



Published in final edited form as:

J Dual Diagn. 2012 January 1; 8(2): 126–130. doi:10.1080/15504263.2012.671717.

A Review of Smoking Cessation in Bipolar Disorder: Implications for Future Research

Tony P. George, M.D., FRCPC^{1,2}, Becky S. Wu, B.Sc.¹, and Andrea H. Weinberger, Ph.D.³

¹Schizophrenia Program, Centre for Addiction and Mental Health (CAMH), Toronto, Ontario, Canada

²Division of Brain and Therapeutics, Department of Psychiatry, University of Toronto, Toronto, Ontario, Canada

³Division of Substance Abuse, Department of Psychiatry, Yale University School of Medicine, New Haven, CT USA 06519

Abstract

Tobacco smoking is common in people with bipolar disorder, and rates of smoking cessation are lower than in the general population. A literature review found eleven clinical research publications on bipolar disorder and tobacco, including only one smoking cessation pharmacotherapy trial. This article will review these findings and discuss possible reasons for the high rates of tobacco addiction among persons with bipolar disorder, as well as specific vulnerability factors that may contribute to tobacco treatment failure. An approach to the clinical assessment and treatment of tobacco dependence is described for this sub-group of smokers. Finally, recommendations are made for planning future treatment studies in persons with bipolar disorder and nicotine dependence.

Keywords

bipolar disorder, smoking cessation, review, tobacco, varenicline, mania, depression, drug safety

The lifetime prevalence of bipolar disorder is estimated at 1.6–2.2% in the U.S. general population (Regier et al., 1990), and 2.2% in a recent Canadian population-based survey (Schaffer et al., 2006). People with bipolar disorder have a very high prevalence of cigarette smoking, in the range of 50–70%, compared to about 20% in the general population (Gonzalez-Pinto et al., 1998; Lasser et al., 2000; Chuang et al., 2008). A recent clinical survey demonstrated that the adjusted odds ratio for the association of current smoking with bipolar disorder is 7.3 (CI [4.3,12.4]), and is 4.0 (CI [2.4,6.7]) for ever smoking, compared to controls (Diaz et al., 2009). By comparison, the odds ratios for the association of smoking with schizophrenia is 5.9 (CI [4.9,6.7]) for current smoking and 3.1 (CI [2.4,3.8]) for ever smoking (de Leon & Diaz, 2005).

Moreover, similar to schizophrenia (Hitsman et al., 2009), there is a lower probability of smoking cessation compared to the general population in smokers with bipolar disorder ($OR=0.13$, CI [0.03,0.24]). This suggests that there may be unique features of the illness

Address for Correspondence: Tony P. George, M.D. FRCPC Centre for Addiction and Mental Health (CAMH) 250 College Street, Room CS 734 Toronto, Ontario Canada M5T 1R8 Tel: (416) 535-8501 ext.4544; Fax: (416) 979-4676 tony_george@camh.net.

DISCLOSURES Dr. George reports that in the past three years, he has received consulting fees and contract support from Pfizer, speaker's fees from Pfizer, Janssen and Astra-Zeneca, and serves on a Data Monitoring Committee for Novartis. Ms. Wu and Dr. Weinberger have no financial disclosures to report.

which predispose people with bipolar disorder to the initiation and maintenance of smoking behaviors (Diaz et al., 2009). Population-based studies have also suggested that, like most subgroups of smokers with mental illness and drug addiction, people with bipolar disorder have much lower quit rates than smokers without a comorbid disorder (Lasser et al., 2000). Bipolar disorder is a chronic relapsing mental disorder similar to these other disorders; however some of the unique features of mania and periods of elevated, expansive and irritable mood, alternating with periods of significant clinical depression may contribute to differences in cessation history. Two general forms of the illness have been described: bipolar I (mania alternating with clinical depression) and bipolar II (mild mania or hypomania, alternating with major depression). There have been several studies investigating biobehavioral factors that may contribute to the initiation and maintenance of tobacco dependence in people with depression, schizophrenia, and other psychotic disorders (see Sacco et al., 2005; George et al., 2006; George, 2007; Hong et al., 2011; Wing et al., 2012; Ziedonis et al, 2008), as well as several reports of cessation in smokers with depression, schizophrenia, and schizoaffective disorder (Evins et al., 2005, Evins et al., 2008; George et al., 2000, George et al., 2002; George et al., 2008; Williams et al., 2012; Ziedonis et al, 2008). In stark contrast, there have been few studies of smoking vulnerability factors or smoking cessation in people with bipolar disorder.

METHODS

Using a PubMed literature search with the terms “bipolar disorder”, “tobacco” and “smoking cessation”, we found eleven clinical studies focusing on bipolar disorder and tobacco addiction, including one smoking cessation treatment study.

RESULTS

A summary of studies of cigarette smoking prevalence and clinical correlates in bipolar disorder is given in Table 1.

Tobacco use in people with bipolar disorder is associated with high rates of other substance abuse, earlier onset of substance abuse, and more suicide attempts (Goldstein et al., 2008; Heffner et al., 2011; Heffner et al., 2008; Ostacher et al., 2007), as well as higher severity of manic and depressive symptoms, rapid cycling features (Waxmonsky et al., 2005), and poorer response to pharmacotherapies for bipolar disorder (Berk et al., 2008). Since tobacco-related medical illness may be the primary cause of morbidity and mortality in bipolar and other mentally ill smokers (BarChana et al., 2008; Hitsman et al., 2009), the development of safe and effective treatments for tobacco use comorbidity in these patients is crucial. A recent online survey of smokers with bipolar disorder suggested that a large proportion of these smokers (74%) are interested in quitting smoking, but only a third of their mental health providers have raised the issue of smoking cessation (Prochaska et al., 2011).

In addition to the clinical associations described in these eleven reports, only two controlled smoking cessation treatment studies in bipolar smokers have been published. The first studied the effects of sustained-release (SR) bupropion, an atypical antidepressant approved for the treatment of tobacco dependence (Weinberger et al., 2008). Although the sample was small ($N=5$), the results demonstrated the feasibility of using bupropion SR in this population. The second, also completed by our group, studied the effects of varenicline, a partial agonist for the alpha4beta2 subtype of nicotinic acetylcholine receptors (nAChRs) (Wu et al., 2012, this issue). This study was also small ($N=5$) but suggested the feasibility of using varenicline with careful screening and clinical monitoring of patients with bipolar disorder.

DISCUSSION

While there are three classes of FDA approved pharmacotherapies for tobacco dependence (nicotine replacement therapy, bupropion SR and varenicline), and several evidence-based behavioral treatments (e.g. brief advice, motivational interviewing, relapse-prevention/coping skills therapies; see George, 2011), there are virtually no such empirical studies for smokers with bipolar disorder. In the accompanying Letter to the Editor, we have described a pilot study of the safety and efficacy of varenicline for smoking cessation in tobacco smokers with bipolar disorder (Wu et al., 2012). Two identical controlled studies in the general population have shown that varenicline is more efficacious than bupropion SR and placebo (Gonzalez et al., 2006; Jorenby et al., 2006), suggesting that it may be the most effective treatment for use in smokers with refractory tobacco dependence, who often include those with psychiatric comorbidity (Hitsman et al., 2009). While varenicline has a generally acceptable safety profile, neuropsychiatric symptoms have emerged in post-marketing reports, including mood alterations, aggression and psychosis (Kohen & Kremen, 2007). Thus, while our small study (Wu et al., 2012) is timely insofar as addressing the issue of the safety of varenicline in smokers with bipolar disorder, more studies are needed to assess the relationship between varenicline and treatment-emergent neuropsychiatric adverse events. Two retrospective analyses of clinical studies of varenicline which included smokers with psychiatric histories (including the presence of modest numbers of smokers with bipolar disorder; Stapleton et al., 2008; McClure et al., 2010) support the safety of this drug in psychiatric smokers.

Our review of the literature on smoking and bipolar illness, and the results of our pilot study with varenicline in smokers with bipolar disorder (Wu et al., 2012), highlight the importance of addressing tobacco dependence in this patient population where there are few published descriptive or treatment studies. Only eleven clinical studies have been conducted in smokers with bipolar disorder. Importantly, only two very small controlled smoking cessation studies have been published, one with sustained-release bupropion (Weinberger et al., 2008; $N=5$), and one with varenicline (Wu et al., 2012; $N=5$). The low eligibility rates (e.g., randomization of only 5/164 smokers with bipolar disorder screened in the varenicline study) attest to the difficulty in recruiting psychiatrically stable people with bipolar disorder who are motivated to quit smoking. Similar to the bupropion trial (Weinberger et al., 2008), only 3% of phone screens in the Wu et al. (2012) study proceeded to successful randomization, which may explain why there are so few smoking cessation studies in people with bipolar disorder. Future studies should use multi-center clinical trial designs to further investigate the safety and efficacy of pharmacotherapies, such as nicotine replacement therapies, sustained-release bupropion and varenicline, in smokers with bipolar disorder. Of note, a recent multi-center placebo-controlled study of varenicline in smokers with schizophrenia or schizoaffective disorder ($N=127$) has demonstrated the safety and efficacy of this agent in smokers with chronic psychoses (Williams et al., 2012).

Anecdotally, it was of interest to note that in conducting in-person screening of potential subjects for the varenicline trial (Wu et al., 2012), many of the psychiatrists and family physicians who we contacted about their patients' participation noted that they were not convinced about the safety of smoking cessation in their patients with bipolar disorder, nor in the use of the smoking cessation agents for these patients. A Clinical Case Conference in the Journal of the American Medical Association highlighted the public health importance of the need to develop evidence-based treatments to address tobacco dependence in smokers with bipolar and other mental illness (Schroeder, 2009). The aid of patient advocacy groups such as the Depression and Bipolar Support Alliance (DBSA) and the National Alliance for the Mentally Ill (NAMI) should be enlisted to raise awareness about the lack of attention to this important comorbidity, particularly amongst psychiatric clinicians, where training on

tobacco dependence assessment and treatment (including basic smoking cessation counselling skills), and integration of tobacco treatment into mental health treatment settings, would be an important goal, as has been described for posttraumatic stress disorder (McFall et al., 2010). Furthermore, clinicians need to use motivational interviewing techniques to engage smokers with bipolar disorder to consider quitting tobacco smoking, as tobacco-related medical illness may be one of the leading causes of morbidity and mortality in smokers with bipolar illness (Heffner et al., 2011; Prochaska et al., 2011). Furthermore, increased federal funding for further research in this field emphasizing behavioral and pharmacological interventions, and research on the best ways by which such evidence-based treatments can be implemented in smokers with bipolar disorder in community settings, is urgently needed.

Acknowledgments

This work was supported in part by operating grants from the Canadian Tobacco Control Research Initiative (CTCRI Grant # 20613) and Canadian Institute for Health Research (CIHR) Operating Grant (MOP#115145 to TPG), the Canadian Foundation of Innovation Leading Opportunity Fund (CFI-LOF #19229, to TPG), the Ontario Mental Health Foundation (OMHF, to TPG), the University Chair in Addiction Psychiatry at the University of Toronto (to TPG), and the National Institute on Drug Abuse (NIDA grant K02-DA-016611 to TPG). We thank Douglas M. Ziedonis, M.D., M.P.H. for his helpful comments on the manuscript.

REFERENCES

- Baethge C, Tondo L, Lepri B, Baldessarini RJ. Coffee and cigarette use: Association with suicidal acts in 352 Sardinian bipolar disorder patients. *Bipolar Disorders*. 2009; 11:494–503. doi: 10.1111/j.1399-5618.2009.00727.x. [PubMed: 19624388]
- BarChana M, Levav I, Lipschitz I, Pugachova I, Kohn R, Weizman A, Grinshpoon A. Enhanced cancer risk among patients with bipolar disorder. *Journal of Affective Disorders*. 2008; 108:43–48. <http://dx.doi.org/10.1016/j.jad.2007.09.003>. [PubMed: 17904227]
- Berk M, Ng F, Wang WV, Tohen M, Lubman DI, Vieta E, Dodd S. Going up in smoke: Tobacco smoking is associated with worse treatment outcomes in mania. *Journal of Affective Disorders*. 2008; 110:126–134. <http://dx.doi.org/10.1016/j.jad.2008.01.018>. [PubMed: 18280579]
- Chuang H, Mansell C, Patten SB. Lifestyle characteristics of psychiatric outpatients. *Canadian Journal of Psychiatry*. 2008; 53:260–266.
- Cassidy F, McEvoy JP, Yang YK, Wilson WH. Smoking and psychosis in patients with bipolar I disorder. *Comprehensive Psychiatry*. 2002; 43:63–64. <http://dx.doi.org/10.1053/comp.2002.29847>. [PubMed: 11788921]
- Corvin A, O'Mahoney E, O'Regan M, Comerford C, O'Connell R, Craddock N, Gill M. Cigarette smoking and psychotic symptoms in bipolar affective disorder. *The British Journal of Psychiatry*. 2001; 179:35–38. doi: 10.1192/bjp.179.1.35. [PubMed: 11435266]
- de Leon J, Diaz FJ. A meta-analysis of worldwide studies demonstrates an association between schizophrenia and tobacco smoking behaviors. *Schizophrenia Research*. 2005; 76:135–157. <http://dx.doi.org/10.1016/j.schres.2005.02.010>. [PubMed: 15949648]
- Diaz F, James D, Botts S, Maw L, Susce MT, de Leon J. Tobacco smoking behaviors in bipolar disorder: A comparison of the general population, schizophrenia and major depression. *Bipolar Disorders*. 2009; 11:154–165. doi: 10.1111/j.1399-5618.2009.00664.x. [PubMed: 19267698]
- Dodd S, Brnabic AJ, Berk L, Fitzgerald PB, de Castella AR, Folia S, Berk M. A prospective study of the impact of smoking on outcomes in bipolar and schizoaffective disorder. *Comprehensive Psychiatry*. 2010; 51:504–509. <http://dx.doi.org/10.1016/j.comppsy.2009.12.001>. [PubMed: 20728008]
- Evins AE, Deckersbach T, Cather C, Freudenreich O, Culhane MA, Henderson DC, Goff DC. Independent effects of tobacco abstinence and bupropion on cognitive function in schizophrenia. *The Journal of Clinical Psychiatry*. 2005; 66:1184–1190. [PubMed: 16187778]
- Evins AE, Culhane MA, Alpert JE, Pava J, Liese BS, Farabaugh A, Fava M. A controlled trial of bupropion added to nicotine patch and behavioral therapy for smoking cessation in adults with

- unipolar depressive disorders. *Journal of Clinical Psychopharmacology*. 2008; 28:660–666. doi: 10.1097/JCP.0b013e31818ad7d6. [PubMed: 19011435]
- George TP, Vessicchio JC, Termine A, Bregartner TA, Feingold A, Rounsaville BJ, Kosten TR. A placebo controlled trial of bupropion for smoking cessation in schizophrenia. *Biological Psychiatry*. 2002; 52:53–61. [http://dx.doi.org/10.1016/S0006-3223\(02\)01339-2](http://dx.doi.org/10.1016/S0006-3223(02)01339-2). [PubMed: 12079730]
- George TP, Ziedonis DM, Feingold A, Pepper WT, Satterburg CA, Winkel J, Kosten TR. Nicotine transdermal patch and atypical antipsychotic medications for smoking cessation in schizophrenia. *The American Journal of Psychiatry*. 2000; 157:1835–1842. doi: 10.1176/appi.ajp.157.11.1835. [PubMed: 11058482]
- George TP, Termine A, Sacco KA, Seyal AA, Dudas MM, Allen TM, Duncan EJ. A preliminary study of the effects of cigarette smoking on prepulse inhibition in schizophrenia: Involvement of nicotinic receptor mechanisms. *Schizophrenia Research*. 2006; 87:307–315. <http://dx.doi.org/10.1016/j.schres.2006.05.022>. [PubMed: 16854565]
- George TP. Neurobiological links between nicotine addiction and schizophrenia. *Journal of Dual Diagnosis*. 2007; 3:27–42. doi: 10.1300/J374v03n03_04.
- George TP, Vessicchio JC, Sacco KA, Creeden CL, Dudas MM, Allen TA, Jatlow PI. A double-blind, randomized, placebo-controlled trial of sustained-release bupropion combined with transdermal nicotine patch for smoking cessation in schizophrenia. *Biological Psychiatry*. 2008; 63:1092–1096. <http://dx.doi.org/10.1016/j.biopsych.2007.11.002>. [PubMed: 18096137]
- George, TP. Nicotine and tobacco. In: Goldman, L.; Schafer, AI., editors. *Goldman's Cecil Medicine*. 24th edition. Elsevier - Health Sciences Division; New York, NY: 2011. p. 142-146.
- Gonzales D, Rennard SI, Nides M, Oncken C, Azoulay S, Billing CB, Reeves KR. Varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs sustained-release bupropion and placebo for smoking cessation: A randomized controlled trial. *JAMA: The Journal of the American Medical Association*. 2006; 296:47–55. doi: 10.1001/jama.296.1.47. [PubMed: 16820546]
- Gonzalez-Pinto A, Gutierrez M, Ezcurra J, Aizpuru F, Mosquera F, Lopez P, de Leon J. Tobacco smoking and bipolar disorder. *The Journal of Clinical Psychiatry*. 1998; 59:225–228. [PubMed: 9632031]
- Goldstein BI, Birmaher B, Axelson DA, Goldstein TR, Esposito-Symthers C, Stober MA, Keller MB. Significance of cigarette smoking among youths with bipolar disorder. *The American Journal on Addictions*. 2008; 17:364–371. doi: 10.1080/10550490802266151. [PubMed: 18770078]
- Heffner JL, Delbello MP, Fleck DE, Anthenelli RM, Strakowski SM. Cigarette smoking in the early course of bipolar illness: Association with ages-at-onset of alcohol and marijuana use. *Bipolar Disorders*. 2008; 10:838–845. doi: 10.1111/j.1399-5618.2008.00630.x. [PubMed: 19032716]
- Heffner JL, Strawn JR, DelBello MP, Strakowski SM, Anthenelli RM. The co-occurrence of cigarette smoking and bipolar disorder: Phenomenology and treatment considerations. *Bipolar Disorders*. 2011; 13:439–453. doi: 10.1111/j.1399-5618.2011.00943.x. [PubMed: 22017214]
- Hitsman B, Moss TG, Montoya ID, George TP. Treatment of tobacco dependence in mental health and addictive disorders. *Canadian Journal of Psychiatry*. 2009; 54:368–378.
- Hong LE, Thaker GK, McMahon RP, Summerfelt A, Rachbeisel J, Fuller RL, Nye A. Effects of moderate-dose treatment with varenicline on neurobiological and cognitive biomarkers in smokers and nonsmokers with schizophrenia or schizoaffective disorder. *Archives of General Psychiatry*. 2011; 68:1195–1206. doi:10.1001/archgenpsychiatry.2011.83. [PubMed: 21810630]
- Jorenby DE, Hays JT, Rigotti NA, Azoulay S, Watsky EJ, Williams KE, Varenicline Phase 3 Study Group. Efficacy of varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation: A randomized controlled trial. *JAMA: The Journal of the American Medical Association*. 2006; 296:56–63. doi: 10.1001/jama.296.1.56. [PubMed: 16820547]
- Kohen I, Kremen N. Varenicline-induced manic episode in a patient with bipolar disorder. *The American Journal of Psychiatry*. 2007; 164:1269–1270. doi: 10.1176/appi.ajp.2007.07010173. [PubMed: 17671294]

- Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness: A population-based prevalence study. *JAMA: The Journal of the American Medical Association*. 2000; 284:2606–2610. doi: 10.1001/jama.284.20.2606. [PubMed: 11086367]
- Law CW, Soczynska JK, Woldeyohannes HO, Miranda A, Brooks JO III, McIntyre RS. Relation between cigarette smoking and cognitive function in euthymic individuals with bipolar disorder. *Pharmacology, Biochemistry, and Behavior*. 2009; 92:12–16. <http://dx.doi.org/10.1016/j.pbb.2008.10.002>.
- McClure JB, Swan GE, Catz SL, Jack L, Javitz H, McAfee T, Zbikowski SM. Smoking outcome by psychiatric history after behavioural and varenicline treatment. *Journal of Substance Abuse Treatment*. 2010; 38:394–402. <http://dx.doi.org/10.1016/j.jsat.2010.03.007>. [PubMed: 20363092]
- McFall M, Saxon AJ, Malte CA, Chow B, Bailey S, Baker DG, CSP 519 Study Team. Integrating tobacco cessation into mental health care for posttraumatic stress disorder: A randomized controlled trial. *JAMA: The Journal of the American Medical Association*. 2010; 304:2485–2493. doi: 10.1001/jama.2010.1769. [PubMed: 21139110]
- Ostacher MJ, Nierenberg AA, Perlis RH, Eidelman P, Borrelli DJ, Tran TB, Sachs GS. The relationship between smoking and suicidal behavior, comorbidity, and course of illness in bipolar disorder. *The Journal of Clinical Psychiatry*. 2006; 67:1907–1911. [PubMed: 17194268]
- Prochaska JJ, Reyes RS, Schroder SA, Daniels AS, Doederlein A, Bergeson B. An online survey of tobacco use, intentions to quit, and cessation strategies among people living with bipolar disorder. *Bipolar Disorders*. 2011; 13:466–473. doi: 10.1111/j.1399-5618.2011.00944.x. [PubMed: 22017216]
- Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, Goodwin FK. Comorbidity of mental disorders with alcohol and other drug abuse: Results from the Epidemiologic Catchment Area (ECA) Study. *JAMA: The Journal of the American Medical Association*. 1990; 264:2511–2518. [PubMed: 2232018]
- Sacco KA, Termine A, Seyal AA, Dudas MM, Vessicchio JC, Krishnan-Sarin S, George TP. Effects of cigarette smoking on spatial working memory and attentional deficits in schizophrenia: Involvement of nicotinic receptor mechanisms. *Archives of General Psychiatry*. 2005; 62:649–659. [PubMed: 15939842]
- Schaffer A, Cairney J, Cheung A, Veldhuizen S, Levitt A. Community survey of bipolar disorder in Canada: Lifetime prevalence and illness characteristics. *Canadian Journal of Psychiatry*. 2006; 51:9–16.
- Schroeder SA. A 51-year old woman with bipolar disorder who wants to quit smoking. *JAMA: The Journal of the American Medical Association*. 2009; 301:522–531. doi: 10.1001/jama.2008.982. [PubMed: 19126801]
- Stapleton JA, Watson L, Spirling LI, Smith R, Milbrandt A, Ratcliffe M, Sutherland G. 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*. 2008; 103:146–154. doi: 10.1111/j.1360-0443.2007.02083.x. [PubMed: 18028247]
- Waxmonsky JA, Thomas MR, Miklowitz DJ, Allen MH, Wisniewski SR, Zhang H, Fossey MD. Prevalence and correlates of tobacco use in bipolar disorder: Data from the first 2000 participants in the Systemic Treatment Enhancement Program (STEP-BD). *General Hospital Psychiatry*. 2005; 27:321–328. [PubMed: 16168792]
- Weinberger AH, Vessicchio JC, Sacco KA, Creeden CL, Chengappa KN, George TP. A preliminary study of sustained-release bupropion for smoking cessation in bipolar disorder. *Journal of Clinical Psychopharmacology*. 2008; 28:584–587. doi: 10.1097/JCP.0b013e318184ba3c. [PubMed: 18794666]
- Williams JM, Anthenelli RM, Morris C, Tredow J, Thompson JR, Yunis C, George TP. A double-blind, placebo-controlled study evaluating the safety and efficacy of varenicline tartarate for smoking cessation in schizophrenia and schizoaffective disorder. *The Journal of Clinical Psychiatry*. in press.
- Ziedonis D, Hitsman B, Beckham JC, Zvolensky M, Adler LE, Audrain-McGovern J, Riley WT. Tobacco use and cessation in psychiatric disorders: National Institute of Mental Health report. *Nicotine & Tobacco Research*. 2008; 10(12):1691–1715. [PubMed: 19023823]

Table 1

Clinical Studies of Cigarette Smoking in Patients With Bipolar Disorder

Study	Design	Results
Wu et al. (2012)	Randomized, double-blind, placebo-controlled trial of varenicline in 5 smokers with bipolar disorder	One smoker in the varenicline group (n=3) quit, and one reduced smoking Placebo treatment was associated with dropout and hypomania.
Prochaska et al. (2011)	Online survey of 685 persons with bipolar disorder who smoked 100 cigarettes lifetime	74% expressed an intention to quit, which was unrelated to current mental health symptoms. Only 33% were advised to quit by a mental health provider. Higher proportion of former versus current smokers (57 vs. 40%) described mental health stability (p=0.011).
Dodd et al. (2010)	Prospective study of self-reported tobacco smoking and mental health outcomes in 240 subjects with bipolar and schizoaffective disorders during a 24-month period	Daily smokers had poorer outcomes on CGI Overall and Depression Score scales than non-daily smokers. Daily smokers had longer length of stays than non-daily smokers.
Ostacher et al. (2009)	Prospective study of the association between cigarette smoking and suicidality in people with bipolar disorder	A higher proportion of smokers versus non-smokers made a suicide attempt during the 9-month observation period (16.1 versus 3.5%; OR=5.25, CI [1.2,23.5]).
Baethe et al. (2009)	Retrospective review of 352 Sardinian patients with bipolar I and II disorder and association between cigarette smoking and suicidal acts	Current smoking was associated with higher rates of suicidal acts compared to non-smoking status. Higher consumption was positively correlated with suicidal behaviors compared to lower consumption.
Law et al. (2009)	Cross-sectional study of the relationship between smoking status and cognitive function in 43 patients with bipolar disorder	No differences in neuropsychological performance between smokers (n=16) and non-smokers (n=27). Presence of tobacco smoking was associated with poorer pre-morbid IQ performance.
Heffner et al. (2008)	Survey of 134 adolescents with bipolar disorder who were hospitalized for a first manic episode	45.5% were smokers Smokers were more likely to report cannabis and alcohol use, and an earlier onset of bipolar disorder than non-smokers. Characteristics of bipolar illness (age of onset, symptom severity, psychosis, rapid cycling) were not linked with smoking status.
Goldstein et al. (2008)	Cross-sectional survey of smoking status (Never, Ever and Daily smoking) and mental illness history in 441 youth with bipolar disorder.	Daily and ever smokers had greater occurrence of lifetime suicide attempts, physical abuse, conduct disorder and SUDs compared to never smokers. Heavy daily smokers had higher SUD prevalence, depression and suicide attempts compared to light daily smokers.
Weinberger et al. (2008)	Randomized, double-blind, placebo-controlled trial of bupropion SR in 5 smokers with bipolar disorder	Two smokers in the bupropion SR group either quit or reduced smoking Placebo treatment was associated with dropout and occurrence of hypomania.
Waxmonsky et al. (2005)	Cross-sectional study of cigarette smoking and clinical correlates of bipolar disorder in 1,904 people with bipolar disorder participating in the STEP-BD study.	31.2% of participants were smokers. Smokers were more likely than non-smokers to be male, poor, and less educated. Smokers were also more likely than non-smokers to have SUDs or other psychiatric comorbidity, more rapid cycling features, and more depressive or manic episodes and symptom severity.

Study	Design	Results
Cassidy et al. (2002)	Survey of 67 recently admitted inpatients with bipolar I disorder (with manic or mixed states) regarding smoking and psychosis outcomes.	No correlations between cigarette smoking and any psychosis outcomes.
Corvin et al. (2001)	Cross-sectional study assessed cigarette smoking and psychopathology in 92 patients with bipolar disorder in Dublin, Ireland.	Strong relationship between smoking consumption and severity of psychosis in bipolar patients.

Note. CGI = Clinical Global Impression; STEP-BD = Systematic Treatment Enhancement Program for Bipolar Disorder; SUD = Substance Use Disorder.