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Author manuscript

*Drug Alcohol Depend.* Author manuscript; available in PMC 2017 August 01.

Published in final edited form as:

*Drug Alcohol Depend.* 2016 August 1; 165: 253–259. doi:10.1016/j.drugalcdep.2016.06.013.

## Gender differences in self-reported withdrawal symptoms and reducing or quitting smoking three years later: A prospective, longitudinal examination of U.S. adults

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### Abstract

**Background**—Little is known about gender differences in withdrawal symptoms among smokers in the community. This study used longitudinal epidemiologic data to examine gender differences in current smokers' report of withdrawal symptoms during past quit attempts and the relationship between withdrawal symptoms and the odds of reducing or quitting smoking three years later.

**Methods**—Data were drawn from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; Wave 1, 2001–2001, n=43,093; Wave 2, 2004–2005, n=34,653). Analyses were conducted on respondents who reported current daily cigarette smoking at Wave 1 (n=6,911). Withdrawal symptoms during past quit attempts were assessed at Wave 1. Current smoking status was assessed at Wave 2.

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#### Contributors

Dr. Weinberger conceived the study and wrote the first draft of the manuscript. Mr. Platt undertook the statistical analyses. Dr. Shuter and Goodwin contributed to the writing of the manuscript. All authors contributed to and approved the final manuscript.

#### Conflicts of Interest

Dr. Weinberger, Mr. Platt, Dr. Shuter, and Dr. Goodwin have no conflicts of interest to report.

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**Results**—Wave 1 current smoking women, compared to men, were more likely to endorse any withdrawal symptoms, withdrawal-related discomfort, and withdrawal-related relapse ( $p < 0.0001$ ). Women endorsed a greater number of withdrawal symptoms than men ( $M = 2.37$ ,  $SE = 0.05$  versus  $M = 1.78$ ,  $SE = 0.04$ ;  $p < 0.0001$ ). The odds of reducing and quitting smoking were significantly lower for respondents who reported any Wave 1 withdrawal symptoms, withdrawal-related discomfort, and withdrawal-related relapse. These relationships did not differ for women versus men. Among men, the odds of reducing smoking at Wave 2 decreased significantly with each cumulative withdrawal symptom compared to women ( $\beta$  interaction = 0.87;  $p = 0.01$ ).

**Conclusions**—Women were more likely to report withdrawal while the relationship between withdrawal symptoms and decreased likelihood of reducing smoking was stronger in men. Identifying gender differences in withdrawal can help develop strategies to help reduce withdrawal for both men and women.

### Keywords

smoking; withdrawal; gender; epidemiology

## 1. INTRODUCTION

Most smoking quit attempts end in relapse to cigarette use within the first week (Piasecki, 2006) when withdrawal symptoms are the strongest (Piasecki et al., 2002). A number of laboratory and clinical studies have reported that women experience both a greater number and a wider variety of withdrawal symptoms than men following either a quit attempt in clinical studies or a period of smoking abstinence in laboratory studies (Jorenby et al., 1995; Leventhal et al., 2007; Pang and Leventhal, 2013; Piasecki et al., 1998, 2003; Wetter et al., 1999). For example, in a laboratory study of 203 smokers (Leventhal et al., 2007), women reported greater increases in negative affect, withdrawal-related distress, and the urge to smoke to relieve withdrawal-related distress after 12 hours of smoking abstinence. In another laboratory study, female smokers reported higher levels of overall negative affect and anxiety during abstinence than male smokers after 16 hours of smoking abstinence (Pang and Leventhal, 2013). In a placebo-controlled clinical trial of transdermal nicotine patch and/or bupropion for smoking cessation, women displayed more day-to-day variability in withdrawal symptoms (Piasecki et al., 2003). Together, clinical and laboratory data suggest that men and women differ in their report of withdrawal symptoms. As the severity of withdrawal symptoms are strongly linked with smoking lapse after quit attempts (Piasecki, 2006), a better understanding of the experience of withdrawal for men and women, and the implications of gender differences in withdrawal for smoking abstinence, is warranted.

While past studies have examined gender differences in withdrawal within specific geographic communities and groups of smokers (e.g., treatment seeking smokers), little is known about gender differences in self-reported withdrawal symptoms using epidemiologic data that is more generalizable to the general population and that assesses smoking behavior over a lengthy period of time. Breslau and colleagues (1992) surveyed 1,007 young adults (ages 21–30) who were members of a health maintenance organization in the metro Detroit area of the U.S. state of Michigan. Among the 241 participants who reported they had

unsuccessfully attempted to quit or cut down on their smoking, there were no differences in the average number of withdrawal symptoms (range 0–12) by gender (men  $M=3.93$ ,  $SD=2.12$ , women  $M=4.39$ ,  $SD=2.23$ ,  $p=n.s.$ ). It is not yet known if there are gender differences in the report of withdrawal symptoms or withdrawal-related experiences (e.g., returning to smoking during a quit attempt to relieve withdrawal symptoms) in more recent samples that are nationally representative of the full U.S. adult population. In addition, it has not yet been examined whether gender differences exist in the association between self-reported withdrawal symptoms and continued smoking versus reducing or quitting smoking over a number of years.

The current study uses longitudinal epidemiologic data from the U.S. adult population to examine gender differences in withdrawal symptoms and the relationship between withdrawal symptoms reported by current daily smokers and the likelihood of reducing or quitting smoking three years later. The first aim of the study was to examine withdrawal symptoms for current daily smoking women versus men. Based on the laboratory and clinical research cited above (e.g., Leventhal et al., 2007), it was expected that current daily smoking women would be more likely to report withdrawal symptoms, withdrawal-related distress, and withdrawal-related relapse to smoking during past quit attempts than current daily smoking men. The second aim was to examine the relationship between self-report withdrawal symptoms during past quit attempts and reducing or quitting smoking three years later. Based on the relationship between withdrawal and smoking relapse (e.g., Piasecki et al., 2006), it was expected that the endorsement of withdrawal symptoms, withdrawal-related distress, and withdrawal-related relapse would be associated with a decreased likelihood of reducing and quitting smoking. The third aim was to explore whether gender differences existed in the relationship between self-reported withdrawal symptoms during past quit attempts and reducing or quitting smoking three years later.

## 2. METHODS

### 2.1. Data Source and Study Population

This study analyzed data from the National Institute on Alcohol Abuse and Alcoholism's National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; Wave 1, 2001–2002,  $n=43,093$ ; Wave 2, 2004–2005,  $n=34,653$ ). Participants were non-institutionalized U.S. civilian adults (ages 18 and older) in all 50 states and the District of Columbia. African-Americans, Hispanics, and young adults (ages 18–24) were oversampled. The response rate for the Wave 1 assessment was 81% and 86% of the eligible Wave 1 participants completed the Wave 2 assessment. Details of the NESARC, including the procedures related to data collection and weighting, have been described in past publications (Grant and Kaplan, 2005; Grant et al., 2003). The sample for the current analyses included participants who reported current daily cigarette smoking at the Wave 1 interview ( $n=6,911$ ).

### 2.2. Material and Methods

**2.2.1. Smoking status**—Smoking behavior was assessed at Wave 1 and Wave 2 using the Alcohol Use Disorders and Associated Disabilities Interview Schedule-DSM-IV (AUDADIS-IV; Grant et al., 2001, 2003). Individuals were classified as Wave 1 current daily

smokers, and included in the analytic sample, if they reported smoking cigarettes every day (i.e., seven days per week) during the past year at the Wave 1 assessment. Smoking status at Wave 2 was categorized into three mutually exclusive groups: current daily smokers (reported smoking every day in the past year at the Wave 2 assessment), current non-daily smokers (reported smoking some days in the past year at the Wave 2 assessment; range: 6 days/week – once a month or less), and current non-smokers (reported no smoking in the past year at the Wave 2 assessment).

**2.2.2. Withdrawal symptoms**—During the Wave 1 interview, participants were asked if they had experienced each of eight symptoms when attempting to quit smoking during the past 12 months: depression, sleep problems, difficulty in concentrating, increased appetite, irritability or frustration, anxiety or nervousness, heart beating more slowly, and restlessness. A response of Yes to each item was coded as a “1” while a response of No to each item was coded as a “0.” The cumulative number of symptoms ranged from 0–8. Participants were considered to have endorsed “any withdrawal symptoms” if they reported at least 1 withdrawal symptom.

Participants were also asked to report whether withdrawal symptoms experienced over the past 12 months caused discomfort, distress, or impairment (“withdrawal-related discomfort”, Yes/No) and whether they used cigarettes to avoid withdrawal symptoms (“withdrawal-related relapse”, Yes/No).

**2.2.3. Demographics**—Wave 1 demographic information was categorized based on previous work (Grant et al., 2004) and included gender (male, female), 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 or Living As Married, Not Married).

**2.2.4. Psychiatric and substance use disorders**—At Wave 1, the AUDADIS-IV assessed mood disorders (major depressive disorder, dysthymia, manic disorder, hypomanic disorder), anxiety disorders (panic disorder with or without agoraphobia, agoraphobia, social phobia, specific phobia, generalized anxiety disorder), alcohol use disorders (abuse and dependence), and substance use disorders (nicotine dependence; abuse and dependence of 10 classes of drugs: cannabis, sedatives, tranquilizers, opiates, heroin, stimulants, cocaine, hallucinogens, inhalants, solvents). Participants were classified into one of two mutually exclusive responses for each disorder category: (1) Lifetime Diagnosis (met criteria for a diagnosis at any point during the lifetime) or (2) Never Diagnosis (no lifetime diagnosis of the disorder).

### 2.3. Statistical Analyses

All tests were completed in STATA using weighted analyses (StataCorp, 2011) to account for residual differences between the sample and the population profile according to the 2000 United States Population Census, as well as to account for nonresponse and sample attrition. The weighted Wave 2 data represent the same baseline population as represented in Wave 1.

Sample frequencies of demographic, psychiatric, and substance use covariates were calculated to compare sample differences between males and females. Also, the proportion of withdrawal symptoms, the mean number of symptoms, and smoking status at Wave 2 follow-up were compared between males and females. Standard errors were computed using Taylor series linearization and bivariate frequencies were tested using Rao Scott chi-squared tests to account for complex survey design. Statistical tests were two-tailed and differences were considered significant when  $p < 0.05$ .

A series of multinomial logistic regression models were run to estimate the odds of reducing smoking or quitting smoking (versus continued smoking) at Wave 2 for four withdrawal variables assessed at Wave 1: (1) the report of any withdrawal symptom, (2) the cumulative number of withdrawal symptoms, (3) the report of withdrawal-related discomfort, and (4) the report of withdrawal-related relapse. Participants were considered to have reduced their smoking if they reported daily smoking at Wave 1 and non-daily smoking at Wave 2 while participants were considered to have quit smoking if they reported daily smoking at Wave 1 and no smoking at Wave 2. First, unadjusted odds ratios (ORs) were calculated for each withdrawal variable. Then a series of models were run to examine these associations with adjustment for potential confounders. The first model adjusted for demographics and smoking quantity at Wave 1 while a second model adjusted for demographics, smoking quantity, substance use disorders, and psychiatric disorders. A third set of models were run for the withdrawal-related discomfort and withdrawal-related relapse that added an adjustment for the mean-centered reported number of withdrawal symptoms as a measure of withdrawal severity. For each of the four withdrawal variables, a final model tested for statistical interaction between the withdrawal variable and gender. If the interaction parameter estimate was significant, two sets of models were run, one without any adjustments and the second adjusting for all covariates from the third model, and stratified by gender. Only the adjusted model results were reported for the stratified models. An odds ratio (OR) and 95% confidence interval (CI) was calculated for each model and were considered to be statistically significant if the 95% CI did not include 1.0.

### 3. RESULTS

#### 3.1. Sample characteristics (Table 1)

See Table 1 for demographics and prevalences of psychiatric and substance use disorders for the full analytic sample and by gender. Just over half of the sample (55.4%) was male and the majority of the sample identified as Caucasian. Though statistically significant due to the large sample, demographic frequencies were generally similar between men and women with the largest gender difference seen for income. Women were significantly more likely to endorse mood and anxiety disorders while men were more likely to report alcohol and substance use disorders.

#### 3.2. Self-reported withdrawal symptoms at Wave 1 (Aim 1; Table 2)

At Wave 1, 69.4% of current daily smoking women and 61.6% of current daily smoking men endorsed at least one withdrawal symptom. Women reported a higher average number of symptoms than men (Women  $M=2.6$ ,  $SE=0.06$ ; Men  $M=2.0$ ,  $SE=0.05$ ;  $p < 0.0001$ ).

Current daily smoking women were significantly more likely to endorse seven out of the eight withdrawal symptoms (with the exception of slower heartbeat; see Table 2). Current daily smoking women were also significantly more likely than current daily smoking men to report experiencing withdrawal-related discomfort and withdrawal-related relapse (see Table 2).

### **3.3. Association between self-reported withdrawal symptoms and the likelihood of reducing or quitting smoking three years later (Aim 2; Table 3)**

At Wave 2, 16.0% of Wave 1 daily smokers reported that they were not currently smoking (men=17.1%, women=14.7%) while 5.3% of Wave 1 daily smokers reported reducing their smoking frequency to non-daily use (men=5.4%; women=5.1%). The unadjusted odds of reducing and quitting smoking at Wave 2 were significantly lower among respondents who at Wave 1 reported (1) any withdrawal symptoms, (2) a greater number of withdrawal symptoms, and (3) withdrawal-related relapse (see Table 3). The unadjusted odds of quitting smoking were also significantly lower among respondents who reported withdrawal-related discomfort. After adjustment for demographics and smoking quantity, the associations were significant in the models for all withdrawal variables including the odds of reducing smoking and withdrawal-related discomfort. After additional adjustment for substance use and psychiatric disorders, the associations between both cumulative withdrawal symptoms and withdrawal-related relapse and smoking cessation outcome remained significant although the relationship of withdrawal-related relapse and smoking cessation outcome relationship was then no longer statistically significant after an additional adjustment for number of withdrawal symptoms. In the fully-adjusted model, the odds of quitting smoking at Wave 2 decreased by 3% for each additional withdrawal symptom reported by respondents at Wave 1 (95% CI= 0.95–0.99).

### **3.4. Gender differences in the association between self-reported withdrawal symptoms and the likelihood of reducing or quitting smoking three years later (Aim 3; Table 3)**

The only withdrawal variable for which the statistical interaction of gender was significant was for cumulative Wave 1 withdrawal symptoms. There was a stronger relationship between the odds of reducing smoking at Wave 2 and greater cumulative withdrawal symptoms at Wave 1 for men compared to women ( $\beta$  interaction= 0.87;  $p=0.01$ ). With each additional reported withdrawal symptom, men who were current smokers at Wave 1 were 6% less likely to have reduced smoking at Wave 2 (95% CI=0.90–0.98). The relationship was not significant for women. The unadjusted stratified models were slightly further from the null association and became attenuated after adjusting for model confounders. Further, there was no interaction between gender and any withdrawal symptom ( $\beta=0.05$ ,  $p=0.75$ ;  $\beta=-0.007$ ,  $p=0.93$ ), withdrawal-related discomfort ( $\beta=0.72$ ,  $p=0.17$ ;  $\beta=0.15$ ,  $p=0.44$ ) or withdrawal-related relapse ( $\beta=0.34$ ,  $p=0.22$ ;  $\beta=0.17$ ,  $p=0.22$ ) in reducing or quitting smoking, respectively.

## **4. DISCUSSION**

The current study is the first to use longitudinal data from a representative sample of U.S. adults to examine gender differences in self-reported withdrawal symptoms during past quit

attempts and in the association of self-reported withdrawal and quitting or reducing smoking. As expected, women were more likely than men to report experiencing withdrawal symptoms, a greater number of withdrawal symptoms, withdrawal-related discomfort, and withdrawal-related relapse. Also as expected, the endorsement of any withdrawal symptoms, cumulative number of withdrawal symptoms, withdrawal-related distress, and withdrawal-related relapse were associated with a decreased likelihood of both reducing smoking and quitting smoking three years later among both men and women. With regard to gender differences in the relationship between withdrawal and reducing or quitting smoking, men and women did not differ in the relationship between withdrawal and reducing or quitting smoking for most withdrawal symptoms. Men reported a stronger relationship between number of withdrawal symptoms and reduced likelihood of reducing smoking with compared to women.

The finding that women were more likely than men to report withdrawal symptoms in a nationally representative sample of U.S. adults is consistent with previous clinical and laboratory studies that were more selected and geographically constrained (e.g., Leventhal et al., 2007; Pang and Leventhal, 2013). While it is possible that women experience greater absolute withdrawal symptoms than men, it is also possible that women are more likely to report or expect (vs. experience) withdrawal symptoms than men. For example, there is evidence that men underreport withdrawal symptoms when assessed retrospectively in contrast to prospective assessment while women report the same number of symptoms retrospectively and prospectively (Pomerleau et al., 1994).

Both the experience and the expectation of more withdrawal symptoms may have an impact on quit behavior. Adults smokers who reported expecting greater risks of quitting smoking (e.g., cravings, depression) then reported greater levels of cravings, withdrawal symptoms, and depressive symptoms during a week of smoking abstinence compared to adults who expected fewer risks of quitting (Weinberger et al., 2008). Greater perceived risks of quitting have also been found to be associated with decreased motivation to quit and less success at quitting (McKee et al., 2005; Toll et al., 2008). With regard to withdrawal symptoms, a greater expectation that withdrawal symptoms will occur during smoking abstinence is associated with the report of greater withdrawal symptoms (Hendricks and Leventhal, 2013). Further, women are more likely than men to expect to have withdrawal symptoms during quit attempts and report lower motivation to quit smoking with withdrawal expectancies mediating the relationship between gender and motivation to quit (Hendricks et al., 2014). Based on the association between expected withdrawal and experienced withdrawal, it may be useful for those who work with smokers, especially female smokers, to identify expectancies about withdrawal prior to quit attempts and include these beliefs as part of pre-quit counseling (e.g., identifying, examining, and modifying these beliefs).

Withdrawal symptoms, withdrawal-related distress, and withdrawal-related relapse were all significantly associated with decreased odds of reducing or quitting smoking three years later for both women and men. While many behavioral and pharmacological treatments (Fiore et al., 2008) focus on reducing withdrawal symptoms, there may be benefits to working with both male and female treatment-seeking smokers on reducing distress related to withdrawal symptoms. Distress tolerance has been associated with smoking lapse (Brown

et al., 2005, 2009; Rohsenow et al., 2015) and decreasing distress tolerance, especially tolerance specifically related to withdrawal symptoms, may be a useful aim to incorporate into treatment in order to improve quit attempt outcomes (Brown et al., 2013). Prophylactic emphasis on avoiding the use of cigarettes to cope with withdrawal symptoms may also help to improve quit outcomes.

In the current study, a significant interaction between gender and cumulative withdrawal symptoms emerged related to smoking reduction. Even though women reported a greater number of withdrawal symptoms than men, the relationship between number of withdrawal symptoms and reducing smoking was stronger for men compared to women. As men may underreport withdrawal symptoms when asked to recall them retrospectively (Pomerleau et al., 1994), the relationship between cumulative withdrawal symptoms and reducing smoking may even be an underestimate of the impact of withdrawal symptoms for men. Future research should examine whether male smokers benefit from education about withdrawal symptoms in order to increase their ability to identify withdrawal symptoms that have impacted them in the past and whether this information can be used in treatment to improve quit outcomes.

While the decreased likelihood of reducing or quitting smoking was significant for all withdrawal variables after adjusting for demographics, several aspects of withdrawal were no longer significant after adjusting for comorbid psychiatric and substance use disorders. Psychiatric and substance use disorders have been associated with greater withdrawal symptoms (e.g., Pomerleau et al., 2005; Smith et al., 2014a; Weinberger et al., 2010, 2009) and lower likelihoods of quitting smoking (e.g., Smith et al., 2014b). The relationship between higher numbers of withdrawal symptoms and reporting relapse to smoking to relieve withdrawal symptoms remained significant after accounting for these disorders suggesting that alcohol and substance use disorders do not fully account for the relationship between withdrawal and quitting.

While there are strengths associated with the use of epidemiologic data (e.g., large sample size, longitudinal data), there are also limitations. First, research would be needed to confirm that these results generalize to persons not included in the NESARC study (e.g., adolescents, adults in countries other than the U.S.). A second potential limitation related to the NESARC data is that of loss to follow-up between Wave 1 and Wave 2. In a sensitivity analysis of our analytic sample (data not shown), non-Hispanic white respondents were significantly more likely to have completed the Wave 2 follow-up interview than other race/ethnicity groups ( $p=0.003$ ). There were no differences in follow-up rates by gender, age, marital status, education, or income. Though this difference was statistically significant, Wave 2 data were weighted to represent the same baseline population as represented in Wave 1. Therefore, it does not appear that the Wave 2 sample represents a meaningfully different population. Nevertheless, these differences could affect the external validity of our findings by impacting the representative of the U.S. population among the sample of NESARC participants who completed both waves of data collection.

Third, the retrospective recall of withdrawal symptoms may be subject to recall bias (Hughes, 2007). For example, smokers are more likely to remember and report quit attempts



that occurred more recently compared to attempts that occurred further in the past (Borland, 2012). Longitudinal data may reduce recall bias compared to cross-sectional data due to a shorter recall period required (Elliot et al., 2008; Morris et al., 2006); however, it must be noted that, even with the longitudinal data used in this study, participants were asked to report on withdrawal symptoms that may have occurred up to 12 months before the interview. Fourth, data were limited to the information collected at the two assessments. There is a lack of information about number of quit attempts, the timing of changes in smoking, reasons for quitting (including gender-specific reasons for quitting such as pregnancy and quitting due to environments where smoking is not allowed such as hospitalization or incarceration), and the context of quitting or relapse at time points between the two assessments. While cravings are an important part of withdrawal (Piper, 2015), they were not assessed by the AUDADIS-IV and therefore could not be examined as part of the analyses. Future research should examine gender differences in the relationship between withdrawal and abstinence in more detail including cravings, the impact of pharmacological and behavioral treatments on outcomes by gender, and the association of withdrawal and quitting over shorter periods of time. Further, while the analyses were adjusted for mood disorders, premenstrual dysphoric disorder (PMDD) was not assessed by the AUDADIS-IV. Withdrawal symptoms overlap with premenstrual symptoms (Allen et al., 2000) and changes in ovarian hormones are associated with differences in a range of smoking behaviors including withdrawal (see Weinberger et al., 2015 for a review). Additional research is needed to understand the role of PMDD in the relationship between withdrawal symptoms and smoking cessation for women.

Further, it is not known whether the respondents who reduced their smoking were doing so with the intention of quitting smoking completely at a later time, as a consequence of a quit attempt that did not achieve full abstinence, or for other reasons. Reviews and meta-analyses have shown that interventions to reduce smoking improve abstinence outcomes (Asfar et al., 2011; Begh et al., 2015; Wu et al., 2015) and have similar outcome to interventions that ask smokers to quit abruptly (Lindson-Hawley et al., 2012). While there is mixed evidence regarding whether smoking reduction decreases the harmful health consequences of smoking such as cancer and respiratory disease (Begh et al., 2015; Gerber et al., 2012; USDHHS, 2014), quitting smoking has clear benefits for reducing mortality and morbidity (Carter et al., 2015; Thun et al., 2013; USDHHS, 2014).

Withdrawal symptoms are a critical factor in the maintenance of smoking behavior (Piper, 2015). The current results suggest that withdrawal symptoms, withdrawal-related distress, and withdrawal-related discomfort are all associated with decreased likelihoods of reducing and quitting smoking for men and women. Men and women in this study displayed similarities regarding the relationship between withdrawal and smoking abstinence after three years; however, there were also a number of areas in which men and women differed. These differences include the reporting of more withdrawal symptoms by women and the stronger relationship between withdrawal symptom number and smoking reduction among men. While it is important to address withdrawal in both men and women who want to quit smoking, there may be additional benefits to understanding which aspects of withdrawal differ for men and women so that strategies can be developed that provide the best quit outcomes for men and women.

## Acknowledgments

### Role of Funding Source

Funding for this study was provided by the National Institutes of Health grant R01-DA20892 (to Dr. Goodwin). The NIH had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

## References

- Allen SS, Hatsukami D, Christianson D, Brown S. Effects of transdermal nicotine on craving, withdrawal and premenstrual symptomatology in short-term smoking abstinence during different phases of the menstrual cycle. *Nicotine Tob Res.* 2000; 2:231–241. [PubMed: 11082823]
- Asfar T, Ebbert JO, Klesges RC, Relyea GE. Do smoking reduction interventions promote cessation in smokers not ready to quit? *Addict Behav.* 2011; 36:764–768. [PubMed: 21420791]
- Begh R, Lindson-Hawley N, Aveyard P. Does reduced smoking if you can't stop make any difference? *BMC Med.* 2015; 13:257. [PubMed: 26456865]
- Borland R, Partos TR, Yong HH, Cummings KM, Hyland A. How much unsuccessful quitting activity is going on among adult smokers? Data from the International Tobacco Control 4-Country cohort survey. *Addiction.* 2012; 107:673–682. [PubMed: 21992709]
- Breslau N, Kilbey MM, Andreski P. Nicotine withdrawal symptoms and psychiatric disorders: findings from an epidemiologic study of young adults. *Am J Psychiatry.* 1992; 149:464–469. [PubMed: 1554030]
- Brown RA, Lejuez CW, Kahler CW, Strong DR, Zvolensky MJ. Distress tolerance and early smoking lapse. *Clin Psychol Rev.* 2005; 25:713–733. [PubMed: 16023275]
- Brown RA, Lejuez CW, Strong DR, Kahler CW, Zvolensky MJ, Carpenter LL, Niaura R, Price LH. A prospective examination of distress tolerance and early smoking lapse in adult self-quitters. *Nicotine Tob Res.* 2009; 11:493–502. [PubMed: 19372572]
- Brown RA, Palm Reed KM, Litvin Bloom E, Minami H, Strong DR, Lejuez CW, Kahler CW, Zvolensky MJ, Gifford EV, Hayes SC. Development and preliminary randomized controlled trial of a distress tolerance treatment for smokers with a history of early lapse. *Nicotine Tob Res.* 2013; 15:2005–2015. [PubMed: 23884317]
- Carter BD, Abnet CC, Feskanich D, Freedman ND, Hartge P, Lewis CE, Ockene JK, Prentice RL, Speizer FE, Thun MJ, Jacobs EJ. Smoking and mortality—beyond established causes. *N Engl J Med.* 2015; 372:631–640. [PubMed: 25671255]
- Elliot, J.; Holland, J.; Thomson, R. Longitudinal and panel studies. In: Alasuutari, P.; Bickman, L.; Brannen, J., editors. *The SAGE Handbook of Social Research Methods.* SAGE Publications Ltd; Thousand Oaks, CA: 2008. p. 228-248.
- Fiore, MC.; Jaén, CR.; Baker, TB.; Bailey, WC.; Benowitz, NL.; Curry, SJ., et al. *Treating Tobacco Use and Dependence: 2008 Update.* U.S. Department of Health and Human Services; Rockville, MD: 2008.
- Gerber Y, Myers V, Goldbourt U. Smoking reduction at midlife and lifetime mortality risk in men: a prospective cohort study. *Am J Epidemiol.* 2012; 175:1006–1012. [PubMed: 22306566]
- Grant, BF.; Dawson, DA.; Hasin, DS. *The Alcohol Use Disorders and Associated Disabilities Interview Schedule-Version for DSM-IV (AUDADIS-IV).* National Institute on Alcohol Abuse and Alcoholism; Bethesda, MD: 2001.
- 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]
- 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]
- Grant, BF.; Kaplan, KD. *Source And Accuracy Statement: The Wave 2 National Epidemiologic Survey On Alcohol And Related Conditions (NESARC).* National Institute On Alcohol Abuse and Alcoholism; Rockville, MD: 2005.

- 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). National Institute on Alcohol Abuse and Alcoholism; Bethesda, MD: 2003.
- Hendricks PS, Leventhal AM. Abstinence-related expectancies predict smoking withdrawal effects: Implications for possible causal mechanisms. *Psychopharmacology (Berl)*. 2013; 230:363–373. [PubMed: 23812761]
- Hendricks PS, Westmaas JL, Ta Park VM, Thorne CB, Wood SB, Baker MR, Lawler RM, Webb Hooper M, Delucchi KL, Hall SM. Smoking abstinence-related expectancies among American Indians, African Americans, and women: potential mechanisms of tobacco-related disparities. *Psychol Addict Behav*. 2014; 28:193–205. [PubMed: 23528192]
- Hughes JR. Measurement of the effects of abstinence from tobacco: a qualitative review. *Psychol Addict Behav*. 2007; 21:127–137. [PubMed: 17563132]
- Jorenby DE, Smith SS, Fiore MC, Hurt RD, Offord KP, Croghan IT, Hays JT, Lewis SF, Baker TB. Varying nicotine patch dose and type of smoking cessation counseling. *JAMA*. 1995; 274:1347–1352. [PubMed: 7563558]
- Leventhal AM, Walters AJ, Boyd S, Moolchan ET, Lerman C, Pickworth WB. Gender differences in acute tobacco withdrawal: effects on subjective, cognitive, and physiological measures. *Exp Clin Psychopharmacol*. 2007; 15:21–36. [PubMed: 17295582]
- Lindson-Hawley N, Aveyard P, Hughes JR. Reduction versus abrupt cessation in smokers who want to quit. *Cochrane Database Syst Rev*. 2012; 11:CD008033. [PubMed: 23152252]
- 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; 30:423–425. [PubMed: 15718060]
- Morris, AS.; Robinson, LR.; Eisenberg, N. Applying a multimethod perspective to the study of developmental psychology. In: Eid, M.; Diener, E., editors. *Handbook Of Multimethod Measurement In Psychology*. American Psychological Association; Washington, DC: 2006. p. 371-384.
- Pang RD, Leventhal AM. Sex differences in negative affect and lapse behavior during active tobacco abstinence: a laboratory study. *Exp Clin Psychopharmacol*. 2013; 21:269–276. [PubMed: 23834551]
- Piasecki TM. Relapse to smoking. *Clin Psychol Rev*. 2006; 26:196–215. [PubMed: 16352382]
- Piasecki TM, Fiore MC, Baker TB. Profiles in discouragement: two studies of variability in the time course of smoking withdrawal symptoms. *J Abnorm Psychol*. 1998; 107:238–251. [PubMed: 9604553]
- Piasecki TM, Jorenby DE, Smith SS, Fiore MC, Baker TB. Smoking withdrawal dynamics: II. Improved tests of withdrawal-relapse relations. *J Abnorm Psychol*. 2002; 112:14–27. [PubMed: 12653410]
- Piasecki TM, Jorenby DE, Smith SS, Fiore MC, Baker TB. Smoking withdrawal dynamics: III. Correlates of withdrawal heterogeneity. *Exp Clin Psychopharmacol*. 2003; 11:276–285. [PubMed: 14599261]
- Piper ME. Withdrawal: expanding a key addiction construct. *Nicotine Tob Res*. 2015; [epub ahead of print]. doi: 10.1093/ntr/ntv048
- Pomerleau CS, Tate JC, Lumley MA, Pomerleau OF. Gender differences in prospectively versus retrospectively assessed smoking withdrawal symptoms. *J Subst Abuse*. 1994; 6:433–440. [PubMed: 7780301]
- 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]
- Rohsenow DJ, Tidey JW, Kahler CW, Martin RA, Colby SM, Sirota AD. Intolerance for withdrawal discomfort and motivation predict voucher-based smoking treatment outcomes for smokers with substance use disorders. *Addict Behav*. 2015; 43:18–24. [PubMed: 25531536]
- Smith PH, Hornish GG, Giovino GA, Kozlowski LT. Cigarette smoking and mental illness: a study of nicotine withdrawal. *Am J Public Health*. 2014a; 104:e127–e133. [PubMed: 24328637]

- Smith PH, Mazure CM, McKee SA. Smoking and mental illness in the US population. *Tob Control*. 2014b; 23:e147–e153. [PubMed: 24727731]
- StataCorp. *Stata Statistical Software: Release 12*. StataCorp LP; College Station, TX: 2011.
- Thun MJ, Carter BD, Feskanich D, Freedman ND, Pretice R, Lopez AD, Hartge P, Gapstur SM. 50-year trends in smoking-related mortality in the United States. *N Engl J Med*. 2013; 368:351–364. [PubMed: 23343064]
- Toll BA, Salovey P, O'Malley SS, Mazure CM, Latimer A, McKee SA. Message framing for smoking cessation: the interaction of risk perceptions and gender. *Nicotine Tob Res*. 2008; 10:195–200. [PubMed: 18188760]
- USDHHS. *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General*. 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; Atlanta, GA: 2014.
- 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]
- Weinberger AH, Krishnan-Sarin S, Mazure CM, McKee SA. Relationship of perceived risks of smoking cessation to symptoms of withdrawal, craving, and depression during short-term smoking abstinence. *Addict Behav*. 2008; 33:960–963. [PubMed: 18384974]
- 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; 18:140–147. [PubMed: 19283566]
- Weinberger AH, Smith PH, Allen SS, Cosgrove KP, Saladin ME, Gray KM, Mazure CM, Wetherington CL, McKee SA. Systematic and meta-analytic review of research examining the impact of menstrual cycle phase and ovarian hormones on smoking and cessation. *Nicotine Tob Res*. 2015; 17:407–421. [PubMed: 25762750]
- Wetter DW, Fiore MC, Young TB, McClure JB, de Moor CA, Baker TB. Gender differences in response to nicotine replacement therapy: objective and subjective indexes of tobacco withdrawal. *Exp Clin Psychopharmacol*. 1999; 7:135–144. [PubMed: 10340153]
- Wetter DW, Kenford SL, Smith SS, Fiore MC, Jorenby DE, Baker TB. Gender differences in smoking cessation. *J Consult Clin Psychol*. 1999; 67:555–562. [PubMed: 10450626]
- Wu L, Sun S, He Y, Zeng J. Effect of smoking reduction therapy on smoking cessation for smokers without an intention to quit: an updated systematic review and meta-analysis of randomized controlled trials. *Int J Environ Res Public Health*. 2015; 12:10235–10253. [PubMed: 26308034]

**Highlights**

- We examined gender differences in self-reported withdrawal symptoms in U.S. adults.
- Women were more likely than men to endorse withdrawal symptoms.
- Women were more likely to endorse withdrawal-related discomfort and relapse.
- Men demonstrated a stronger relationship between withdrawal symptoms and lower likelihood of reducing smoking.

Demographic, smoking, psychiatric disorder, and substance use disorder covariates for the full sample of Wave 1 current daily smoking adults (n=6,911) and by gender.

**Table 1**

Variable	Total		Men (n=3,391)		Women (n=3,520)		p-value
	N <sup>a</sup>	(%) <sup>b</sup>	N <sup>a</sup>	(%) <sup>b</sup>	N <sup>a</sup>	(%) <sup>b</sup>	
<i>Age</i>							
18–29	1108	(18.1)	519	(17.8)	589	(18.6)	
30–44	2182	(31.7)	982	(30.1)	1200	(33.6)	<0.0001
45–64	2775	(39.2)	1472	(41.6)	1303	(36.1)	
65+	846	(11.0)	418	(10.5)	428	(11.6)	
<i>Race/Ethnicity</i>							
NH White	4508	(76.6)	2234	(75.4)	2274	(78.2)	
NH Black	1264	(10.1)	549	(9.7)	715	(10.5)	
NH Native American / AK Native	188	(3.5)	87	(3.3)	101	(3.7)	<0.0001
NH Asian/ Pacific Islander	114	(2.2)	71	(2.8)	43	(1.4)	
Hispanic	837	(7.6)	450	(8.8)	387	(6.2)	
<i>Marital status</i>							
Current	3312	(57.9)	1780	(60.6)	1532	(54.5)	
Widowed, separated, divorced	2151	(23.5)	860	(18.6)	1291	(29.5)	<0.0001
Never	1448	(18.7)	751	(20.8)	697	(16.0)	
<i>Personal income</i>							
\$0–19,999	3289	(46.1)	1235	(35.0)	2054	(59.8)	
\$20–34,999	1753	(25.2)	890	(26.2)	863	(24.0)	
\$35–69,999	1481	(22.4)	971	(29.5)	510	(13.5)	<0.0001
\$70,000+	388	(6.4)	295	(9.3)	93	(2.7)	
<i>Education</i>							
Less than HS degree	1365	(19.1)	695	(20.3)	670	(17.6)	
High school degree	3960	(58.4)	1914	(57.1)	2046	(59.9)	<0.0001
More than HS	1586	(22.6)	782	(22.7)	804	(22.4)	
<i>Psychiatric and substance use disorders – lifetime diagnosis</i>							
Mood disorders <sup>c</sup>	1065	(14.7)	379	(10.6)	686	(19.8)	<0.0001

Variable	Total		Men (n=3,391)		Women (n=3,520)		p-value
	N <sup>a</sup>	(%) <sup>b</sup>	N <sup>a</sup>	(%) <sup>b</sup>	N <sup>a</sup>	(%) <sup>b</sup>	
Anxiety disorders <sup>d</sup>	2317	(32.9)	970	(28.5)	1347	(38.3)	<0.0001
Alcohol use disorders <sup>e</sup>	1052	(16.1)	676	(20.2)	376	(10.9)	<0.0001
Substance use disorders <sup>f</sup>	337	(5.2)	202	(6.1)	135	(4.0)	<0.0001
<i>Wave 1 Smoking quantity</i>							
Number of daily cigarettes (mean, SE)	17.5	(0.2)	18.8	(0.26)	16.0	(0.21)	<0.0001

Note. NH, non-Hispanic; AK, Alaska; HS, high school; PY, past year; SE, standard error

<sup>a</sup>Unweighted N

<sup>b</sup>Weighted %

<sup>c</sup>A lifetime diagnosis of major depressive disorder, dysthymia, manic disorder, or hypomanic disorder

<sup>d</sup>A lifetime diagnosis of panic disorder with or without agoraphobia, agoraphobia, social phobia, specific phobia, or generalized anxiety disorder

<sup>e</sup>A lifetime diagnosis of alcohol abuse or dependence

<sup>f</sup>A lifetime diagnosis of nicotine dependence and/or abuse or dependence of at least one of 10 classes of drugs: cannabis, sedatives, tranquilizers, opiates, heroin, stimulants, cocaine, hallucinogens, inhalants, solvents

Self-reported withdrawal symptoms and withdrawal-related experiences for the full sample of Wave 1 current daily smoking adults (n=6,911) and by gender.

**Table 2**

	Total		Men (N=3,391)		Women (N=3,520)		
	N <sup>a</sup>	(%) <sup>b</sup>	N <sup>a</sup>	(%) <sup>b</sup>	N <sup>a</sup>	(%) <sup>b</sup>	p-value
<b>Past-Year Withdrawal Symptoms<sup>c</sup></b>							
Any withdrawal symptoms	4415	(65.1)	2024	(61.6)	2391	(69.4)	<0.0001
Depression	1303	(19.2)	512	(15.4)	791	(23.9)	<0.0001
Trouble Sleeping	1084	(16.6)	463	(14.6)	621	(19.0)	<0.0001
Difficulty Concentrating	1321	(20.1)	583	(17.9)	738	(22.7)	<0.0001
Weight Gain	2889	(41.8)	1224	(36.9)	1665	(47.8)	<0.0001
Irritable	3201	(48.4)	1394	(43.9)	1807	(53.9)	<0.0001
Anxious	2836	(42.2)	1235	(38.1)	1601	(47.2)	<0.0001
Heart beat slower	366	(5.3)	167	(5.1)	199	(5.6)	0.216
Restless	2191	(33.0)	971	(29.7)	1220	(37.0)	<0.0001
<b>Past-Year Withdrawal-Related Experiences</b>							
Withdrawal-related discomfort	686	(10.6)	265	(8.6)	421	(13.0)	0.0001
Withdrawal-related relapse	1048	(15.3)	408	(12.6)	640	(18.7)	<0.0001

<sup>a</sup>Unweighted N

<sup>b</sup>Weighted %

<sup>c</sup>Past-year refers to the 12 months directly preceding the Wave 1 interview.



Wave 1 withdrawal symptoms and the odds of reducing and quitting smoking (vs. continuing smoking)

Table 3

Wave 2 Smoking status <sup>a</sup>	Any Wave 1 withdrawal symptoms		Cumulative Wave 1 withdrawal symptoms		Withdrawal-related discomfort		Withdrawal-related relapse		
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	
Unadjusted	Quit	0.82	0.76, 0.89	0.93	0.91, 0.95	0.82	0.70, 0.95	0.68	0.60, 0.78
	Reduced	0.86	0.76, 0.98	0.93	0.90, 0.97	0.72	0.51, 1.00	0.64	0.47, 0.87
AOR1 <sup>b</sup>	Quit	0.82	0.75, 0.89	0.93	0.91, 0.95	0.85	0.73, 0.99	0.72	0.62, 0.82
	Reduced	0.81	0.71, 0.91	0.92	0.89, 0.95	0.67	0.48, 0.95	0.59	0.43, 0.81
AOR2 <sup>c</sup>	Quit	0.97	0.89, 1.07	0.97	0.95, 0.99	1.07	0.91, 1.26	0.85	0.74, 0.97
	Reduced	1.06	0.93, 1.21	0.99	0.96, 1.03	0.93	0.64, 1.34	0.74	0.53, 1.04
AOR3 <sup>d</sup>	Quit	---	---	---	---	1.13	0.96, 1.34	0.88	0.74, 1.05
	Reduced	---	---	---	---	0.93	0.64, 1.35	0.71	0.50, 1.00
AOR4 <sup>e1</sup>	Quit			0.97	0.94, 1.00				
	Reduced			0.94	0.90, 0.98				
AOR4 <sup>e2</sup>	Quit		<i>f</i>	0.97	0.94, 1.00		<i>f</i>		<i>f</i>
	Reduced			1.05	1.00, 1.11				

<sup>a</sup>Reduced: Wave 1 daily smoker who reported non-daily smoking at Wave 2; Quit: Wave 1 daily smoker who reported non-smoking at Wave 2

<sup>b</sup>AOR1 + additional adjustment for demographics and smoking quantity

<sup>c</sup>AOR2 + additional adjustment for substance use disorders and psychiatric disorders

<sup>d</sup>AOR3 + additional adjustments for number of withdrawal symptoms

<sup>e</sup>Fully adjusted for all model covariates, stratified by gender where significant (4e1=men; 4e2=women)

<sup>f</sup>Interaction term non-significant