Published in final edited form as:

Addiction. 2012 October ; 107(10): 1847–1856. doi:10.1111/j.1360-0443.2012.03889.x.

The relationship of major depressive disorder and gender to changes in smoking for current and former smokers: Longitudinal evaluation in the U.S. population

Andrea H. Weinberger, Ph.D.^{1,2}, Corey E. Pilver, Ph.D.³, Rani A. Desai, Ph.D., MPH^{1,3,4}, Carolyn M. Mazure, Ph.D.^{1,2}, and Sherry A. McKee, Ph.D.^{1,2}

¹Divisions of Substance Abuse and Women's Behavioral Health Research, Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06519 USA

²Women's Health Research at Yale, Yale University School of Medicine, New Haven, CT 06520 USA

³National Center for PTSD, Evaluation Division; VA CT Healthcare Center, West Haven, CT 06516 USA

⁴Department of Public Health, Yale University School of Medicine, New Haven, CT 06510 USA

Abstract

Aims—Although depression and smoking are highly correlated, the relationship of Major Depressive Disorder (MDD) to smoking cessation and relapse remains unclear. This study compared changes in smoking for current and former smokers with and without Current and Lifetime MDD over a three year period.

Design—Analysis of two waves of longitudinal data from the National Institute on Alcohol Abuse and Alcoholism's National Epidemiologic Survey on Alcohol and Related Conditions (Wave 1, 2001–2002; Wave 2, 2004–2005).

Setting—Data were collected through face-to-face interviews from non-institutionalized United States civilians, 18 years and older, in 50 states and the District of Columbia.

Participants—11,973 adults (46% female) classified as Current or Former Daily Smokers at Wave 1 and completed Wave 2.

Measurements—Classification as Current or Former Smokers at Wave 1 and Wave 2.

Findings—Smoking status remained stable for most participants. Wave 1 Current Daily Smokers with Current MDD (OR=1.38, 95% CI=1.03, 1.85) and Lifetime MDD (OR=1.48, 95% CI=1.18, 1.85) were more likely than those without the respective diagnosis to report continued smoking at Wave 2. Wave 1 Former Daily Smokers with Current MDD (OR=0.44, 95% CI=0.26, 0.76) were less likely to report continued abstinence at Wave 2. None of the gender by MDD diagnosis interactions were significant. Patterns of results remained similar when analyses were limited to smokers with nicotine dependence.

Conclusions—Current and Lifetime Major Depressive Disorder are associated with a lower likelihood of quitting smoking and Current Major Depressive Disorder is associated with greater likelihood of smoking relapse.

Corresponding Author: Andrea H. Weinberger, Ph.D., Assistant Professor of Psychiatry, Yale University School of Medicine, 34 Park Street, SAC, Room S-211, New Haven, CT 06519 USA, Tel: (203) 974-7598, Fax: (203) 974-7366, andrea.weinberger@yale.edu.

Declaration of Interest: None

INTRODUCTION

Major Depressive Disorder (MDD) is one of the most common psychiatric illnesses in the U.S. (1) and there is a significant association between smoking and MDD. Lifetime and Current MDD are associated with higher smoking rates while smoking is associated with a greater prevalence of a lifetime MDD, greater symptoms of depression, and more frequent episodes of depression (2–5). The high prevalence of MDD and high rates of smoking among adults with MDD translate into millions of adults affected by the enormous negative personal and societal consequences of smoking (6, 7).

Nicotinic acetylcholine receptors (nAChRs) are the primary neuronal targets of nicotine. Through nAChRs, nicotine impacts multiple neurotransmitters (e.g., serotonin, norepinephrine) which modulate response to stress and depression (8–10) and both nicotine and nicotinic agents reduce depressive symptoms (11), supporting the high rates of comorbidity. Chronic nicotine exposure results in nAChR desensitization and upregulation of nicotine binding sites (8, 10, 12). Desensitization of nAChRs results in decreased depression symptoms and an increased desire to smoke when desensitized nAChRs become unoccupied (9, 10, 12) which may make it more difficult for adults with MDD to quit smoking.

However, research has been equivocal regarding the impact of MDD on smoking cessation success. While some clinical studies and cross-sectional epidemiological data suggest that smokers with depression have more difficulty quitting smoking (4, 13–15); other studies find conflicting results (e.g., 16, 17; see 3 for a review). Most studies analyze post-hoc data from clinical trials (e.g., 18, 19) or longitudinal data from gender-specific subgroups of smokers (e.g., 14, 20, 21), smokers from a specific geographical region (e.g., 22), or smokers with co-morbid disorders (e.g., 23) which limit generalizability to a general adult population. Further, most studies only include smokers with Lifetime MDD (e.g., 17, 24–26) limiting generalizability to adults with Current MDD. The use of longitudinal epidemiological data would clarify the mixed findings on the role of MDD in changes in smoking behavior and identify smokers who need more intensive smoking treatments and/or smoking treatments that also specifically address depression.

Thirteen percent of adults meet criteria for current nicotine dependence (27) diagnosed by reports of daily smoking, evidence of tolerance (i.e., lack of aversive effects of nicotine such as nausea), and the presence of withdrawal symptoms upon smoking cessation (e.g., dysphoria, irritability, cravings) (28). Adults with Current and Lifetime MDD report higher rates of nicotine dependence than other adults (27, 29); therefore, it is important to consider nicotine dependence in the relationship of MDD and changes in smoking behavior.

Women report higher rates of Current and Lifetime MDD (27); exhibit a stronger relationship between Current and Lifetime MDD and smoking (30) and between Lifetime MDD and duration of withdrawal (31); and are more likely to report concerns about post-cessation negative affect (32). Both Current and Lifetime MDD appear to exert a greater negative impact on the ability of women to quit smoking (33–37, although see also 17, 38), highlighting the need to consider gender in the relationship between MDD and smoking behavior.

Aims of the current study

The primary aim of this study was to use longitudinal data from a large, nationally representative sample of the adult U.S. population to examine the main and gender-specific effects of current and lifetime MDD on changes in smoking behavior over a three year period. It was hypothesized that diagnoses of Current and Lifetime MDD would be related

to greater continued smoking for Current Smokers and greater smoking relapse for Former Smokers. It was expected that these relationships would remain significant for smokers who met criteria for nicotine dependence. Finally, it was hypothesized that the relationship between MDD and smoking would be stronger for women than men.

METHODS

Participants and Procedures

Data were taken from two waves of the National Institute on Alcohol Abuse and Alcoholism's National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; Wave 1, 2001–2002; Wave 2, 2004–2005). During Wave 1, face-to-face interviews were conducted with 43,093 non-institutionalized United States civilians in 50 states and the District of Columbia. Participants were ages 18 and older with an oversampling of African-Americans, Hispanics, and young adults (ages 18–24). Approximately eighty-six percent of the Wave 1 sample ($n=34,653$ out of 39,959 eligible participants) completed face-to-face Wave 2 interviews with a mean interval between interviews of 36.6 months. See Grant and colleagues (39, 40) for more details about the sampling, purpose, and weight procedures for the NESARC.

Analytic sample

We limited our analysis to two, non-overlapping subsamples of the NESARC population, Wave 1 Current Daily Smokers and Wave 1 Former Daily Smokers. Smoking behavior was assessed at each wave using the Alcohol Use Disorders and Associated Disabilities Interview Schedule-DSM-IV (AUDADIS-IV; 41), a structured interview administered by trained lay interviewers which shows good reliability in the assessment of smoking behavior ($ICCs=0.60–0.92$; 42). Definitions of current and former smoking behavior were consistent with the categories used by the U.S. Department of Health and Human Service's Centers for Disease Control and Prevention (43) and other investigations using NESARC data (29, 30).

Wave 1 Current Daily Smokers were defined as individuals who indicated that they (1) had smoked 100 or more cigarettes in their lifetime; (2) had smoked cigarettes in the 12 months preceding the Wave 1 assessment; and, (3) currently smoked cigarettes every day. We identified 8,213 individuals who met these criteria for Wave 1 Current Daily Smoking. From this subsample, we excluded 1,668 individuals who did not complete the Wave 2 assessment or did not provide valid data for smoking status at Wave 2. The final sample of Wave 1 Current Daily Smokers included 6,545 individuals.

Wave 1 Former Daily Smokers were defined as individuals who indicated that they (1) had smoked 100 or more cigarettes in their lifetime; (2) had smoked cigarettes before the 12 months preceding the Wave 1 assessment (but not during those 12 months); and, (3) usually smoked cigarettes every day, in the period when they had last smoked. We identified 6,622 individuals who met these criteria for Wave 1 Former Daily Smoking. From this subsample, we excluded 1,194 individuals who did not complete the Wave 2 assessment or did not provide valid data for smoking status at Wave 2. The final sample of Wave 1 Former Daily Smokers included 5,428 individuals.

For the purposes of additional analyses, we created two more subsamples: Wave 1 Current Daily Smokers with a past-year diagnosis of Nicotine Dependence ($n=3,556$) and Wave 1 Former Daily Smokers with a past diagnosis of Nicotine Dependence ($n=1,118$). Nicotine Dependence was assessed through the AUDADIS-IV.

Current Smokers were less likely to complete the Wave 2 assessment than Former Smokers (80.2% versus 83.2%, $p<0.001$). Participants with lifetime nicotine dependence were less

likely to complete the Wave 2 assessment than participants without lifetime nicotine dependence (83.1% versus 80.9%, $p < 0.01$).

Measures

Changes in Smoking (Dependent Variables)—Among Wave 1 Current Daily Smokers, the binary dependent variable of interest was “Persistence of smoking.” Persistence of smoking was defined according to smoking status at Wave 2, and denoted whether Wave 1 Current Smokers were stable current smokers at Wave 2 (coded as “1”) or quitters at Wave 2 (coded as “0”). Individuals were categorized as Stable Current Smokers if they indicated that they smoked cigarettes in the 12 months preceding the Wave 2 interview. Individuals who had not smoked cigarettes in the 12 months preceding the Wave 2 interview were characterized as Quitters.

Among Wave 1 Former Smokers, the binary dependent variable of interest was “Persistence of non-smoking.” Persistence of non-smoking was defined according to smoking status at Wave 2, and denoted whether Wave 1 Former Smokers remained former smokers at Wave 2 (coded as “1”) or had relapsed to smoking at Wave 2 (coded as “0”). Individuals were categorized as Stable Former Smokers if they indicated that they had not smoked 100 or more cigarettes in the period since the Wave 1 interview. Individuals who indicated that they had smoked cigarettes in the 12 months preceding the Wave 2 interview were characterized as Relapsers.

Major Depressive Disorder (Dependent Variables)—Psychiatric disorders including MDD were assessed using the AUDADIS-IV (41) which assesses symptoms based on DSM-IV diagnostic criteria (28) and has demonstrated adequate reliability for the assessment of Axis I disorders (κ s=0.40–0.63;42).

The independent variables of interest were diagnoses of Lifetime MDD and Current MDD (both assessed at Wave 1). A diagnosis of MDD was given to participants who reported 5 of the following symptoms for at least a 2-week period that was also marked by significant distress and/or impairment: depressed mood, loss of interest or pleasure in activities, changes in weight or appetite, changes in sleep, psychomotor agitation or sedation, loss of energy, feelings of worthlessness or guilt, diminished concentration, and suicidality (28). A diagnosis of Current MDD was given if participants met criteria for MDD within the twelve months prior to the Wave 1 assessment and a diagnosis of Lifetime MDD was given if participants met criteria for MDD in their lifetime but not during the previous 12 months.

Additional disorders that were assessed by the AUDADIS-IV included dysthymia (28), minor depression (44), anxiety disorders (i.e., participants who met criteria for any of the following: panic disorder, agoraphobia, specific phobia, social phobia, and generalized anxiety disorder), alcohol abuse/dependence, drug abuse/dependence, and manic disorder. Similar to MDD, disorders were assessed at Wave 1 and classified as “current” if the most recent episode began during the 12 months prior to the Wave 1 interview, and “lifetime” if the disorder was experienced during the participants’ lifetime but not within the 12 months prior to the Wave 1 interview.

Demographics—The following information was assessed at Wave 1: gender, age (18–29, 30–44, 45 and older), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Non-Hispanic Other, Hispanic), education (Less than High School, High School Graduate, Attended/Completed College), and marital status (Married, Not Married). These categorizations were based on the work of Grant and colleagues (27).

Statistical Analyses

Data were analyzed using SUDAAN (45), a software package that adjusts for characteristics of complex survey sampling designs. NESARC-calculated weights were used to account for nonresponse; attrition; oversampling of African-Americans, Hispanics, and young adults, and to be representative of the US civilian population based on the 2000 decennial census. Statistical tests were two-tailed and differences were considered significant when $p < 0.05$. Statistical significance was determined with the Wald Chi-square test.

Analyses proceeded in several steps. First, we descriptively examined the demographic characteristics of the sample using the PROC CROSSTAB procedure for categorical variables. We then examined whether Wave 1 Current Smokers and Wave 1 Former Smokers differed on these characteristics. We also examined the bivariate distribution of MDD (Current and Lifetime) and the dependent variables of interest (persistence of smoking among Wave 1 Current Daily Smokers with and without a past-year diagnosis of nicotine dependence, and persistence of non-smoking among Wave 1 Former Daily Smokers with and without a lifetime diagnosis of nicotine dependence), stratified by gender. For these descriptive statistics, we presented the unweighted N and weighted prevalence estimates.

In the modeling stage of our analysis, we built a series of binary logistic regression models using PROC RLOGIST. These models were constructed separately for Wave 1 Current Smokers, Wave 1 Current Daily Smokers with a past-year diagnosis of nicotine dependence, Wave 1 Former Daily Smokers, and Wave 1 Former Daily Smokers with a lifetime diagnosis of nicotine dependence. The dependent variables of interest were persistence of smoking for Wave 1 Current Daily Smokers and persistence of non-smoking for Wave 1 Former Daily Smokers. We ran one set of models with Current MDD as the main independent variable, and another set of models with Lifetime MDD as the main independent variable.

The first analysis included only the independent variable of interest (i.e. Lifetime or Current MDD assessed at Wave 1). For these analyses, we calculated the main effect of MDD and present this as an unadjusted odds ratio (OR) and its associated 95% Confidence Interval (95% CI). The second analysis examined the gender-specific effects of MDD diagnosis on changes in smoking and included MDD, gender, and the MDD by gender interaction term. For these analyses, we calculated the unique effects of MDD among women and among men (the gender-specific ORs and their associated 95% CIs), as well as the interaction ORs. The interaction OR is the ratio of the gender-specific effects; in other words, it is effect of MDD among women divided by the effect of MDD among men ($\text{Interaction OR} = \text{OR}_{\text{women}} / \text{OR}_{\text{men}}$). An interaction is considered to be statistically significant when the 95% CI of the interaction OR does not include 1.0 (the corresponding p-value is less than 0.05). The pattern of results for all analyses remained the same after controlling for co-morbid psychiatric and substance use disorders.

RESULTS

Wave 1 Demographics

The sample was primarily male, 45 years or older, non-Hispanic White, married, and had at least a high school education. Wave 1 Current Daily Smokers were more likely to be female, younger, an ethnic minority, unmarried, and to not have attended or completed college compared to Wave 1 Former Daily Smokers (see Table 1). Fifty-five percent of Wave 1 Current Daily Smokers met criteria for current nicotine dependence while twenty-one percent of Wave 1 Former Daily Smokers met criteria for lifetime nicotine dependence.

Prevalence of Current and Lifetime MDD at Wave 1

The prevalence of Current and Lifetime MDD was at least two times higher for women compared to men. Among Wave 1 Current Daily Smokers, the prevalence of Current MDD was 16.0% for women and 7.9% for men ($p<0.0001$); the prevalence of Lifetime MDD was 28.0% for women and 14.4% for men ($p<0.0001$). Among Wave 1 Former Daily Smokers, the prevalence of Current MDD was 8.6% for women and 3.6% for men ($p<0.0001$); the prevalence of Lifetime MDD was 22.2% for women and 9.0% for men ($p<0.0001$).

Changes in Smoking for Wave 1 Current and Former Smokers

Smoking status remained stable for the majority of Wave 1 Current and Former Daily Smokers over the three year period. Eighty-five percent of Wave 1 Current Daily Smokers remained Current Smokers while 15% reported that they had quit smoking at Wave 2. Ninety-five percent of Wave 1 Former Daily Smokers reported that they remained Former Smokers while five percent reported that they were Current Smokers at Wave 2.

The Main and Gender-Specific Effects of MDD on Smoking Cessation. (Table 2)

The Main Effect of MDD on Smoking Cessation—Individuals with Current MDD and Lifetime MDD, respectively, were 38% and 48% more likely than individuals without these disorders to continue to smoke at Wave 2 (Table 2). The association between Lifetime MDD and continued smoking remained significant for participants with current nicotine dependence.

The Gender-Specific Effects of MDD on Smoking Cessation—In the full sample, the association of Current MDD and continued smoking was significant for women, but not men. However, the interactions of gender and Current MDD diagnosis were not significant in either the full sample or for participants with nicotine dependence suggesting that the overall effect of Current MDD on continued smoking was essentially the same for men and women.

The association between Lifetime MDD and persistent smoking was significant for women, but not men, in the full sample and for participants who met criteria for lifetime nicotine dependence. However, the interactions of gender and Current MDD diagnosis were not significant in either analysis.

The Main and Gender-Specific Effects of MDD on Smoking Relapse (Table 3)

The Main Effect of MDD on Smoking Relapse—Individuals with Current MDD and Lifetime MDD were 56% and 35% less likely than individuals without the respective diagnoses to have remained abstinent from smoking at Wave 2 (Table 3). The association between Current MDD and continued smoking remained significant for participants with current nicotine dependence. The association between Lifetime MDD and continued smoking was not significant for participants with lifetime nicotine dependence.

The Gender-Specific Effects of MDD on Smoking Relapse—While the association of Current MDD and smoking relapse was significant for women but not men in the full sample, the interactions of gender and Current MDD diagnosis were not significant in either analysis suggesting that the overall effect of Current MDD on smoking relapse was essentially the same for men and women. The interactions of gender and Lifetime MDD diagnosis were not significant.

DISCUSSION

Our study was the first to use longitudinal data from a large epidemiological survey of adults in the U.S. to examine the gender-specific relationship of Current and Lifetime MDD to changes in smoking for Current and Former Smokers. Smoking status remained stable for most participants over the 3-year period. Smokers with Current or Lifetime MDD were more likely to continue smoking (i.e., were less likely to quit smoking) than smokers without the respective diagnosis. Former smokers with Current MDD were more likely to report smoking relapse than those without Current MDD. The pattern of results remained the same when analyses were limited to smokers with nicotine dependence although the association of Current MDD and continued smoking and Lifetime MDD and relapse were no longer statistically significant in the restricted analyses. Contrary to expectation, the relationship between MDD and changes in smoking did not differ by gender.

Most previous studies of the relationship of depression to smoking behavior examined outcomes for specific smoking cessation treatments or used cross-sectional data to examine changes in smoking retrospectively. In both cases, the findings were mixed (see (10) for a review). Further, most past research excluded participants with Current MDD, resulting in little information about the relationship between Current MDD and smoking quit behavior. Our data advances this past work to show that MDD is negatively related to changes in smoking in a general adult population. Our data further show that this relationship applies to smokers with current MDD as well as those with past MDD and that the detrimental impact of MDD on smoking behavior is similar for men and women.

The mechanisms behind the association of MDD to greater continued smoking and smoking relapse are not clear. Smokers with depression report greater tobacco withdrawal (46, 47), smoking expectancies (48, 49), smoking cue reactivity (50, 51), and smoking reward (52). Neurobiological findings related to the nAChR system also suggest that smokers with depression would experience greater cravings to smoke when attempting to quit (9, 10, 12). In order to successfully quit smoking, adults with MDD, current or past, may need smoking interventions that target withdrawal and cravings as well as depressive symptoms. Adults with Current MDD may also need longer treatment durations and monitoring after smoking cessation to catch and intervene early in relapse situations.

Women in this sample reported higher rates of Current and Lifetime MDD than men similar to other research findings (27, 53, 54). The relationship of MDD to changes in smoking was similar for men and women consistent with a meta-analysis of smoking cessation clinical trials (17). However, MDD would still be expected to have an overall greater impact on the smoking behavior of women due to the larger numbers of women suffering from MDD. Women are more susceptible to some smoking-related illnesses (55, 56), face gender-specific consequences of smoking (57), and appear to have more trouble quitting smoking than men (37, 58, 59). Future research should continue to identify variables differentially associated with changes in smoking for women to improve cessation interventions for female smokers.

Several limitations to this study should be noted. The NESARC study surveyed non-institutionalized adults in the United States and may not generalize to adults in other countries, adults with severe MDD requiring residential living, or smokers younger than 18. While one strength of the NESARC study is the careful and psychometrically sound assessment of smoking behavior and Axis I disorders, the dataset is limited with regard to other variables. For example, there are no data provided on the pattern of smoking between the two waves of data collection (e.g., number of quit attempts, smoking cessation treatments utilized, experience of withdrawal symptoms during specific quit attempts).

Future research should examine how MDD relates to cessation success with specific behavioral and pharmacological interventions. Future research should also examine the impact of MDD course and treatment (e.g., chronicity of MDD, timing since MDD onset, and antidepressant use), other depressive disorders (e.g., dysthymia, minor depression), and co-morbid psychiatric and substance use disorders on changes in smoking in population and clinical samples.

Current and Lifetime MDD are associated with a lower likelihood of quitting smoking and Current MDD is associated with greater likelihood of smoking relapse. While women showed higher rates of depression, the impact of depression on changes in smoking was similar for men and women. Consideration of both depression and gender is critical for improving our knowledge of why some groups of smokers are less likely to achieve smoking cessation. Further, considering depression and gender when working with smokers in clinical settings will help to provide appropriate levels of care in assisting these smokers to quit and remain abstinent, thereby decreasing the enormous negative individual and societal consequences of smoking.

Acknowledgments

This work was supported by the National Institutes of Health grants R03-DA027052 (to AHW), K12-DA000167 (to AHW), and RL1DA024857 (to SAM); *Women's Health Research at Yale*; and the State of Connecticut, Department of Mental Health and Addiction Services.

References

1. Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al. National Comorbidity Survey Replication. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA*. 2003; 289:3095–105. [PubMed: 12813115]
2. Wiesbeck GA, Kuhl HC, Yaldirli O, Wurst FM. WHO/ISBRA Study Group on Biological State and Trait Markers of Alcohol Use and Dependence. Tobacco smoking and depression--results from the WHO/ISBRA study. *Neuropsychobiology*. 2008; 57:26–31. [PubMed: 18424908]
3. Ziedonis D, Hitsman B, Beckham JC, Zvolensky M, Adler LE, Audrain-McGovern J, et al. Tobacco use and cessation in psychiatric disorders: National Institute of Mental Health report. *Nicotine Tob Res*. 2008; 10:1691–715. [PubMed: 19023823]
4. Wilhelm K, Wedgwood L, Niven H, Kay-Lambkin F. Smoking cessation and depression: Current knowledge and future directions. *Drug Alcohol Rev*. 2006; 25:97–107. [PubMed: 16492582]
5. Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness: A population-based prevalence study. *JAMA*. 2000; 284:2606–10. [PubMed: 11086367]
6. USDHHS. The Health Consequences of Smoking: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2004.
7. CDC. Smoking-attributable mortality, years of potential life lost, and productivity losses---United States, 2000–2004. *Morbidity and Mortality World Report (MMWR)*. 2008; 57:1226–8.
8. Picciotto MR, Addy NA, Mineur YS, Brunzell DH. It is not “either/or”: Activation and desensitization of nicotinic acetylcholine receptors both contribute to behaviors related to nicotine addiction and mood. *Prog Neurobiol*. 2008; 84:329–42. [PubMed: 18242816]
9. Mineur YS, Picciotto MR. Nicotine receptors and depression: Revisiting and revising the cholinergic hypothesis of depression. *Trends Pharmacol Sci*. 2010; 31:580–6. [PubMed: 20965579]
10. Picciotto MR, Brunzell DH, Caldarone BJ. Effect of nicotine and nicotinic receptors on anxiety and depression. *Neuro Report*. 2002; 13:1097–106.
11. Weinberger AH, McKee SA, Picciotto MR, Mazure CM. Examining antidepressant drug response by smoking status: Why is it important and how often is it done? *J Psychopharmacol*. 2011; 25:1269–76. [PubMed: 21169392]

12. Benowitz NL. Neurobiology of nicotine addiction: implications for smoking cessation treatment. *Am J Med.* 2008; 121:S3–S10. [PubMed: 18342164]
13. Piper ME, Smith SS, Schlam TR, Fleming MF, Bittrich AA, Brown JL, et al. Psychiatric disorders in smokers seeking treatment for tobacco dependence: Relations with tobacco dependence and cessation. *J Consult Clin Psychol.* 2010; 78:13–23. [PubMed: 20099946]
14. Walsh Z, Epstein A, Munisamy G, King A. The impact of depressive symptoms on the efficacy of naltrexone in smoking cessation. *J Addict Dis.* 2008; 27:65–72. [PubMed: 18551889]
15. McClave AK, Dube SR, Strine TW, Kroenke K, Caraballo RS, Mokdad AH. Associations between smoking cessation and anxiety and depression among U.S. adults. *Addict Behav.* 2009; 34:491–7. [PubMed: 19217720]
16. Johnson EO, Breslau N. Is the association of smoking and depression a recent phenomenon? *Nicotine Tob Res.* 2006; 8:257–62. [PubMed: 16766418]
17. Hitsman B, Borrelli B, McChargue DE, Spring B, Niaura R. History of depression and smoking cessation outcome: A meta-analysis. *J Consult Clin Psychol.* 2003; 71:657–63. [PubMed: 12924670]
18. Niaura R, Britt DM, Shadel WM, Goldstein M, Abrams D, Brown R. Symptoms of depression and survival experience among three samples of smokers trying to quit. *Psychol Addict Behav.* 2001; 15:13–7. [PubMed: 11255933]
19. Brown R, Niaura AR, Lloyd-Richardson EE, Strong DR, Kahler CW, Abrantes AM, et al. Bupropion and cognitive-behavioral treatment for depression in smoking cessation. *Nicotine Tob Res.* 2007; 9:721–30. [PubMed: 17577801]
20. Kinnunen T, Haukka A, Korhonen T, Quiles ZN, Spiro A 3rd, Garvey AJ. Depression and smoking across 25 years of the Normative Aging Study. *Int J Psychiatry Med.* 2006; 36:413–26. [PubMed: 17407995]
21. McDermott L, Dobson A, Owen N. Occasional tobacco use among young adult women: A longitudinal analysis of smoking transitions. *Tob Control.* 2007; 16:248–54. [PubMed: 17652240]
22. Breslau N, Peterson EL, Schultz LR, Chilcoat HD, Andreski P. Major depression and stages of smoking. A longitudinal investigation. *Arch Gen Psychiatry.* 1998; 55:161–6. [PubMed: 9477930]
23. Friend KB, Pagano ME. Time-varying predictors of smoking cessation among individuals in treatment for alcohol abuse and dependence: Findings from Project MATCH. *Alcohol Alcohol.* 2007; 42:234–40. [PubMed: 17526633]
24. Haas AL, Munoz RF, Humfleet GL, Reus VI, Hall SM. Influences of mood, depression history, and treatment modality on outcomes in smoking cessation. *J Consult Clin Psychol.* 2004; 72:563–70. [PubMed: 15301640]
25. Burgess ES, Brown RA, Kahler CW, Niaura R, Abrams DB, Goldstein MG, et al. Patterns of change in depressive symptoms during smoking cessation: Who's at risk for relapse? *J Consult Clin Psychol.* 2002; 70:356–61. [PubMed: 11952193]
26. Kinnunen T, Henning L, Nordstrom BL. Smoking cessation in individuals with depression: Recommendations for treatment. *CNS Drugs.* 1999; 11:93–103.
27. Grant BF, Hasin DS, Chou P, Stinson FS, Dawson DA. Nicotine dependence and psychiatric disorders in the United States. *Arch Gen Psychiatry.* 2004; 61:1107–15. [PubMed: 15520358]
28. APA. Diagnostic and statistical manual of mental disorders. 4. Washington DC: American Psychiatric Association; 1994. (DSM-IV)
29. Dierker L, Donny E. The role of psychiatric disorders in the relationship between cigarette smoking and DSM-IV nicotine dependence among young adults. *Nicotine Tob Res.* 2008; 10:439–46. [PubMed: 18324562]
30. Husky MM, Mazure CM, Paliwal P, McKee SA. Gender differences in the comorbidity of smoking behavior and major depression. *Drug Alcohol Depend.* 2008; 93:176–9. [PubMed: 17850991]
31. Weinberger AH, Maciejewski PK, McKee SA, Reutenauer EL, Mazure CM. Gender differences in associations between lifetime alcohol, depression, panic disorder, and posttraumatic stress disorder and tobacco withdrawal. *Am J Addict.* 2009; 18:140–7. [PubMed: 19283566]
32. McKee SA, O'Malley SS, Salovey P, Krishnan-Sarin S, Mazure C. Perceived risk and benefits of smoking cessation: Gender-specific predictors of motivation and treatment outcome. *Addict Behav.* 2005; 30:423–5. [PubMed: 15718060]

33. Reynoso J, Susabda A, Cepeda-Benito A. Gender differences in smoking cessation. *J Psychopathol Behav Assess.* 2004; 27:227–34.
34. Schnoll RA, Patterson F, Lerman C. Treating tobacco dependence in women. *J Women's Health.* 2007; 16:1211–8.
35. Borland R. Slip-ups and relapse in attempts to quit smoking. *Addict Behav.* 1990; 15:235–45. [PubMed: 2378283]
36. Glassman AH, Covey LS, Dalack GW, Stetner F, Rivelli SK, Fleiss J, et al. Smoking cessation, clonidine, and vulnerability to nicotine among dependent smokers. *Clin Pharmacol Ther.* 1993; 54:670–9. [PubMed: 8275622]
37. Perkins KA. Smoking cessation in women: Special considerations. *CNS Drugs.* 2001; 15:391–411. [PubMed: 11475944]
38. John U, Meyer C, Rumpf H-J, Hapke U. Depressive disorders are related to nicotine dependence in the population but do not necessarily hamper smoking cessation. *J Clin Psychiatry.* 2004; 65:169–76. [PubMed: 15003069]
39. Grant, BF.; Moore, TC.; Shepard, J.; Kaplan, K. Source and accuracy statement for wave 1 of the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Bethesda, MD: National Institute on Alcohol Abuse and Alcoholism; 2003.
40. Grant, BF.; Kaplan, KD. Source and accuracy statement: The wave 2 national epidemiologic survey on alcohol and related conditions (NESARC). Rockville, MD: National Institute on Alcohol Abuse and Alcoholism; 2005.
41. Grant, BF.; Dawson, DA.; Hasin, DS. The Alcohol Use Disorders and Associated Disabilities Interview Schedule-Version for DSM-IV (AUDADIS-IV). Bethesda, MD: National Institute on Alcohol Abuse and Alcoholism; 2001.
42. Grant BF, Dawson DA, Stinson FS, Chou PS, Kay W, Pickering R. The Alcohol Use Disorder and Associated Disabilities Schedule (AUDADIS): Reliability of alcohol consumption, tobacco use, family history of depression, and psychiatric diagnostic modules in a general population. *Drug Alcohol Depend.* 2003; 71:7–16. [PubMed: 12821201]
43. CDC. Cigarette Smoking among Adults - United States, 2006. Morbidity and Mortality World Report (MMWR). 2007; 56:1157–61.
44. APA. Diagnostic and statistical manual of mental disorders. 4. Washington, DC: American Psychiatric Association; 2002. text revision (DSM-IV-TR)
45. SUDAAN Software. computer program. Research Triangle Institute; Research Triangle Park: 2001.
46. Breslau N, Kilbey MM, Andreski P. Nicotine withdrawal symptoms and psychiatric disorders: Findings from an epidemiologic study of young adults. *Am J Psychiatry.* 1992; 149:464–9. [PubMed: 1554030]
47. Weinberger AH, Desai R, McKee SA. Nicotine withdrawal in U.S. smokers with current mood, anxiety, alcohol, and substance use disorders. *Drug Alcohol Depend.* 2010; 108:7–12. [PubMed: 20006451]
48. Weinberger AH, George TP, McKee SA. Differences in smoking expectancies in smokers with and without a history of major depressive disorder. *Addict Behav.* 2011; 36:434–7. [PubMed: 21239119]
49. Currie SR, Hodgins DC, el-Guebaly N, Campbell W. Influence of depression and gender on smoking expectancies and temptations in alcoholics in early recovery. *J Subst Abuse.* 2001; 13:443–58. [PubMed: 11775075]
50. Pomerleau OF, Pomerleau CS, Mehringer AM, Snedecor SM, Ninowski R, Sen A. Nicotine dependence, depression, and gender: Characterizing phenotypes based on withdrawal discomfort, response to smoking, and ability to abstain. *Nicotine Tob Res.* 2005; 7:91–102. [PubMed: 15804681]
51. Weinberger AH, McKee SA, George TP. Smoking cue reactivity in adult smokers with and without depression: A pilot study. *Am J Addict.* 2011; 36:434–7.
52. Spring B, Pingitore R, McChargue DE. Reward value of cigarette smoking for comparably heavy smoking schizophrenic, depressed, and nonpatient smokers. *Am J Psychiatry.* 2003; 160:316–22. [PubMed: 12562579]

53. Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: Results from the national comorbidity survey. *Arch Gen Psychiatry*. 1994; 51:8–19. [PubMed: 8279933]
54. Kessler RC, McGonagle KA, Swartz M, Blazer DG, Nelson CB. Sex and depression in the National Comorbidity Survey. I: Lifetime prevalence, chronicity and recurrence. *J Affect Disord*. 1993; 29:85–96. [PubMed: 8300981]
55. Ceribelli A, Pino MS, Cecere FL. Gender differences: Implications for clinical trials and practice. *J Thorac Oncol*. 2007; 2:S15–S8. [PubMed: 17457223]
56. Kiyohara C, Ohno Y. Sex differences in lung cancer susceptibility: A review. *Gen Med*. 2010; 7:381–401.
57. USDHHS. Women and smoking: A report of the Surgeon General. Washington, DC: YS Department of Health and Human Services, Centers for Disease Prevention and Control, National Center for Chronic Disease Prevention and Promotion, Office on Smoking and Health; 2001.
58. Perkins KA, Scott J. Sex differences in long-term smoking cessation rates due to nicotine patch. *Nicotine Tob Res*. 2008; 10:1245–51. [PubMed: 18629735]
59. Wetter DW, Kenford SL, Smith SS, Fiore MC, Jorenby DE, Baker TB. Gender differences in smoking cessation. *J Consult Clin Psychol*. 1999; 67:555–62. [PubMed: 10450626]

Table 1

Wave 1 Demographics for the Full Sample and by Wave 1 Smoking Status.

Wave 1 Demographics	Total Sample (n=11,973)	Wave 1 Current Daily Smokers (n=6,545)	Wave 1 Former Daily Smokers (n=5,428)	p-value
Gender				
Male	54.2%	52.7%	56.1%	0.0036
Female	45.8%	47.3%	43.9%	
Age				
18–29	15.6	25.0	4.1	<0.0001
30–44	27.4	34.9	18.3	
45+	57.0	40.1	77.5	
Race				
Non-Hispanic, White	79.1	76.3	82.6	<0.0001
Non-Hispanic, Black	8.7	10.3	7.0	
Non-Hispanic, Other	5.1	5.7	4.4	
Hispanic	7.1	7.8	6.1	
Marital Status				
Married	64.2	55.5	74.8	<0.0001
Not Married	35.8	44.5	25.2	
Education				
Less than HS	17.9	19.7	15.6	<0.0001
Graduated HS	33.6	36.8	29.6	
Attended/Completed College	48.5	43.4	54.8	

Key: HS, high school

Table 2

The Main and Gender-Specific Effects of Major Depressive Disorder Diagnosis on Changes in Smoking for Wave 1 Current Daily Smokers.

	Wave 1 Current Daily Smokers			Wave 1 Current Daily Smokers with Current Nicotine Dependence		
	% Stable Current Smokers (n= 5,546)	% Quitters (n=999)	OR	95% CI	p-value	
Main Effects of MDD						
Current MDD	88.4	11.6	1.38	1.03, 1.85	0.05	10.7
No Current MDD	84.7	15.3	1.00	--		13.6
Gender * MDD Interaction						
Women						
Current MDD	88.7	11.3	1.45	1.04, 2.04	0.03	10.7
No Current MDD	84.4	15.6	1.00	--		14.5
Men						
Current MDD	87.8	12.2	1.28	0.78, 2.08	0.32	10.7
No Current MDD	84.9	15.1	1.00	--		12.7
Interaction OR (Women vs. Men)			0.88	0.50, 1.53	0.64	0.85
Main Effects of MDD						
Lifetime MDD	88.7	11.3	1.48	1.18, 1.85	0.0008	10.6
No Lifetime MDD	84.2	15.8	1.00	--		14.1
Gender * MDD Interaction						
Women						
Lifetime MDD	88.9	11.1	1.57	1.17, 2.11	0.003	10.6
No Lifetime MDD	83.6	16.4	1.00	--		15.5
Men						
Lifetime MDD	88.4	11.6	1.38	0.95, 2.01	0.09	10.7
No Lifetime MDD	84.6	15.4	1.00	--		12.9
Interaction OR (Women vs. Men)			0.88	0.54, 1.44	0.60	0.81

Key: OR, odds ratio; CI, confidence interval; MDD, Major Depressive Disorder

Table 3

The Main and Gender-Specific Effects of Major Depressive Disorder Diagnosis on Changes in Smoking for Wave 1 Former Daily Smokers.

	Wave 1 Former Daily Smokers			Wave 1 Former Daily Smokers with Lifetime Nicotine Dependence		
	% Stable Former Smokers (n=5,189)	% Relapsers (n=239)	OR	95% CI	p-value	
Main Effects of MDD						
Current MDD	90.8	9.2	0.44	0.26, 0.76	0.004	
No Current MDD	95.2	4.8	1.00	--	--	0.04
Gender * MDD Interaction						
Women						
Current MDD	90.8	9.2	0.50	0.27, 0.92	0.03	0.13
No Current MDD	95.2	4.8	1.00	--	--	--
Men						
Current MDD	92.6	7.4	0.44	0.15, 1.25	0.12	0.19
No Current MDD	96.6	3.4	1.00	--	--	--
Interaction OR (Women vs. Men)			0.88	0.26, 2.92	0.83	0.76
Main Effects of MDD						
Lifetime MDD	94.1	5.9	0.65	0.41, 1.03	<i>0.06</i>	0.42
No Lifetime MDD	96.1	3.9	1.00	--	--	--
Gender * MDD Interaction						
Women						
Lifetime MDD	94.2	5.8	0.85	0.50, 1.46	0.56	0.10
No Lifetime MDD	95.0	5.0	1.00	--	--	--
Men						
Lifetime MDD	93.8	6.2	0.51	0.24, 1.08	<i>0.08</i>	0.10
No Lifetime MDD	96.8	3.3	1.00	--	--	--
Interaction OR (Women vs. Men)			0.60	0.25, 1.44	0.25	0.09

Key: OR, odds ratio; CI, confidence interval; MDD, Major Depressive Disorder