

Smoking and Schizophrenia: *Treatment Approaches within Primary Care*

Amanda L. Baker, BA (Hons), MPsychol, PhD, Dan I. Lubman MB ChB, PhD,
and Leanne Hides, BBehSc(Hons), PhD

ABSTRACT

Tobacco dependence is common among people with psychotic disorders and is associated with significant morbidity and mortality. Illness, socio-demographic, lifestyle, institutional, and tobacco industry influences are all associated with this high prevalence. While many smokers with psychotic disorders are willing to quit or reduce smoking, they are often provided with limited support within the healthcare system. Numerous randomized controlled trials among smokers with psychotic disorders have demonstrated that smoking cessation interventions can be effective in the short-term, with smoking reduction a common finding. Support for smoking cessation can be offered within primary health settings, and should include adequate and longer-term pharmacotherapies combined with psychosocial counseling. Psychosocial strategies that can readily be incorporated into primary care settings include brief motivational interventions, the encouragement of social support, behavioral strategies such as avoidance of high risk situations and activity scheduling, cognitive strategies to cope with cravings and negative moods and to improve lifestyle, and relapse prevention. As smoking is a chronic and relapsing condition, numerous change attempts should be encouraged and normalized, with flexible combinations of pharmacotherapies and counseling employed.

FOCUS POINTS

- Many smokers with psychotic disorders are motivated to quit smoking.
- A combination of pharmacotherapies and psychosocial counselling offered over a sustained period of time can help people with psychotic disorders quit smoking.
- Numerous change attempts may be needed, using flexible combinations of pharmacotherapy and counseling to address relapse.

INTRODUCTION

A recent review of the literature on smoking and mental illness¹ posed the following question: “Is there any reason why all the efforts put into reducing smoking should not be applied equally to people with mental illness?” As 44% of all cigarettes smoked in the United States are smoked by people with mental or substance use disorders,² it is intriguing that this question has been posed more than 50 years after the harmful effects of tobacco smoking were identified.³ This article addresses a similar question: Is there any reason why all the efforts put into smoking by primary care physicians (PCPs) and general practitioners should not be applied equally to people with psychotic disorders (including bipolar and schizophrenia spectrum disorders)? In order to address this question, the authors overview the harms associated with smoking in people with psychotic disorders, factors associated with their smoking patterns, whether smokers with psychotic disorders are willing to quit, and studies examining interventions for smoking cessation. Finally, the article offers recommendations on smoking interventions for people with psychotic disorders that can be applied within primary care set-

Dr. Baker is professor and NHMRC senior research fellow at the Centre for Brain and Mental Health Research at the University of Newcastle in New South Wales, Australia. Dr. Lubman is associate professor and Dr. Hides is senior research fellow at the Orygen Youth Health Research Centre at the University of Melbourne in Australia.

Disclosure: The authors report no affiliation with or financial interest in any organization that may pose a conflict of interest.

Acknowledgments: The authors would like to thank Louise Thornton and Vanessa Clark for their assistance in preparation of the manuscript.

Please direct all correspondence to: Amanda L. Baker, Centre for Brain and Mental Health Research, University of Newcastle, University Drive, Callaghan, NSW, 2308, Australia; Tel: 61-2- 40335690; Fax: 61-2-40335692; E-mail: Amanda.Baker@newcastle.edu.au.

tings.

PREVALENCE

The prevalence of smoking is extremely high (70% to 80%) among people with psychotic disorders,⁴ compared to other psychiatric disorders (50%) and the general population (21%).³ Hughes⁵ reported that the prevalence of smoking among psychiatric outpatients was 1.6 times that of population-based control groups after controlling for age, sex, marital status, socio-economic status, and alcohol use. People with schizophrenia have also been found to be twice as likely to smoke as other people with mental illnesses with similar disadvantaged backgrounds,⁶ to smoke heavily, and have high levels of nicotine dependence.⁷

According to one study,⁸ smokers are at higher risk for the onset of schizophrenia. A follow-up (4–16 years) study of 14,248 18-year-old males conscripted to the Israeli Defence Force found male adolescents who smoked 1–9 cigarettes per day at 18 years of age were 1.4 times more likely to be hospitalized for schizophrenia during the follow-up period. Those who smoked ≥ 10 cigarettes per day were at 2.3 times greater risk. These differences remained statistically significant after controlling for cognitive performance, social adjustment, presence of non-psychotic mental illness, and socioeconomic status. However, a major limitation of this study was the fact that the impact of cannabis use was not examined, despite the accumulating evidence for an association between cannabis use and the onset of schizophrenia.⁹

HARMS ASSOCIATED WITH SMOKING

The harms associated with tobacco smoking in schizophrenia are substantial, particularly in terms of the costs to health, finances, and quality of life. Most of the excess mortality (excluding suicides and accidents) for schizophrenia is associated with cigarette smoking,¹⁰ with many patients dying at a younger age from illnesses related to smoking (eg, coronary heart disease (CHD), cancer, cerebrovascular disease, respiratory disease). For lung cancer alone, the mortality ratio is twice that found in the general population,¹⁰ while at least 33% of people with schizophrenia suffer with CHD.¹¹ Mortality rates due to CHD among people with psychotic disorders are around twice that seen in the general population.¹² Indeed, CHD accounts for more premature deaths than suicide among people with schizophrenia.¹³

Smoking also increases the metabolism of several antipsychotics (through induction of the liver cytochrome P450 1A2 isoform) as well as some antidepressant and anxiolytic drugs. As a result, smokers on such medications require larger doses compared with non-smokers,¹⁴ increasing the likelihood of

adverse side-effects.^{14,15} Apart from harmful consequences to health, the financial burden of tobacco use is large, particularly among low-income earners, including many people with chronic psychotic disorders. It has been estimated that smoking costs at least 33% of an individual's weekly income,² with obvious consequences for their quality of life.¹⁶

FACTORS ASSOCIATED WITH SMOKING

In addition to the well recognized socio-demographic and lifestyle factors associated with smoking,⁴ it appears that illness factors may be associated with the high prevalence of smoking among people with schizophrenia. Altered expression and function of brain $\alpha 7$ nicotinic receptors have been implicated in information-processing deficits in schizophrenia,¹⁷ and there is accumulating evidence for self-medication of cognitive dysfunction in schizophrenia (eg, sensory gating, sustained attention and spatial working memory).¹⁸ Furthermore, people with psychotic disorders report smoking for similar reasons to smokers without a psychiatric illness,¹⁹ but also report smoking to alleviate negative psychotic symptoms and/or medication side effects.¹⁶ Nevertheless, Srinivasan and Thara²⁰ have argued that smoking in schizophrenia is not inevitable, and economic and social factors are important to address, even if neurochemical factors are involved.

Mental health staff and institutional practices also appear to have done little to discourage smoking among people with psychotic disorders.^{21,22} Many staff within mental health facilities smoke cigarettes and/or use cigarettes as a form of reinforcement (eg, to encourage medication compliance or to discourage assaultive behaviors).²² Indeed, nurses who are smokers themselves are less in favor of encouraging patients to stop smoking and report that it may be therapeutic to smoke with patients.²³ Such attitudes and practices do little to discourage tobacco smoking among patients in psychiatric wards, and may even increase the risk of other patients taking up smoking because of peer pressure to smoke, lack of other ward activities, and reinforcement by the institution.²¹ Further, mental health providers tend not to routinely diagnose nicotine dependence.^{24,25} A national survey of smoking cessation activities among 184 child and adolescent psychiatrists in America found that only 14% reported consistently assessing and documenting cigarette use.²⁶ In addition, only 19% reported that they consistently assessed the willingness of youths to quit smoking, while 30% consistently gave messages urging the smoker to quit. Finally, the psychiatrists estimated that only 46% of youths with schizophrenia smoked, despite the higher reported prevalence rates of smoking in this population. Together these findings highlight the need for more training in the assessment²⁶ and treatment of tobacco dependence across a range of mental health professionals.^{24,25}

At a wider level, examination of previously secret tobacco industry documents has revealed that the tobacco industry promoted smoking in psychiatric settings, supported efforts to block hospital smoking bans, and made efforts to slow treatment for tobacco dependence in this population.²⁷

DO SMOKERS WITH PSYCHOTIC DISORDERS WANT TO QUIT?

Among smokers with severe mental disorders, there is evidence that interest in quitting and cutting down is high,^{28,29} and such reductions are not associated with symptom exacerbations.⁴ However, smokers with psychotic illnesses are less likely to quit smoking compared to people without mental disorders, most likely due to higher levels of nicotine dependence.³⁰ Given the low level of smoking cessation care provided to people with psychotic disorders in mental health settings²⁴ and the comparatively high frequency with which smokers with psychotic disorders attend general practice surgeries,³¹ guidelines for smoking cessation interventions within primary care and routine psychiatric settings have been developed.^{3,32}

WHAT IS THE EVIDENCE FOR SMOKING CESSATION INTERVENTIONS AMONG PEOPLE WITH PSYCHOTIC DISORDERS?

Although there have been a number of randomized controlled trials of smoking cessation interventions conducted among people with psychotic disorders,^{5,33-38} methodologic problems such as the use of heterogeneous, small samples and poorly defined interventions and control groups³⁹ limit the conclusions that can be drawn from these studies. Interventions have usually consisted of nicotine replacement therapy (NRT) with cognitive-behavioral therapy (CBT),^{4,33} NRT alone,³⁸ bupropion and CBT,³⁴⁻³⁷ or bupropion with CBT and NRT.^{32,40} While smoking cessation was achieved among very few participants at follow up, smoking reduction (which may eventually lead to cessation⁵) was common.³⁹

Pharmacotherapy for smoking cessation has been well described.^{3,30} Each of the NRTs (patch, gum, inhaler, nasal spray, lozenge) work by reducing the severity of nicotine withdrawal symptoms and craving, so that the quitter can focus more on overcoming behavioral associations as well as triggers of tobacco use.³⁰ Sustained-release bupropion is an antidepressant (chemically unrelated to other antidepressants) with a mechanism of action on tobacco dependence which is unclear and independent of depression.³⁰ Bupropion is contraindicated in patients with a history of seizures or eating disorders and patients taking monoamine oxidase

inhibitors, and should be used with caution in people taking medications which may lower seizure threshold, such as oral hypoglycaemic agents.⁴¹ Some caution should also be exercised in using bupropion in people with bipolar disorder due to the possible risk of precipitating a manic episode, as with all antidepressants.⁴² Numerous other pharmacotherapies are used in smoking cessation, most notably varenicline, a selective nicotinic receptor partial agonist which mitigates the reinforcing effects of smoking.³⁰ Only NRT and bupropion are recommended as first-line therapies in people with psychosis.⁴¹ No randomized controlled trials of varenicline among smokers with psychotic disorders have been published, and as such, it should be used with caution. Indeed, varenicline-induced mania in a patient with bipolar disorder⁴³ and exacerbation of schizophrenia by varenicline⁴⁴ have been reported. Foulds and colleagues³⁰ point out that clinicians should remain mindful of the effect of atypical antipsychotics on smoking behaviors and quit attempts, as they have been associated with more success among people with psychosis.

RECOMMENDATIONS FOR SMOKING CESSATION INTERVENTIONS AMONG PEOPLE WITH PSYCHOTIC DISORDERS IN PRIMARY CARE SETTINGS AND ROUTINE PSYCHIATRY PRACTICE

It is important to note that as smoking is a chronic and relapsing condition, repeated quit attempts should be encouraged as the aggregate effect of this will be larger over time⁴⁵ and prolonged treatment is necessary for many smokers.⁴⁶ Based on existing guidelines, the following strategies are suggested to enhance smoking cessation among people with psychotic disorders.^{3,47} Before conducting any smoking intervention with an individual with a psychotic disorder, psychiatric and substance use assessments should be conducted,⁴⁸ either within the context of their mental health case plan or by the PCP. Given the multiple health issues associated with tobacco smoking, screening for physical illnesses should be considered a priority, with a low threshold for further investigations if clinically indicated. The Fagerstrom Test for Nicotine Dependence⁴⁹ is useful to assess the severity of current smoking patterns and to monitor progress. Individuals should be provided with personalized, informal assessment feedback on the results of their psychiatric, substance use, and physical health assessments. With regard to tobacco use, particular reference should be made to the frequency, quantity, and likely impact of tobacco use on the individual's mental and physical health as well as their financial, social, and occupational functioning. When providing feedback, the elicit-provide-elicited approach (ie, first ask for permission, offer the information,

and then ask for the client's response) is recommended.⁵⁰ It is also important to congratulate people for not smoking and/or their previous attempts to quit smoking. This message should be reinforced by providing the individual with psychoeducational information (with their permission) on the high rates of nicotine dependence and the harms associated with smoking among individuals with schizophrenia. It is important to note that interventions are best offered when psychiatric symptoms are not severe.³ However, admission to a smoke-free inpatient unit can sometimes motivate a person to quit.⁴⁷

Zwar and Richmond⁴¹ have recommended that as with all smokers, every opportunity should be taken to offer clear advice and support to help people with psychotic disorders stop smoking. They recommend that brief interventions might include advice to stop smoking and assessment of the patient's commitment to quit. Commitment can be assessed via a Contemplation Ladder (Figure 1)⁵¹ or through direct questioning regarding how interested the person is in quitting over the next month⁴⁸ (eg, "On a scale of 1–10, how important is quitting smoking in the next month?"⁵⁰). This can be used to reinforce the importance or to enhance motivation by eliciting motivational statements (such as asking, "So, a '5'—why not a '2'?").

Discussion can then occur around the positive reasons for change. Zwar and Richmond⁴¹ discuss the benefits of encouraging all smokers to quit whenever the opportunity arises, as expressed interest in quitting in the period leading up to the attempt is unrelated to success. Possible barriers, such as smoking among others in the household and/or close friends, may need to be addressed.⁴⁷

FIGURE 1
THE CONTEMPLATION LADDER⁵¹

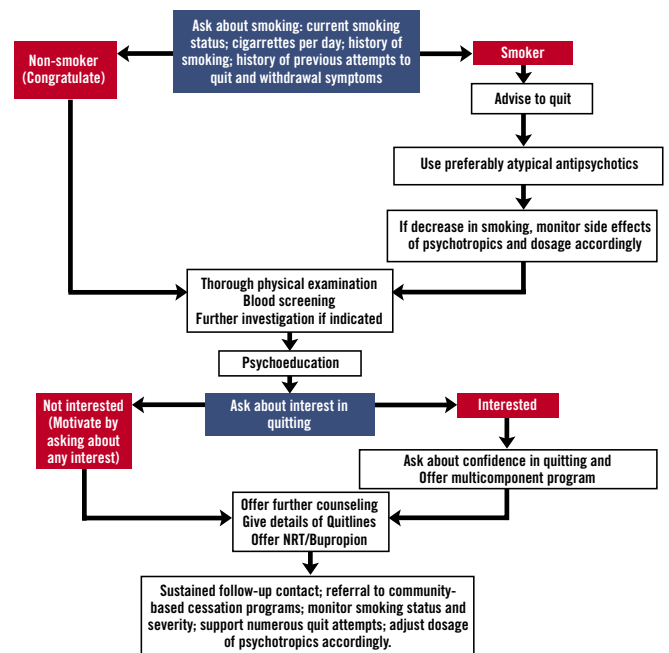
- • 10 Taking action to quit (eg, cutting down, enrolling in a program)
- • 9
- • 8 Starting to think about how to change my smoking patterns.
- • 7
- • 6
- • 5 Think I should quit but not quite ready.
- • 4
- • 3
- • 2 Think I need to consider quitting someday.
- • 1
- • 0 No thought about quitting.

Each rung on this ladder represents where various smokers are in their thinking about quitting. Circle the number that indicates where you are now.

Baker AL, Lubman DI, Hides L. *Primary Psychiatry*. Vol 17, No 1. 2010.

Zwar and Richmond⁴¹ state that an offer of pharmacotherapy and counseling (if available and appropriate) should be made and self-help material and referral to other more intensive support given. Intensive support is recommended for smokers with psychosis.^{7,30,47} Confidence in quitting can be assessed in the same way as importance (eg, "On a scale of 1–10, how confident are you about quitting?"⁵⁰). This information will assist in preparation for psychoeducation about pharmacotherapy and behavioral interventions. It is important that the practitioner maximizes compliance with pharmacotherapies by explaining the importance of an adequate dosage and duration of therapy, including long-term and combination pharmacotherapy, such as NRT.³⁰ Preferences for pharmacotherapy and individual versus group support should be discussed.⁴⁷ Although abrupt cessation is usually recommended, gradual reduction should be considered if the patient prefers and, if possible, a quit date should be set.⁴⁷ A follow-up appointment 1–3 days after the quit date should be made, with additional follow-ups scheduled.⁴⁷ Withdrawal symptoms should be monitored and a withdrawal scale, such as the Minnesota Withdrawal Scale,⁵² may be useful. Hughes and colleagues⁵³ recommended that for people with schizophrenia, NRT should be modified according to individual withdrawal symptoms, with a combination of patch and

FIGURE 2
FLOWCHART OF INTERVENTIONS FOR SMOKING IN THE PRIMARY CARE SETTING²¹



NRT=nicotine replacement therapy.

Baker AL, Lubman DI, Hides L. *Primary Psychiatry*. Vol 17, No 1. 2010.

titratable forms of NRT up to 42 mg/day for as long as withdrawal symptoms, including craving, continue.

As smoking reduces, it is important that the treating clinician monitors the effects of other psychotropic medications,^{3,21} particularly if an individual's medication can be affected by cigarette smoking (eg, olanzapine, clozapine). Side effects can develop during the first 3–6 weeks after smoking cessation or meaningful reduction due to elevated plasma concentrations of these agents, and clinicians may need to reduce the dosage accordingly. Clinicians should discuss this process with the patient before smoking cessation is attempted. Figure 2 outlines a possible smoking cessation intervention process for primary care.²¹

Psychosocial interventions augment smoking cessation outcomes with pharmacotherapies⁴⁷ and can be incorporated into primary care. These include the following. First, social support provided by a spouse, partner, or buddy system. Second, brief motivational interventions as described above. Third, behavioral therapies involving strategies such as avoidance of high risk situations and activity scheduling. Fourth, CBT involving both behavioral and cognitive strategies to cope with cravings and mood (see Baker and colleagues⁵⁴ for a treatment manual). CBT can also be targeted towards an overall healthy lifestyle approach and early evidence for this is promising.⁵⁵ At the very least, advice should be given regarding physical activity and healthy eating strategies (possible abstinence from alcohol associated with relapse), and reduction in caffeine consumption (as smoking increases the metabolism of caffeine).⁴⁷ Fifth, addressing relapse by considering the adequacy of pharmacotherapy for withdrawal symptoms, with consideration given to an alternative form of pharmacotherapy or a different formulation or dose; and implementation of more intensive behavior therapy or a different format of therapy, with referral to a health professional who specializes in nicotine dependence if necessary.⁴⁷

CONCLUSION

The answer to the question posed at the beginning of this article (“Is there any reason why all the efforts put into smoking by PCPs, psychiatrists, and general practitioners should not be applied equally to people with psychotic disorders?”) must be a resounding “No.” There is a very high rate of smoking among this population, with associated harmful effects on health, finances, and quality of life. While illness, socio-demographic, social, institutional, and tobacco industry influences promote smoking among people with psychotic disorders, such patients are motivated to quit smoking. Multiple change attempts involving adequate dosages and prolonged use of pharmacotherapies accompanied by psychosocial counseling are recommended. From a primary care perspective, all smokers should be identified and offered advice to quit, with an

option for longer-term pharmacotherapy and counseling for those with psychotic disorders. **PP**

REFERENCES

- Ragg M, Ahmed T. *Smoke and Mirrors: A Review of the Literature on Smoking and Mental Illness*. Sydney, Australia: Cancer Council NSW; 2008:12.
- Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness: a population-based prevalence study. *JAMA*. 2000;284(20):2606-2610.
- U.S. Public Health Service. *Treating Tobacco Use and Dependence: Clinical Practice Guidelines Update*. Washington, DC: U.S. Department of Health and Human Services; 2008.
- Baker A, Richmond R, Haile M, et al. Randomized controlled trial of a smoking cessation intervention among people with a psychotic disorder. *Am J Psychiatry*. 2006;163(11):1934-1952.
- Hughes JR. Dependence on and abuse of nicotine replacement medications: an update. In: Benowitz NL, ed. *Nicotine Safety and Toxicity*. New York, NY: Oxford University Press; 1998:147-157.
- de Leon J, Dadvand M, Canuso C, White AO, Stanilla JK, Simpson GM. Schizophrenia and smoking: an epidemiological survey in a state hospital. *Am J Psychiatry*. 1995;152(3):453-455.
- Williams JM, Foulds J. Successful tobacco dependence treatment in schizophrenia. *Am J Psychiatry*. 2007;164(2):222-227.
- Weiser M, Reichenberg A, Grotto I, et al. Higher rates of cigarette smoking in male adolescents before the onset of schizophrenia: a historical-prospective cohort study. *Am J Psychiatry*. 2004;161(7):1219-1223.
- Moore TH, Zammit S, Lingford-Hughes A, et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet*. 2007;370(9584):319-328.
- Brown S, Inskip H, Barraclough B. Causes of the excess mortality of schizophrenia. *Br J Psychiatry*. 2000;177:212-217.
- AHW. Australia's Health 2000. *The 7th Biennial Health Report of the Australian Institute of Health and Welfare*. Canberra, Australia: Australian Institute of Health and Welfare; 2000.
- Weiss AP, Henderson DC, Weiburg JB. Treatment of cardiac risk factors among patients with schizophrenia and diabetes. *Psychiat Serv*. 2006;57(8):1145-1152.
- Hennekens CH. Increasing global burden of cardiovascular disease in general populations and patients with schizophrenia. *J Clin Psychiatry*. 2007;68(Suppl 4):4-7.
- Williams JM, Ziedonis D. Addressing tobacco among individuals with a mental illness or an addiction. *Addict Behav*. 2004;29(6):1067-1083.
- Carosella A, Ossip-Klein DJ, Owens CA. Smoking attitudes, beliefs, and readiness to change among acute and long term care inpatients with psychiatric diagnoses. *Addict Behav*. 1999;24(3):331-344.
- Dalack GW, Healy DJ, Meador-Woodruff JH. Nicotine dependence in schizophrenia: clinical phenomena and laboratory findings. *Am J Psychiatry*. 1998;155(11):1490-1501.
- Leonard S, Breeze C, Adams C, et al. Smoking and schizophrenia: abnormal nicotinic receptor expression. *Eur J Pharmacol*. 2000;393(1-3):237-242.
- Sacco KA, Bannon KL, George TP. Nicotinic receptor mechanisms and cognition in normal states and neuropsychiatric disorders. *J Psychopharmacol*. 2004;18(4):457-474.
- Reichler H, Baker A, Lewin T, Carr V. Smoking among in-patients with drug-related problems in an Australian psychiatric hospital. *Drug Alcohol Rev*. 2001;20(2):231-237.
- Srinivasan TN, Thara R. Smoking in schizophrenia—all is not biological. *Schizophr Res*. 2002;56(1-2):67-74.
- Olivier D, Lubman DI, Fraser R. Tobacco smoking within psychiatric inpatient settings: biopsychosocial perspective. *Aust N Z J Psychiatry*. 2007;41(7):572-580.
- Lawn S. Cigarette smoking in psychiatric settings: occupational health, safety, welfare and legal concerns. *Aust NZ J Psychiatry*. 2005;39(10):886-891.
- Dickens GL, Stubbs JH, Haw CM. Smoking and mental health nurses: a survey of clinical staff in a psychiatric hospital. *J Psychiatr Ment Health Nurs*. 2004;11(4):445-451.
- Wye P, Bowman J, Wiggers J, et al. Smoking restrictions and treatment for smoking: policies and procedures in Australia. *Psychiat Serv*. 2009;60(1):100-107.
- Montoya ID, Herbeck DM, Svikis DS, Pincus HA. Identification and treatment of patients with nicotine problems in routine clinical psychiatry practice. *Am J Addict*. 2005;14(5):441-454.
- Price JH, Sidani J, Price JA. Child and adolescent psychiatrists' practices in assisting their adolescent patients who smoke to quit smoking. *Am Acad Child Adolesc Psychiatry*. 2007;46(1):60-67.
- Prochaska JJ, Hall SM, Bero LA. Tobacco use among individuals with schizophrenia: what role has the tobacco industry played? *Schizophr Bull*. 2008;34(3):555-567.
- Moeller-Saxone K. Cigarette smoking and interest in quitting among consumers at a psychiatric disability rehabilitation and support service in Victoria. *Aust NZ J Publ Health*. 2008;32(5):479-481.
- Baker A, Kay-Lambkin FJ, Lewin TJ. Co-existing mental health and drug and alcohol problems: steps towards better treatment. In: Baker A, Velleman R, eds. *Clinical Handbook of Co-existing Mental Health and Drug and Alcohol Problems*. London, England: Routledge; 2007:1-19.
- Foulds J, Steinberg MB, Williams JM, Ziedonis DM. Developments in pharmacotherapy for tobacco dependence: past, present and future. *Drug Alcohol Rev*. 2006;25(1):59-71.
- Carr VJ, Lewin TJ, Barnard RE, et al. Comparisons between schizophrenia patients recruited from Australian general practices and public mental health services. *Acta Psychiatr Scand*. 2002;105(5):346-355.
- 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(11):1092-1096.
- George TP, Ziedonis DM, Feingold A, et al. Nicotine transdermal patch and atypical antipsychotic medications for smoking cessation in schizophrenia. *Am J Psychiatry*. 2000;157(11):1835-1842.
- George TP, Vessicchio JC, Termine A, et al. A placebo controlled trial of bupropion for smoking cessation in schizophrenia. *Biol Psychiatry*. 2002;52(1):53-61.
- Evins AE, Mays VK, Rigotti NA, et al. A pilot trial of bupropion added to cognitive behavioral therapy for

- smoking cessation in schizophrenia. *Nicotine Tob Res.* 2001;3(4):397-403.
36. Evins AE, Cather C, Deckersbach T, et al. A double-blind placebo-controlled trial of bupropion sustained-release for smoking cessation in schizophrenia. *J Clin Psychopharmacol.* 2005;25(3):218-225.
 37. Evins A, Cather C, Rigotti N, et al. Two-year follow-up of a smoking cessation trial in patients with schizophrenia: increased rates of smoking cessation and reduction. *J Clin Psychiatry.* 2004;65(3):307-311.
 38. Chou KR, Chen R, Lee JF, Ku CH, Lu RB. The effectiveness of nicotine-patch therapy for smoking cessation in patients with schizophrenia. *Int J Nurs Stud.* 2004;41(3):321-330.
 39. McChargue DE, Gulliver SB, Hitsman B. Would smokers with schizophrenia benefit from a more flexible approach to smoking treatment? *Addiction.* 2002;97(7):785-793.
 40. Evins A, Cather C, Culhane M, Birnbaum A, Horowitz J, Hsieh E. 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 Psychopharmacol.* 2007;27(4):380-386.
 41. Zwar N, Richmond R, Borland R, et al. *Smoking Cessation Pharmacotherapy: An Update for Health Professionals.* Melbourne Australia: Royal Australian College of General Practitioners; 2007.
 42. Williams JM, Hughes JR. Pharmacotherapy treatments for tobacco dependence among smokers with mental illness or addiction. *Psychiatr Ann.* 2003;33:457-466.
 43. Kohen I, Kremen N. Varenicline-induced manic episode in a patient with bipolar disorder. *Am J Psychiatry.* 2007;164(8):1269-1270.
 44. Freedman R. Exacerbation of schizophrenia by varenicline. *Am J Psychiatry.* 2007;164(8):1269.
 45. West R. The clinical significance of "small" effects of smoking cessation treatments. *Addiction.* 2007;102(4):506-509.
 46. Etter JF, Stapleton JA. Nicotine replacement therapy for long-term smoking cessation: a meta-analysis. *Tobacco Control.* 2006;15(4):280-285.
 47. Kleber HD, Weiss RD, Anton RF, et al. *Practice Guideline for the Treatment of Patients with Substance Use Disorders.* 2nd ed. Washington, DC: American Psychiatric Association; 2006.
 48. Weinberger AH, Sacco KA, George TP. Comorbid tobacco dependence and psychiatric disorders. *Psychiatr Times.* 2006;25(1):35-37.
 49. Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom KO. The Fagerstrom Test for Nicotine Dependence: a revision of the Fagerstrom Tolerance Questionnaire. *Br J Addict.* 1991;86(9):1119-1127.
 50. Rollnick S, Mason P, Butler C. *Health Behaviour Change: A Guide for Practitioners.* Edinburgh, UK: Churchill Livingstone; 1999.
 51. Biener L, Abrams DB. The Contemplation Ladder: validation of a measure of readiness to consider smoking cessation. *Health Psychol.* 1991;10(5):360-365.
 52. Hughes JR, Hatsukami D. Signs and symptoms of tobacco withdrawal. *Arch Gen Psychiatry.* 1986;43(3):289-294.
 53. Hughes JR, Lesmus DK, Hatsukami DK, et al. Are higher doses of nicotine replacement more effective for smoking cessation? *Nicotine Tob Res.* 1999;1(2):169-174.
 54. Baker A, Kay-Lambkin F, Bucci S, Haile M, Richmond R, Carr V. *Intervention for Tobacco Dependence among People with a Mental Illness.* Sydney, Australia: National Drug and Alcohol Research Centre; 2004.
 55. Baker A, Richmond R, Castle D, et al. Coronary heart disease risk reduction intervention among overweight smokers with a psychotic disorder: pilot trial. *Aust N Z J Psychiatry.* 2009;43(2):129-135.