPs can be effective in helping them to do so.²¹

This article examines the close link between smoking and mental illness, in particular anxiety disorders and depression, which are common in general practice, and schizophrenia and bipolar disorder in which smoking rates are highest.^{22,23} We explore the reasons for the high smoking prevalence in these disorders and the misinformation that has led to low intervention rates by health professionals. The evidence for treatment for smokers with specific mental illnesses is discussed, with practical advice to assist doctors in helping these smokers to quit.

Dr Mendelson is a General Practitioner and Tobacco Treatment Specialist at the Brain & Mind Research Institute, Sydney. Dr Montebello is a Senior Staff Specialist in Addiction Psychiatry for the South Eastern Sydney Local Health District Drug and Alcohol Service; and Conjoint Lecturer, National Drug and Alcohol Research Centre, University of New South Wales, Sydney, NSW.

TABLE 1. MYTHS ABOUT SMOKING AND MENTAL ILLNESS

| Myth | Fact |
|---|---|
| Smokers with mental illness are not motivated to quit smoking | People with mental illness are at least as motivated to quit as the general population; 85% have tried to quit in the past (versus 78% without mental illness); and more than half are contemplating quitting within six months ^{2,9,10} |
| Smokers with mental illness are not able to quit smoking | Smokers with mental illnesses such as depression, schizophrenia and anxiety disorders can quit successfully but generally have lower quit rates ¹¹⁻¹³ |
| Quitting smoking worsens mental illness | Quitting does not generally cause deterioration of mental illnesses such as depression, schizophrenia or post-traumatic stress disorder ¹⁴⁻¹⁸ |
| Smoking is a lower priority for patients with mental illness | Smokers with mental illness are more likely to die from smoking-related disease than from mental illness. ¹⁹ Most of the excess mortality in smokers with mental illness is caused by smoking ⁵ |
| Smoking helps smokers cope with stress | Smoking increases stress levels overall. Former smokers often report feeling less stressed than when they were smokers ^{14,20} |

SMOKING RATES IN MENTAL ILLNESS

Thirty two per cent of Australians with a current mental illness smoke compared with 16% of those without mental illness.¹ In general, the more severe the psychiatric diagnosis the higher the smoking prevalence (Figure).^{2,22} Smokers with mental illness also smoke more heavily than other smokers and are more nicotine-dependent.^{2,22} Daily cigarette intake increases with the severity of the mental illness.^{2,22}

WHY DO PEOPLE WITH MENTAL ILLNESS SMOKE?

There are several possible explanations for the higher prevalence of smoking among people with mental illness. There appears to be a shared genetic predisposition to smoking and mental illnesses such as depression and schizophrenia.^{24,25} In addition, common environmental factors such as stress can increase the risk of both smoking and mental illness.

Nicotine has antidepressant and anti-anxiety effects and is used for short-term symptom relief.²⁶ In schizophrenia, it also improves cognitive deficits, such as attention and memory deficits, and may improve negative symptoms, including lack of motivation and energy.^{23,27} Smoking can also relieve boredom and facilitate social interaction.

Cigarette smoke also reduces the side effects of many psychotropic medications, such as sedation, by accelerating their metabolism and lowering blood levels.²⁸

WHY SHOULD PEOPLE WITH MENTAL ILLNESS QUIT?

Health effects of smoking

Smokers with mental illness have reduced life expectancy compared with people without mental illness and most of the excess mortality is due to smoking.^{5,19} They are far more likely to die from smoking-related disorders than from mental illness. The leading cause of premature death and illness in this population is cardiovascular disease, and smoking is the most significant contributing risk factor.^{4,5}

Nicotine-dependent smokers also have a 77% increased risk of suicide attempts compared with nonsmokers.²⁹ After a year's abstinence, the risk of suicide drops dramatically.²⁹ The quitting process itself is not associated with an increased risk of suicide.³⁰

The stress paradox

Smokers often report that smoking helps them cope with stress. Nicotine has a transient anxiolytic action and can have a calming effect on the smoker. An additional benefit of a cigarette break is having time out

and taking deep breaths while smoking.

However, smoking actually increases stress levels overall and former smokers often report feeling less stressed than when they smoked.^{8,20,31} Smokers experience frequent periods of nicotine withdrawal during the day between cigarettes and are often thinking about when and how they can smoke next. Much of the apparent calming effect of smoking is due to the relief of nicotine withdrawal.²⁰ In addition, nicotine stimulates the release of hormones such as noradrenaline and cortisol, which can increase stress levels.²⁶

GPs should advise smokers that smoking is not an effective strategy for coping with stress. Healthier strategies should be discussed, such as time out without a cigarette, deep breathing, exercise, mindfulness, cognitive behavioural therapy or counselling.

CAN SMOKERS WITH MENTAL ILLNESS QUIT SAFELY?

Smokers with mental illness can quit successfully but have lower quit rates than the general population.²² Smoking cessation may be more challenging for this group because of their heavier smoking, higher levels of nicotine dependence and chronic stress.^{2,11,32} Other possible barriers to quitting include less social support and diminished cognitive and coping skills.

Health professionals are often reluctant to encourage quitting because of concerns that it will exacerbate mental illness.⁸ However, there is good evidence these fears are mostly unfounded.¹⁴⁻¹⁸

The same evidence-based therapies used in the general population are recommended for smokers with mental illness.³³ However, counselling and support may need to be more intensive or prolonged.^{12,34,35} Additional help may be needed to address issues relevant to the mental illness, such as coping skills for stress and management of negative mood caused by quitting. Also, because of higher levels of nicotine dependence, many smokers with mental illness will require higher doses of medications used to aid smoking cessation, combination pharmacotherapy and a longer duration of therapy.^{36,37}

EFFECT OF QUITTING ON PSYCHOTROPIC DRUG LEVELS

Chemicals in tobacco smoke accelerate the metabolism of many common psychotropic medications, including antipsychotics, antidepressants and benzodiazepines, by inducing the cytochrome P450 enzyme, CYP1A2 (Table 2).³⁸⁻⁴¹ This can substantially lower the serum concentrations and effectiveness of these medications in smokers.

Conversely, smoking cessation increases blood levels of these medications. Patients who quit smoking should be monitored for adverse effects, and dose reductions may be required. Immediate dose reductions should be considered for medications with a narrow therapeutic index, such as olanzapine and clozapine, to avoid medication toxicity.

Special care should be taken with bupropion because of potential interactions with other psychotropic medications.⁴² In particular, the risk of seizure may be increased when bupropion is combined with antidepressants or antipsychotics.⁴²

SMOKING AND SPECIFIC ILLNESSES

Anxiety disorders

Anxiety disorders (generalised anxiety disorder, post-traumatic stress disorder, panic disorder, agoraphobia, simple phobia and social phobia) comprise the largest

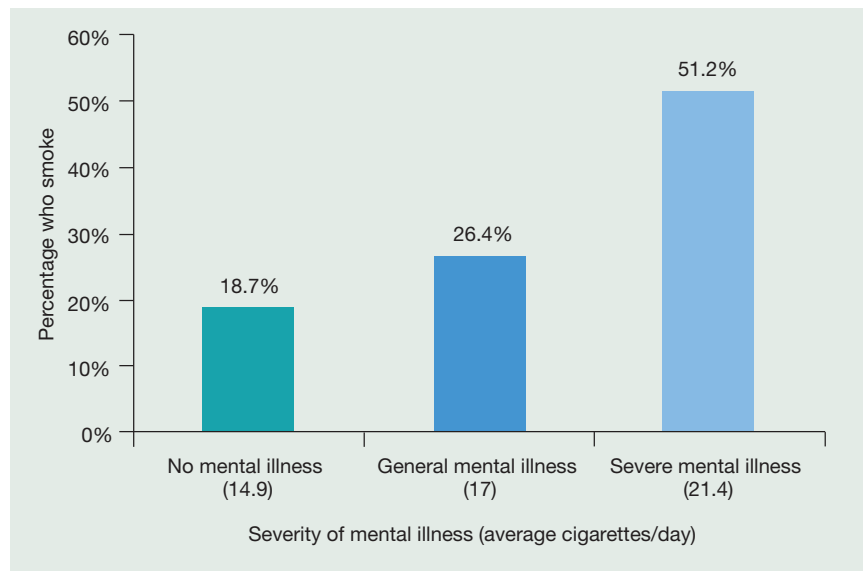


Figure. Rates of smoking and average number of cigarettes per day by mental illness status in Australia (based on South Australian data for 2005–2007).² Severe mental illness is defined as receiving a disability pension on the basis of a psychological or psychiatric illness.

mental health diagnostic group among smokers. People with anxiety disorders have approximately double the smoking rate of the general population.²² They have higher levels of nicotine dependence, more severe withdrawal and lower quit rates.¹¹

A large trial in patients with anxiety disorders demonstrated a 28% quit rate at six months, compared with 36% for smokers without an anxiety disorder.¹¹ Modest results were also found in another study in post-traumatic stress disorder.¹⁷

Anxious smokers should be taught alternative ways to manage their anxiety (see *The stress paradox* above). There is no evidence to support the use of anxiolytics to assist in quitting.⁴³

Depression

People with depression are twice as likely to smoke as those without depression, and they smoke more cigarettes per day.²² However, they are highly motivated to quit, possibly more than smokers in the general population.⁹ A meta-analysis of 42 trials found that smokers with a history of depression had a 19% lower rate of long-term abstinence compared with smokers without a history of

depression.¹² Quit rates are lower in those with recurrent depression than in those with a single episode.

Smokers with a history of depression may experience more severe negative mood, cravings and withdrawal symptoms when they quit.⁴⁴ However, studies show no increase in relapse of major depression or suicide as a result of quitting.^{14,15,18} On the contrary, some studies report an improvement in mood after treatment.⁴⁵

Nicotine replacement therapy is effective in patients with depression, with similar quit rates to the general population.⁴⁶ Bupropion appears to be equally effective in smokers with and without a history of depression.⁴⁵ Bupropion has been linked to depression and suicide although causality has not been proven.⁴⁵

There has been limited research to date on the use of varenicline in patients with depression. However, no increase in psychiatric events has been found in trials in the general population⁴⁷ and in patients with mental illness.⁴⁸ There have been post-marketing case reports of depressed mood, agitation, changes in behaviour, suicide ideation and suicide in patients using

TABLE 2. EFFECT OF SMOKING CESSATION ON BLOOD LEVELS OF PSYCHOTROPIC MEDICATIONS³⁸⁻⁴¹

| Medication | Effect of smoking cessation |
|---|--|
| Antipsychotics | |
| Olanzapine, clozapine | Blood levels increase; therefore reduce dose by about a third after quitting |
| Haloperidol, chlorpromazine, fluphenazine | Blood levels increase |
| Antidepressants | |
| Duloxetine | Blood levels increase by 30% |
| Fluvoxamine | Blood levels increase by 25% |
| Tricyclic antidepressants | Blood levels increase |
| Mirtazapine | Blood levels increase |
| Benzodiazepines | |
| Alprazolam, oxazepam, diazepam | Blood levels increase |

varenicline. These are also symptoms of nicotine withdrawal, and a causal relationship with varenicline has not been demonstrated.^{49,50} Patients should be advised of a possible risk and monitored regularly for mood or behaviour changes.

The addition of cognitive behavioural therapy for mood management to conventional smoking cessation treatment for patients with a history of depression has also been shown to enhance success rates.⁴⁴

Schizophrenia

Seventy per cent of patients with schizophrenia smoke,³ and they smoke more intensely than other smokers.⁵¹ However, they are at least as motivated to quit as the general population.¹⁰ Nevertheless, smokers with schizophrenia have overall quit rates that are only about half those of the general population.²⁵ Importantly, smoking cessation does not generally cause a deterioration in their mental health.^{16,18,36,52}

Bupropion has the strongest evidence supporting its use for smokers with schizophrenia. A recent Cochrane review found that bupropion was well tolerated and tripled quit rates compared with placebo at six months.¹⁶ The same review also reported

that the limited evidence to date did not demonstrate a benefit of nicotine replacement therapy in schizophrenia.¹⁶ However, nicotine replacement therapy may relieve agitation and aggression after quitting in schizophrenia, and it is reasonable to use this therapy in these patients until more evidence becomes available.⁵³

Varenicline appears to be safe, well tolerated and effective in trials to date in people with schizophrenia,^{13,54} although there have been some case reports of increased psychiatric symptoms. Varenicline should be used with caution in this group until further research results are available.

Bipolar disorder

Although 60% of patients with bipolar disorder smoke,³ there have been no published studies of smoking cessation in these patients. Standard treatments are recommended, although more intensive counselling may be beneficial.⁵⁵ Bupropion should be used only in conjunction with a mood stabiliser.⁵⁵

CONCLUSION

Smokers with mental health disorders comprise a large proportion of the Australian smoking population, and their smoking is

often neglected by healthcare providers. However, smoking is the major contributor to the excess disease burden in this group. GPs need to proactively address this hidden epidemic. Smokers with mental illness are motivated to stop smoking and can quit successfully, usually without any exacerbation of their psychiatric condition. The same evidence-based interventions used for the general population are recommended, with some special considerations in the choice of pharmacotherapy. More intensive or prolonged counselling, support and pharmacotherapy may give better results. **MI**

REFERENCES

A list of references is included in the website version (<http://www.medicinetoday.com.au>) and the iPad app version of this article.

COMPETING INTERESTS: Dr Mendelsohn has received honoraria for teaching, consulting and travel from Pfizer, GlaxoSmithKline and Johnson and Johnson. He sits on Pfizer's Champix Advisory Board and has served on GlaxoSmithKline's Nicotine Replacement Therapy Expert Panel. Dr Montebello has received honoraria for teaching, consulting and travel from Pfizer and sits on Pfizer's Champix Advisory Board.

Online CPD Journal Program



© ISTOCKPHOTO/MARKFGD

Are patients with mental illness less motivated to quit smoking than those without mental illness?

Review your knowledge of this topic and earn CPD/PDP points by taking part in **MedicineToday's** Online CPD Journal Program.

Log in to
www.medicinetoday.com.au/cpd

Smokers with mental illness

Breaking down the myths

COLIN MENDELSON MB BS(Hons)
MARK E. MONTEBELLO MB BS, FRANZCP, FACHAM

REFERENCES

1. Australian Bureau of Statistics. National survey of mental health and wellbeing: summary of results, 2007. Canberra: ABS, 2008. Cat. No. 4326.0.
2. Bowden JA, Miler CL, Hiller JE. Smoking and mental illness: a population study in South Australia. *Aust N Z J Psychiatry* 2011; 45: 325-331.
3. Cooper J, Mancuso SG, Borland R, Slade T, Galletly C, Castle D. Tobacco smoking among people living with a psychotic illness: the second Australian survey of psychosis. *Aust N Z J Psychiatry* 2012; 46: 851-863.
4. Lawrence DM, D'Arcy C, Holman J, Jablensky AV, Hobbs MST. Death rate from ischaemic heart disease in Western Australian psychiatric patients 1980-1998. *Br J Psychiatry* 2003; 182: 31-36.
5. Brown S, Inskip H, Barraclough B. Causes of excess mortality of schizophrenia. *Br J Psychiatry* 2000; 177: 212-217.
6. Steinberg ML, Williams JM, Ziedonis DM. Financial implications of cigarette smoking among individuals with schizophrenia. *Tob Control* 2004; 13: 206.
7. Szatkowski L, McNeill A. The delivery of smoking cessation interventions to primary care patients with mental health problems. *Addiction* 2013; 108: 1487-1494.
8. Prochaska JJ. Smoking and mental illness – breaking the link. *N Engl J Med* 2011; 365: 196-198.
9. Haukkala A, Uutela A, Vartiainen E, McAlister A, Knekt P. Depression and smoking cessation: the role of motivation and self-efficacy. *Addict Behav* 2000; 25: 311-316.
10. Siru R, Hulse GK, Tait RJ. Assessing motivation to quit smoking in people with mental illness: a review. *Addiction* 2009; 104: 719-733.
11. Piper ME, Cook JW, Schlam TR, Jorenby DE, Baker TB. Anxiety diagnoses in smokers seeking cessation treatment: relations with tobacco dependence, withdrawal, outcome and response to treatment. *Addiction* 2010; 106: 418-427.
12. Hitsman B, Papandonatos GD, McChargue DE, et al. Past major depression and smoking cessation outcome: a systematic review and meta-analysis update. *Addiction* 2013; 108: 294-306.
13. Pachas GN, Cather C, Pratt SA, et al. Varenicline for smoking cessation in schizophrenia: safety and effectiveness in a 12-week, open-label trial. *J Dual Diagn* 2012; 8: 117-125.
14. Prochaska JJ. Failure to treat tobacco use in mental health and addiction treatment settings: a form of harm reduction? *Drug Alcohol Depend* 2010; 110: 177-182.
15. Tsoi JY, Humfleet GL, Munoz RF, Reus VI, Hartz DT, Hall SM. Development of major depression after treatment for smoking cessation. *Am J Psychiatry* 2000; 157: 368-374.
16. Tsoi DT, Porwal M, Webster AC. Interventions for smoking cessation and reduction in individuals with schizophrenia. *Cochrane Database Syst Rev* 2013; 2: CD007253.
17. McFall M, Saxon AJ, Thompson CE, et al. Improving the rates of quitting smoking for veterans with posttraumatic stress disorder. *Am J Psychiatry* 2005; 162: 1311-1319.
18. Ragg M, Gordon R, Ahmed T, Allan J. The impact of smoking cessation on schizophrenia and major depression. *Australas Psychiatry* 2013; 21: 238-245.
19. Colton CW, Manderscheid RW. Congruencies in increased mortality rates, years of potential life lost and causes of death among public mental health clients in eight states. *Prev Chronic Dis* 2006; 3: (2): A42. Epub 2006 Mar 15.
20. Parrott AC, Murphy RS. Explaining the stress-inducing effects of nicotine to cigarette smokers. *Hum Psychopharmacol Clin Exp* 2012; 27: 150-155.
21. Ong MK, Zhou Q, Sung HY. Primary care providers advising smokers to quit: comparing effectiveness between those with and without alcohol, drug or mental disorders. *Nicotine Tob Res* 2011; 13: 1193-1201.
22. Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness. A population-based prevalence study. *JAMA* 2000; 284: 2606-2610.
23. Kalman D, Morissette SB, George TP. Co-morbidity of smoking in patients with psychiatric and substance use disorders. *Am J Addict* 2005; 14: 106-123.
24. Kendler KS, Neale MC, MacLean CJ, Heath AC, Eaves LJ, Kessler RC. Smoking and major depression. A causal analysis. *Arch Gen Psychiatry* 1993; 50: 36-43.

- Res 2005; 76: 135-137.
26. Picciotto MR, Brunzell DH, Caldarone BJ. Effect of nicotine and nicotinic receptors on anxiety and depression. *Neuroreport* 2002; 13: 1097-1106.
 27. Barr RS, Culhane MA, Jubelt LE, et al. The effects of transdermal nicotine on cognition in nonsmokers with schizophrenia and nonpsychiatric controls. *Neuropsychopharmacology* 2008; 33: 480-490.
 28. Matthews AM, Wilson VB, Mitchell SH. The role of antipsychotics in smoking and smoking cessation. *CNS Drugs* 2011; 25: 299-315.
 29. Yaworski D, Robinson J, Sareen J, Bolton JM. The relation between nicotine dependence and suicide attempts in the general population. *Can J Psychiatry* 2011; 56: 161-170.
 30. Hughes JR. Smoking and suicide: a brief overview. *Drug Alcohol Depend* 2008; 98: 169-178.
 31. Hajek P, Taylor T, McRobbie H. The effect of stopping smoking on perceived stress levels. *Addiction* 2010; 105: 1466-1471.
 32. Moeller-Saxone K. Cigarette smoking and interest in quitting among consumers at a psychiatric disability rehabilitation and support service in Victoria. *Aust N Z J Public Health* 2008; 32: 479-481.
 33. Zwar N, Richmond R, Borland R, et al. Supporting smoking cessation: a guide for health professionals. Melbourne: Royal Australian College of General Practitioners; 2011. Available online at: <http://www.racgp.org.au/guidelines/smokingcessation> (accessed July 2013).
 34. Hall SM, Prochaska JJ. Treatment of smokers with co-occurring disorders: emphasis on integration in mental health and addiction treatment settings. *Annu Rev Clin Psychol* 2009; 5: 409-431.
 35. Schroeder SA, Morris CD. Confronting a neglected epidemic: tobacco cessation for persons with mental illness and substance abuse problems. *Annu Rev Public Health* 2010; 31: 297-314.
 36. Evins AE, Cather C, Culhane M, et al. A 12-week double-blind, placebo-controlled study of bupropion sr added to high-dose dual nicotine replacement therapy for smoking cessation or reduction in schizophrenia. *J Clin Psychopharmacology* 2007; 27: 380-386.
 37. George TP, Vessicchio JC, Sacco KA, et al. A placebo-controlled trial of bupropion combined with nicotine patch for smoking cessation in schizophrenia. *Biol Psychiatry* 2008; 63: 1092-1096.
 38. Schaffer SD, Yoon S, Zadezensky I. A review of smoking cessation: potentially risky effects on prescribed medications. *J Clin Nursing* 2009; 18: 1533-1540.
 39. Knadler M, Lobo E, Chappell J, Bergstrom R. Duloxetine: clinical pharmacokinetics and drug interactions. *Clinical Pharmacokinet* 2011; 50: 281-294.
 40. Desai HD, Seabolt J, Jann MW. Smoking in patients receiving psychotropic medications: a pharmacokinetic perspective. *CNS Drugs* 2001; 15: 469-494.
 41. Aubin HJ, Rollema H, Svensson TH, Winterer G. Smoking, quitting, and psychiatric disease: a review. *Neurosci Biobehav Rev* 2012; 36: 271-284.
 42. GlaxoSmithKline Australia. Product information Zyban sustained release tablets. GlaxoSmithKline Australia; 2010. Available online at: http://www.gsk.com.au/resources.ashx/prescriptionmedicinesproductschilddataproinfo/269/FileName/2036C2E04A5E25F86CA4E73A4A574553/PI_Zyban.pdf%20 (accessed July 2013).
 43. Hughes JR, Stead LF, Lancaster T. Anxiolytics for smoking cessation. *Cochrane Database Syst Rev* 2000; 4: CD002849.
 44. Hall S, Tsoh JY, Prochaska J, et al. Treatment for cigarette smoking among depressed mental health patients: a randomised clinical trial. *Am J Public Health* 2006; 96: 1808-1814.
 45. Hughes JR, Stead LF, Lancaster T. Antidepressants for smoking cessation. *Cochrane Database Syst Rev* 2007; 1: CD000031.
 46. Gierisch JM, Bastian LA, Calhoun PS, McDuffie JR, Williams JW Jr. Comparative effectiveness of smoking cessation treatments for patients with depression: a systematic review and meta-analysis of the evidence. Washington (DC): Department of Veterans Affairs; 2010.
 47. Tonstad S, Davies S, Flammer M, Russ C, Hughes J. Psychiatric adverse events in randomised double-blind, placebo-controlled clinical trials of varenicline. *Drug Safety* 2010; 33: 289-301.
 48. Stapleton JA, Watson L, Spiriling LI, et al. Varenicline in the routine treatment of tobacco dependence: a pre-post comparison with nicotine replacement therapy and an evaluation in those with mental illness. *Addiction* 2007; 103: 146-154.
 49. Williams JM, Steinberg MB, Steinberg ML, Gandhi KK, Ulpe R, Foulds J. Varenicline for tobacco dependence: panacea or plight? *Exp Opin Pharmacotherapy* 2011; 12: 1799-1812.
 50. Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. *Cochrane Database Syst Rev* 2011; 2: CD006103.
 51. Tidey JW, Rohsenow DJ, Kaplan GB, Swift RM. Cigarette smoking topography in smokers with schizophrenia and matched non-psychiatric controls. *Drug Alcohol Depend* 2005; 80: 259-265.
 52. Baker A, Richmond R, Haile M, et al. A randomised controlled trial of a smoking cessation intervention among people with a psychotic disorder. *Am J Psychiatry* 2006; 163: 1934-1942.
 53. Allen MH, Debanne M, Lazignac C, Adam E, Dickinson LM, Damsa C. Effect of nicotine replacement therapy on agitation in smokers with schizophrenia: a double-blind, randomized, placebo-controlled study. *Am J Psychiatry* 2011; 168: 395-399.
 54. Williams JM, Anthenelli RM, Morris CD, Treadow J, Thompson JR, Yunis C. A randomised, double-blind, placebo-controlled study evaluating the safety and efficacy of varenicline for smoking cessation in patients with schizophrenia or schizoaffective disorder. *J Clin Psychiatry* 2012; 73: 654-660.
 55. Heffner JL, Strawn JR, DelBello MP, Strakowski SM, Anthenelli RM. The co-occurrence of cigarette smoking and bipolar disorder: phenomenology and treatment considerations. *Bipolar Disord* 2011; 13: 439-453.