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Smoking and suicidal behaviors in a sample of US adults with low mood: a prospective analysis

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ABSTRACT

Objective: To investigate whether: 1) smoking predicts suicide related outcomes (SRO) independently of socio-demographic and psychiatric risk factors, 2) smoking abstinence affects the suicide risk, 3) the relationship is bi-directional.

Design: Longitudinal data obtained in Wave 1 (2001-2002) and Wave 2 (2004-2005) of the National Epidemiologic Survey of Alcohol and Related Conditions.

Setting: Face-to-face interviews conducted with persons in the community.

Participants: US adults (43,093) aged 18 years or older were interviewed in Wave 1; 34,653 participants were re-interviewed three years later. For the present study, the sample was the subset of persons (N=7,352) who at the Wave 2 interview answered affirmatively regarding the presence of low mood lasting two weeks or more during the past three years. Females were 64.1%; the ethnic/racial distribution was White=71.4%, Blacks=10.6%; Hispanic =11.2%; Asian/Pacific Islander = 3.5%; American Indian = 3.3%.

Main outcome measures: SRO composed of any of three items: 1) want to die, 2) suicidal ideation, 3) suicide attempt.

Results: Current and former smoking in Wave 1 predicted increased risk for Wave 2 SRO independently of socio-demographic characteristics, psychiatric history, and prior SRO measured in Wave 1 (Adjusted Odds Ratio (AOR) =1.41, 95% CI=1.28 to1.55 for current smoking, and 1.32, 95% CI=1.21 to 1.43 for former smoking). In comparisons with persistent non-smokers, risk for future SRO was highest among relapsers (AOR=3.42, 95% CI=2.85 to 4.11); next highest among beginning smokers (AOR=1.82, 95% CI=1.51 to 2.19); and lowest among long-term (four+ years) former smokers (AOR=1.22, 95% CI=1.12-1.34). In comparisons with

persistent current smokers, risk reduction was evident with long-term (p=0.0001) but not shorter-term (p=0.17) abstinence. A bi-directional relationship was not observed.

Conclusion: Suicidal behaviour is another harmful consequence of smoking. Further research is needed to understand how regular smoking and smoking abstinence affect the risk of SRO.

INTRODUCTION

Suicide is a leading cause of death worldwide. Close to one million persons die from suicide each year. The World Health Organization predicts that by 2020 suicide deaths will rise to 1.5 million (1). Completed suicides are largely predicted by the wish to die, thoughts of suicide, and unsuccessful previous suicidal attempts (2), making it important to understand the risks posed by suicide related outcomes (SRO). A history of mental disorders (3-5) and particular demographic characteristics (female gender, younger age, unmarried status, and unemployment) are putative risk factors for suicide and SRO (2). Tobacco use, long known as a major risk factor for numerous medical illnesses (6), and recently, for psychiatric outcomes as well (7, 8) has received increasing attention for its potential contribution to the risk of completed suicides and SRO (9). The veracity and dynamics of such a pernicious relationship has implications for suicide prevention. Smoking is a modifiable behaviour; reducing the prevalence of smoking may offer a pathway towards reducing the suicide rate.

A link between smoking and suicide was observed as early as 1976 by Doll and Peto in their study of mortality due to smoking in male British doctors (10). Numerous clinical and epidemiological studies that subsequently investigated the issue are in general, but not universal, agreement in finding a significant association between smoking and suicide and suicidal behaviors. Three studies based on cross-sectional epidemiological data that used the nicotine dependence diagnosis to assess smoking behavior found a positive association between smoking and SRO (11-13); none could infer causality, however, due to lack of information on the relative timing between smoking behaviors and the SRO. More relevant to the aims of the present study are the findings from several longitudinal studies which utilized community based data. Three of those prospective studies (14-16) found that current smoking predicted suicidal behaviors even after controlling for the effects of demographic and psychiatric variables; four studies did not

find a positive relationship (17-20). The effect of smoking abstinence on risk of SRO is also unclear. A study of young adults followed for 10 years found that current, but not past, cigarette smoking predicted suicidal thoughts and attempt (14). Another study found that former smokers initially showed higher age-adjusted incidence rates of suicidal ideation compared to non-smokers (16); however, after more extensive adjustment with depressive disorder, anxiety symptoms, and alcohol dependence, the difference was no longer statistically significant. A study based on data from the NESARC Wave 1 initially found that longer duration of abstinence decreased risk for SRO, but this effect disappeared upon controlling for psychiatric comorbidity (21). A protective or exacerbating impact of smoking abstinence on the risk of suicide-related behaviors would have considerable significance for promoting and managing smoking cessation attempts and preventing SRO and suicide. A further question of theoretical and practical importance is whether there is mutual causation between smoking and suicidal behaviors. In longitudinal data obtained from adolescents, the single study that has addressed this question thus far found that smoking predicted subsequent suicidal ideation and suicide attempts but prior suicidality was not associated with subsequent smoking (15).

The present study was conducted to address these conundrums of the smoking-suicide relationship: 1) whether smoking predicts SRO independently of putative demographic and psychiatric risk factors, 2) whether smoking abstinence, and its corollary, duration of smoking abstinence affects the suicide risk, and 3) whether the relationship is uni- or bi-directional. Important methodological conditions permitting valid assessment of these questions were present, concomitantly, in the two-wave format of the National Epidemiological Survey of Alcohol and Related Conditions (NESARC) (22): a longitudinal design, a large sample, and extensive data on important potential confounders. In addition, access to a sample of persons

with low mood, who are recognized to have a greater probability of experiencing suicidal behaviours (3, 4), provided the more sensitive context for detecting a more valid and precise estimate of the risk potential of smoking for future SRO (23).

METHODS:

Sample: The NESARC interviews were conducted with persons in households, military personnel living off base, and individuals living in group quarters such as boarding houses, shelters, and college dorms. Data were collected to obtain a representative national sample of US adults. In Wave 1 (2001-2002), face-to-face interviews were completed with 43,093 persons aged 18 years or older. The overall response rate was 81.0%. Blacks, Hispanics, and young adults (18-24 years) were oversampled. The Wave 1 sample was re-interviewed in Wave 2 (2004-2005) three years later (mean interval=36.6 months, s.e.=2.62) with an overall response rate based on the Wave 1 sample of 86.7% (N=34,653). Data for the present study were obtained from a subset (N=7,352) comprised of persons who answered affirmatively at the Wave 2 interview to the question concerning the presence of low mood and, as a result, were further queried regarding the occurrence of an SRO during the three years prior to the Wave 2 interview.

The NESARC sample size was chosen to be sufficiently large to produce nationally representative proportions for the study of substance abuse and dependence and mental disorders by demographic group with confidence intervals equal to or smaller than extant studies. The NESARC study used a complex survey design and sampling weights upon responses to adjust for sample selection procedures, non-response from selected households or individuals, oversampling (of young adults, Blacks, and Hispanics), and non-response at the Wave 2 time point. The weights and survey design effects have been incorporated into the following results.

Other methodological details of the NESARC Wave 1 and Wave 2 studies have been described extensively elsewhere (24-26).

Variables: The dependent variable was SRO, comprised by the items on want to die, suicidal ideation, suicidal attempt reported in Wave 2, measured as a dichotomous variable (none of the three=0; any of the three=1). The main predictor variable was smoking status in Wave 1, i.e., non-smoker, former smoker, or current smoker. A non-smoker had responded "No" to each of the questions regarding lifetime use of at least 100 cigarettes, at least 50 cigars, smoked a pipe at least 50 times, used snuff at least 20 times, and used chewing tobacco at least 20 times. Following the coding rule used in the NESARC, all tobacco users were labelled as smokers for the present analysis. A former smoker was defined as a "Yes" responder to the prior questions who also reported having stopped smoking or tobacco use at least one year ago. A current smoker was a "Yes" respondent who had smoked or used tobacco within the past year. Users of cigars, pipes, snuff, or chewing tobacco who did not smoke cigarettes comprised 2% (129/7352) of the sample.

The smoking status variable (i.e., never, former, current) rather than nicotine dependence was selected to assess tobacco use history because: 1) the adequacy of the DSM-IV criteria, followed in the AUDADIS-IV, as a valid measure of nicotine dependence remains controversial (27,28), and 2) response to the question on never, current or former smoking is easier to elicit in the clinical setting, with more validity, than responses to a multi-item measure of tobacco use for which no consensus, stand-alone instrument yet exists (27, 28). To categorize respondents' long-term or recent status as former or current smokers, a smoking change variable was created with the following subgroups according to their report of smoking at Waves 1 and 2: 1) non-smoker to non-smoker, 2) former smoker to former smoker, 3) current smoker to former smoker, 4)

current smoker to current smoker, 5) non-smoker to current smoker, 6) former smoker to current smoker, and 7) non-smoker to former smoker.

Covariates considered potential confounders or effect modifiers because of their known correlations with smoking and/or SRO and measured at Wave 1 were: demographic characteristics (age, gender, race/ethnicity, marital status, education, employment status, income, urban residence, geographic region), the DSM-IV Axis I and Axis II disorders, and prior SRO. The Axis I disorders were categorized into lifetime mood disorders (major depressive disorder, dysthymia, bipolar I and bipolar II), anxiety disorders (panic disorder, social phobia, specific phobia, post-traumatic stress disorder, generalized anxiety disorder), alcohol use disorders (alcohol abuse or dependence), and other substance use disorders (drug abuse or dependence). A history of Attention Deficit Hyperactivity Disorder (ADHD), queried only at Wave 2, was used among the Wave 1 predictors, its lifetime quality presumed since the DSM-IV criteria for ADHD include the presence of ADHD symptoms before age seven. All ten of the Axis II personality disorders measured in AUDADIS-IV (shown in Table 1) were included as well.

Assessment: For both Waves 1 and 2, the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-IV) was administered by interviewers from the U.S. Census Bureau. The reliability and validity of the DSM-IV diagnoses obtained through the AUDADIS-IV have been demonstrated in clinical and general samples in the U.S. and in other countries (29).

Statistical Analysis: Percentages for categorical independent variables were calculated within the analytical, at-risk, sample (Table 1) and the complementary Wave 2 sample (no low mood, Supplemental Data Table S1). For the at-risk sample, the crude effects on Wave 2 SRO of individual Wave 1 variables were assessed by unadjusted odds ratios (OR) and 95% confidence

intervals (CI) obtained from univariate logistic regressions. To control for potential confounding and determine the independent effects of the latter predictor variables on Wave 2 SRO, multiple logistic regression models were performed and adjusted odds ratios (AOR) and 95% confidence intervals (CI) were obtained. A complementary regression as specified in Granger (30) was used to test the opposite temporal relationship – that is, whether prior SRO exerted an effect on current smoking status in Wave 2. All models were estimated with the PROC SURVEYLOGISTIC function of SAS statistical software version 9.2, with the results verified through an internal statistical review at the U.S. Census Bureau.

For most demographic control variables, missing values, reported in Table 1, were replaced through imputation. The exception to this method was for the identification of suicide related outcomes (SRO), where the 12-18 individuals reporting "unknown" for the three SRO-defining questions in Wave 2 were set to "no" responses for the purposes of classification. We conducted sensitivity analysis (a) comparing results from the at-risk subsample to those from the entire Wave 2 NESARC sample, (b) using different measurements of smoking status (including additional quitting cut points in time for short-term cessation), (c) using different categorizations of changes in smoking status, (d) using different sets of control variables with and without education, Axis II personality disorders, and census region, and (e) including help-seeking behavior controls.

RESULTS

Sample characteristics at Wave 1

The prevalence of any SRO was 25.6%. Prevalence rates for individual SROs were 23.4% for "wish to die", 19.3% for "suicidal ideation", and 6.1% for "suicide attempt". By

smoking status, 31.7% were current smokers, 17.8% were former smokers, and 50.5% were never smokers. Weighted percentages and standard errors for categories of the study variables are shown in Table 1, Columns 1 and 2.

Distributions from the at-risk sample (N=7,352) and from the complementary sample of 27,301 Wave 2 respondents (shown in Supplemental Data Table S1) were compared. The complementary sample had included respondents who were skipped out of the SRO section of the interview because they did not report depressed mood. Chi-squared tests found statistically significant differences between the at-risk and the complementary samples for all of the variables reported in the supplemental table, a function of the large sample sizes and the survey design effects of the NESARC. Confirming the at-risk status of the analytical sample, the prevalence rates of the psychiatric disorders (DSM-IV Axis I and Axis II) were markedly higher among them than the rest of the sample. Other demographic characteristics previously associated with higher risk of suicide and SROs were also higher in the at-risk subsample: more females, more lower and fewer high income responders, fewer married, and more separated or never married, and more unemployed individuals. Differences by race/ethnicity, age, urban versus rural residence, and geographic area were also observed.

Effects of Wave 1 predictors on Wave 2 SRO

For reference, the unadjusted odds ratios and 95% CI for risk of future SRO of individual study variables, indicating relationships uncontrolled for covariance effects are shown in Table 1, Columns 3 and 4. The adjusted odds ratios and 95% CI based on a multivariate model on Wave 2 SRO, controlling for covariance from the Wave 1 predictors , are shown in Table 1, Columns 5 and 6.

The adjusted analysis showed significantly higher risk for Wave 2 SRO of both Wave 1 current smokers (AOR=1.41, 95% CI= 1.28-1.55) and former smokers (AOR=1.32, 95% CI=1.21-1.43) relative to nonsmokers. The difference in point estimates of risk between current versus former smokers was not significant ($\chi 2$=1.95, p = 0.16).

The multivariate model also showed significant, independent risk for future SRO for female gender, Hispanic race/ethnicity, young age, cohabiting/divorced/separated marital status, lower income, being unemployed, residence other than the Northeast region. Having reported a SRO in Wave 1 was the strongest predictor of reporting a Wave 2 SRO (AOR=3.49, 95% CI= 3.18- 3.84). Of the DSM-IV Axis I disorders, only anxiety disorders (AOR= 1.08, 95% CI=1.01-1.17) and attention deficit hyperactivity disorder (AOR=1.56, 95% CI=1.36-1.79) showed significant independent prediction of Wave 2 SRO. The adjusted odds ratio for mood disorders indicated a decreased risk of future SRO (AOR= 0.77, 95% CI= 0.70-0.84), in contrast to the increased risk observed in the simple regression (OR=2.04, 95% CI=1.92-2.17). Likewise, the significant predictive effects on Wave 2 SRO for the alcohol use disorders and the substance use disorders seen in the simple regressions were not apparent in the multivariate model. Significantly elevated risk for Wave 2 SRO was seen for only three of the DSM-IV Axis II disorders: borderline personality, schizotypal, and avoidant personality. Ranked in decreasing order, the statistically significant predictors of SRO risk, other things being equal, in the present sample of adults reporting low mood were: prior SRO, borderline personality disorder, ADHD, schizotypal disorder, current smoking, former smoking, avoidant personality disorder, and selected demographic characteristics.

Smoking status change from Wave 1 to Wave 2: effects on Wave 2 SRO

Table 2 shows that the great majority of the sample (90.5%) did not change their smoking status between Waves 1 and 2. Among the remaining 9.5%, over half (5.3%) had made a shift from being current smokers to former smokers; more than a fourth (2.6%) were non-smokers in Wave 1 who became current smokers in Wave 2; and a much smaller proportion (<2%) were former smokers in Wave 1 had relapsed to smoking in Wave 2. A seventh category, non-smokers in Wave 1 who reported former smoking status in Wave 2, produced a sample size that was too small for further assessment.

Table 2 shows the risk for SRO among all categories of ever-smokers compared to the persistent non-smokers. The highest risk was seen for smokers who had relapsed (former to current smoker) (AOR=3.42, 95% CI=2.85-4.11); the new smokers (non-smoker to current smoker) showed the next highest risk (AOR=1.82, 95% CI=1.51-2.19); and the persistent former smokers (reported abstinence status at both Wave 1 and 2 interviews) showed the lowest risk (AOR=1.22, 95% CI=1.12-1.34).

Long-term abstinence, relapse, and new smoking

The risk for Wave 2 SRO of a) long-term quitters relative to recent quitters and b) that of new current smokers in Wave 2 (relapsed or began to smoke) relative to the risk of smokers during both study Waves was examined. Given the three-year interval between Waves 1 and 2 and the coding requirement that former smoking status is assigned only upon reporting of at least 12 months of abstinence, persons in Category 2 of Table 2 (former to former smokers) would have been abstinent for at least four years. Persons who shifted from current smoking in Wave 1 to former smoking in Wave 2 (Category 3) would have been abstinent for a maximum of three years. Pair-wise chi squared tests for equality of the coefficients compared the AOR among the

group categories, as shown below Table 2. The lower risk of recent former smokers (Category 3) when compared to the persistent current smokers (Category 4) was not significant (p=0.26), whereas the lower risk of long-term smokers (Category 2) compared to the persistent current smokers (Category 4) was significant (p=0.0001). These data suggest that a reduction in risk for future SRO with past smoking, relative to current smoking, becomes apparent only after a considerable period of smoking abstinence.

The second comparison which focused on new smoking in Wave 2 found that, relative to persistent current smokers, those who relapsed or began to smoke in Wave 2 had significantly higher risks for Wave 2 SRO than the persistent current smokers (p=0.0001, p=0.04, respectively).

Is there a bi-directional relationship?

Section A in Table 3 shows the results of multivariate models for predicting Wave 2 SRO as a function of smoking in Wave 1 and other Wave 1 covariates. Section B in Table 3 shows results for predicting Wave 2 current smoking as a function of SRO history in Wave 1 and other Wave 1 covariates, following the Granger test for directional causality (30). As in Table 1, Table 3A shows a predictive effect of Wave 1 current smoking and former smoking on Wave 2 SRO. Table 3B shows that persons with Wave 1 SROs were *less* likely to report current smoking status at Wave 2 (AOR=0.81, 95% CI=0.72-0.90). These results refute the hypothesis of a bi-directional temporal relationship whereby there might be mutual causation between SRO and smoking.

To understand these temporal relationships further, the effects of the interaction of Wave 1 smoking status (current vs. nonsmoker and former vs. nonsmoker) with history of prior SRO

(Table 4, Panels A and B) were examined. The outcome variable in Table 4, Panel A is Wave 2 SRO; the outcome variable in Table 4, Panel B, is Wave 2 current smoking. In each model, the reference group comprised the non-smokers with no prior SRO at Wave 1.

Table 4, Panel A shows the following: 1) in the presence of prior SRO, the risk for Wave 2 SRO is much higher across the smoking categories (for current, former, and non-smokers, (AORs > 3.5) than for their counterparts with no prior SRO; 2) in the absence of prior SRO, the risk estimates for Wave 2 SRO among current and former smokers in Wave 1 are significantly higher (95% CI are 1.41-1.74 and 1.28-1.57, respectively) compared to the reference group (while notably lower than their counterparts with prior SRO), 3) also in the absence of prior SRO, the risk for Wave 2 SRO among Wave 1 former smokers is lower than for Wave 1 current smokers (AORs=1.42 and 1.56, respectively), but the difference is small and not statistically significant (Wald chi-square=2.69, p-value = 0.101). Thus, other characteristics (e.g., demographics and psychopathology) being equal, current smoking and former smoking are valid predictors of an *initial* SRO; however, once a person has had a SRO, the risk of *recurrence* is fully predicted by that prior SRO and smoking status information does not significantly adjust the risk prediction.

The predictive model on Wave 2 current smoking in Panel B of Table 4 shows that, as would be expected, Wave 1 current smokers, regardless of prior SRO, have a considerably higher risk of being a current smoker in Wave 2 compared to the reference group of Wave 1 nonsmokers with no prior SRO. Wave 1 former smokers with no prior SRO showed a significantly higher risk for current smoking in Wave 2 (AOR=2.20; 95% CI=1.77- 2.31); by contrast, their counterparts with prior SRO did not (AOR=1.15; 95% CI=0.83, 1.61). Nonsmokers with prior SRO showed a risk for Wave 2 SRO that was lower than nonsmokers

without prior SRO. Thus, the effects of prior SRO upon current smoking at Wave 2 differ by smoking status at Wave 1 – no net effect of prior SRO upon among smokers, but, for former smokers and nonsmokers, prior SROs predicted a *reduction* in the likelihood of current smoking in Wave 2. Overall, analysis of the interaction of prior SRO and Wave 1 smoking status shows nuances but does not fundamentally change the finding from the analysis of main effects seen in Table 2 that smoking predicts increased risk of SRO but the reverse relationship does not hold.

DISCUSSION

The main findings of the present study are: 1) smoking history, whether current or past, increases the risk for SRO independently of demographics, psychiatric factors, and prior SRO; 2) long-term smoking abstinence can reduce that risk; 3) new smoking due to relapse after a period of abstinence or to current smoking among former non-smokers was associated with an increased risk of SRO relative to persistent current smoking; 4) the smoking-suicide relationship is not bi-directional.

Strengths and limitation of the study are worth noting. An important strength is the concomitance of rigorous methods and materials not always present in prior work on the smoking-suicide question – face-to-face interviews, a longitudinal design, a validated instrument, a comprehensive range of putative predictors, and a large and clinically relevant sample that permitted statistical control of the key background factors and comorbidities. A further strength relevant to the real-world setting is the use of a simple yet meaningful measure of smoking status (i.e., never, former or current smoking status), that is easy for a questioner to administer and the respondent to recall and understand. At the same time, study limitations call for cautious interpretation of the findings. The survey excluded persons who had completed suicide attempts.

Using the U.S. rate of 11.1 per 100,000 population per year (31), the Wave 1 sample of 43,093 could be expected to include about 14 persons with completed suicides before Wave 2 (95% CI= 6.8-21.6); introducing a non-trivial, although likely small, selection bias. Second, the present study sample comprised the self-selected 22% of the 34,653 NESARC Wave 2 participants who reported low mood during the three-year interval between the interviews. This selectivity yields findings relevant to mental health settings that are more likely to serve persons experiencing mood problems; however, they may not generalize to the rest of the NESARC sample or to the national population. Nevertheless, allowing for missing data from persons who did not report depressed mood, further analysis on the total sample using the same regression model applied to the present, at-risk sample also showed significant, although lower, predictive effects of current and former smoking history on future SRO (AOR=1.36, 95% CI=1.25-1.48 and AOR=1.18, 95% CI=1.08-1.28, respectively). Third, the present study did not assess the effects of medical conditions which are possibly causally related, albeit in different directions, to smoking and to SRO. A fourth limitation and a direction for further research is the aggregate nature of the dependent variable (i.e., SRO); analysis of individual SRO could yield more meaningful findings.

Other than the present one, there have been seven prospective epidemiological studies of smoking and SRO (14-20). The positive prediction of future SRO reported here was also observed in three studies (14-16). Problems of recall due to the large, ten year interval between data time points could explain the negative finding of the study by Kessler et al (17) while the younger age of the samples in two studies (19-20), could have masked a future effect. Of clinical and public health importance is the finding, not reported in prior studies, that longer abstinence from smoking or tobacco exposure decreased the risk for SRO. The differential risk

of SRO according to duration of abstinence observed in the present study but not considered in the two negative findings regarding past smoking (14, 16) could account for the inconsistent findings. Notably, the divergence of effects according to longevity of abstinence is consistent with evidence regarding lung cancer and other smoking-related disorders that risk reduction from stopping smoking occurs only after multiple years of abstinence (32, 33). Also a new finding made possible by the longitudinal nature of the data is the increased risk for future SRO among former smokers and nonsmokers in Wave 1 who relapsed or began to smoke in Wave 2 compared to persistent current smokers. Although both latter effects occurred in small proportions of the sample, their observed impact on future SRO was high. Relapse and new smoking during adulthood could be signals of a future SRO. Finally, the data did not indicate a reverse temporal relationship, as also seen in the study of adolescents (15). Former and non-smokers with prior SRO in Wave 1 showed lower risk for current smoking in Wave 2 compared to their counterparts with no prior SRO. Perhaps those former and non-smokers, already inclined towards the more healthy behaviour of not smoking, were spurred by the prior SRO to undertake therapeutic actions which included avoidance of smoking. Of interest, exploratory analysis of Wave 1 data revealed a significant correlation (r=0.43, p=0.0001) between prior SRO and help-seeking during the last three years.

This analysis provided clarifying information to the long-standing controversies regarding the effect of current smoking and past smoking on SRO, introduced new information regarding a protective effect of sustained abstinence for the purpose of reducing risk of SRO, and disconfirmed the hypothesis tested thus far only in an adolescent sample (15) of a bi-directional association between smoking and SRO. The neurobiological, genetic, psychiatric and psychological underpinnings of these observations and their invariance across segments of the

wider population (i.e., by age groups, gender, race/ethnicity, cultural groups, and among healthy versus medically or psychiatrically ill persons) need further investigation. The worrisome, new observation of increased risk for SRO following relapse or new smoking among former non-smokers compared to persistent current smokers was observed in a very small proportion of the ever-smokers; replicating those findings in a larger sample would provide more assurance of their certainty and the need for therapeutic attention. Furthermore, since significant prediction from several factors acting as moderators (e.g., gender and race/ethnicity) or mediators (e.g., psychiatric illness) was observed, the interactions of those covariates with smoking as they influence the risk of SRO warrant investigation. Finally, a prospective study of smoking and individual SRO (16) observed different levels of risk associated with suicidal ideation and combinations of ideation with suicidal plans and attempts. Thus, the findings yielded by the present focus on an aggregate measure of SRO warrant testing similar models as applied herein to the relationships between smoking and individual SRO and combinations of SRO.

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spouses of the authors had financial relationships that may be relevant to the submitted work; 6) none of the authors had a non-financial interest that may be relevant to the submitted work.

Lirio Covey and Ivan Berlin conceptualized this study and, with Mei-Chen Hu, designed the analysis. Jahn Hakes had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Lirio Covey was the lead writer of the manuscript. All authors participated in the interpretation of findings and writing of the manuscript. All authors had full access to the statistical reports, tables, and the manuscript; and take responsibility for the integrity of the data and the accuracy of the data analysis.
The employers of the authors had no role in the study design, implementation of the study, analysis and interpretation of data, in the writing of the report, and the decision to submit the article for publication.

The study is a secondary analysis of data collected by the National Institute of Health-National Institute of Alcohol and Alcohol Abuse of the US government. Before data collection, each respondent was informed of the nature of the survey and its potential uses, ensured of confidentiality, and told that participation was voluntary. All participants signed a consent form prior to participating in the interviews. The US Census Bureau and the US Office of Management and Budget reviewed and approved the ethics protocol. Individual data files are de-identified to prevent full anonymity of participants. Approval for conducting this secondary analysis of previously collected data was not required.

In order to safeguard sensitive personal information, NESARC data are not available for public use. The restricted use data sets are maintained by the U.S. Census Bureau on behalf of NIAAA,

and any requests to use NESARC data for replication or other purposes may be directed to the NIAAA coordinator for NESARC, Aaron White (whitea4@mail.nih.gov).

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Supplemental Data:

Table S1: Comparison of Wave 1 characteristics of the at-risk sample with the rest of the Wave 2 NESARC sample. Weighted percentages (%) and standard error (s.e)

Variable	Total Wave 2 sample %	s.e.	At-risk Sample %	s.e.	Rest of sample %	s.e.
Female	52.08	0.16	64.13	0.40	49.02	0.17
Race/Ethnicity						
White	70.93	0.24	71.39	0.40	70.81	0.25
Black	10.75	0.20	10.61	0.22	10.79	0.21
Hispanic	11.56	0.10	11.20	0.15	11.65	0.12
Asian/Pac. Islander	4.36	0.06	3.50	0.10	4.58	0.06
Amer. Indian/Alaska Native	2.40	0.11	3.29	0.20	2.17	0.11
Age: 18-19	4.02	0.07	4.47	0.15	3.91	0.08
20-29	17.78	0.14	19.28	0.30	17.40	0.15
30-44	30.90	0.17	32.28	0.29	30.54	0.18
45-64	31.08	0.15	31.64	0.24	30.94	0.17
65and over	16.22	0.10	12.32	0.25	17.21	0.12
Household Income:						
Less than $20,000	20.35	0.17	25.07	0.32	19.15	0.19
$20,000 to $34,999	19.62	0.13	20.84	0.27	19.31	0.15
$35,000 to $59,999	26.27	0.16	24.85	0.31	26.63	0.17
$60,000 and over	33.76	0.16	29.24	0.33	34.91	0.17
Marital status:						
Married	59.81	0.17	54.75	0.35	61.10	0.17
Cohabiting	3.25	0.06	3.60	0.11	3.16	0.07
Widowed	6.04	0.07	5.37	0.12	6.21	0.08
Divorced	8.45	0.06	10.73	0.19	7.87	0.07
Separated	1.98	0.04	2.98	0.12	1.73	0.04
Never Married	20.46	0.17	22.57	0.33	19.93	0.17
Education:						
Less than HS	14.65	0.13	16.25	0.26	14.24	0.14
High School diploma	29.03	0.18	29.35	0.35	28.95	0.20
College	56.32	0.22	54.40	0.38	56.81	0.23
Unemployed	7.16	0.09	12.31	0.25	5.85	0.09
Urban	28.89	0.26	30.59	0.41	28.46	0.25
Northeast	19.67	0.08	18.57	0.15	19.95	0.10
Midwest	23.15	0.16	23.52	0.32	23.05	0.21
South	35.21	0.15	34.89	0.39	35.29	0.19
West	21.97	0.11	23.02	0.23	21.71	0.15

Table S1, continued.

Variable	Total W2 sample	(std. err.)	At-risk Proportion	(std. err.)	Rest of sample	(std. err.)
Alcohol Use Disorder	30.43	0.20	33.57	0.39	29.63	0.20
Substance Use Disorder	10.42	0.11	15.06	0.26	9.25	0.11
Nicotine Dependence	17.47	0.13	24.33	0.37	15.73	0.13
Anxiety disorder	17.88	0.17	31.00	0.34	14.55	0.17
Mood disorder	21.09	0.13	41.82	0.33	15.82	0.13
ADHD	2.51	0.06	5.82	0.19	1.67	0.05
Personality Disorders						
Borderline	5.89	0.08	18.44	0.28	2.70	0.07
Schizotypal	3.93	0.06	11.20	0.24	2.09	0.05
Narcissistic	6.18	0.08	11.88	0.23	4.74	0.08
Avoidant	2.32	0.05	6.14	0.17	1.36	0.05
Antisocial	3.63	0.07	5.86	0.21	3.07	0.07
Dependent	0.43	0.02	1.36	0.09	0.19	0.01
Obsessive-Compulsive	8.07	0.10	13.50	0.31	6.69	0.09
Paranoid	4.33	0.07	9.66	0.21	2.98	0.06
Schizoid	3.06	0.06	6.44	0.21	2.21	0.05
Histrionic	1.80	0.04	3.68	0.15	1.32	0.04
Any Axis I or Axis II Disorder	54.70	0.22	69.72	0.35	50.89	0.24
Smoking status:						
Current smoker – W1	27.02	0.17	31.65	0.38	25.85	0.19
Former smoker – W1	19.58	0.16	17.84	0.28	20.02	0.17
Never smoked – W1	53.40	0.19	50.51	0.42	54.13	0.20
Total	n=34,653		n= 7,352		n=27,301	

NOTES: Values for control variables in this table (demographics and psychiatric history) are taken from Wave 1 of NESARC, but weighted using W2WEIGHT, as inclusion in sample requires knowing whether respondent had an SRO between waves. All psychiatric disorders are assigned only a lifetime diagnosis.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Table 1: Demographic characteristics, lifetime psychiatric and prior SRO (n=7352)[§]*. Frequencies, odds ratios, and adjusted odds ratios for Wave 2 SRO**

Variable	(1) Weighted mean %	(2) Standard error of mean	(3) OR	(4) 95% CI	(5) AOR	(6) 95% CI
Smoking history						
Current smoker in Wave 1	31.65	0.38	1.77	1.64, 1.90	1.41	1.28, 1.55
Former Smoker in Wave 1	17.84	0.28	1.16	1.07, 1.25	1.32	1.21, 1.43
Never Smoker in Wave 1	50.51	0.42	1.00		1.00	
Demographics						
Female	64.13	0.40	1.05	0.98, 1.12	1.13	1.04, 1.22
Male			1.00		1.00	
White	71.39	0.40	1.00		1.00	
Black	10.61	0.22	0.91	0.84, 0.99	0.84	0.76, 0.92
Hispanic	11.20	0.15	1.10	1.04, 1.17	1.26	1.16, 1.36
Asian/Pacific Islander	3.50	0.10	0.74	0.67, 0.82	0.93	0.82, 1.06
American Indian	3.29	0.20	0.94	0.71, 1.25	0.69	0.51, 0.92
Age 18-19	4.47	0.15	1.00		1.00	
Age 20-29	19.28	0.30	0.83	0.69, 0.98	0.77	0.63, 0.94
Age 30-44	32.28	0.29	0.75	0.64, 0.88	0.73	0.60, 0.90
Age 45-64	31.64	0.24	0.66	0.56, 0.78	0.69	0.56, 0.84
Age 65 and over	12.32	0.25	0.47	0.39, 0.57	0.68	0.54, 0.86
Married	54.75	0.35	1.00		1.00	
Cohabiting	3.60	0.11	1.67	1.42, 1.96	1.27	1.07, 1.51
Widowed	5.37	0.12	0.97	0.85, 1.10	0.92	0.78, 1.07
Divorced	10.73	0.19	1.70	1.57, 1.84	1.20	1.10, 1.32
Separated	2.98	0.12	1.85	1.58, 2.15	1.29	1.06, 1.56
Never married	22.57	0.33	1.35	1.24, 1.46	0.97	0.87, 1.09
Less than High School	16.25	0.26	1.17	1.04, 1.32	1.09	0.95, 1.25
High School Diploma	29.35	0.35	1.00		1.00	
Some College or more	54.40	0.38	0.94	0.87, 1.02	1.08	1.00, 1.17
Household income:						
Less than $20,000	25.07	0.32	1.71	1.57, 1.85	1.31	1.18, 1.44
$20,000 to $34,999	20.84	0.27	1.41	1.30, 1.52	1.18	1.07, 1.30
$35,000 to $59,999	24.85	0.31	1.30	1.20, 1.42	1.21	1.11, 1.32
$60,000 and over	29.24	0.33	1.00		1.00	
Unemployed	12.31	0.25	1.84	1.68, 2.03	1.28	1.13, 1.45
Northeast	18.57	0.15	1.00		1.00	
Midwest	23.52	0.32	1.34	1.25, 1.42	1.33	1.21, 1.46
South	34.89	0.39	1.18	1.09, 1.27	1.14	1.04, 1.25
West	23.02	0.23	1.24	1.16, 1.33	1.25	1.15, 1.35
Urban	30.59	0.41	1.08	1.02, 1.15	1.03	0.97, 1.10
Rural			1.00			

Table 1, continued.

Variable	(1) Weighted mean %	(2) Standard error of mean	(3) OR	(4) 95% CI	(5) AOR	(6) 95% CI
Psychiatric History						
Suicide related outcomes In Wave 1	25.55	0.27	3.84	3.60, 4.10	3.49	3.18, 3.84
Lifetime Axis I Disorders						
Alcohol Use	33.57	0.39	1.40	1.31, 1.49	0.95	0.87, 1.04
Substance Use	15.06	0.26	1.75	1.61, 1.89	0.98	0.88, 1.09
Anxiety	31.00	0.34	1.72	1.62, 1.83	1.08	1.01, 1.17
Mood	41.82	0.33	2.04	1.92, 2.17	0.77	0.70, 0.84
Attention Deficit Hyperactivity Disorder	5.82	0.19	2.87	2.56, 3.22	1.56	1.36, 1.79
Personality Disorders						
Borderline	18.44	0.28	4.49	4.22, 4.77	2.91	2.69, 3.16
Schizotypal	11.20	0.24	3.44	3.09, 3.84	1.50	1.31, 1.72
Narcissistic	11.88	0.23	2.08	1.89, 2.29	1.03	0.92, 1.14
Avoidant	6.14	0.17	2.97	2.66, 3.32	1.29	1.05, 1.58
Antisocial	5.86	0.21	1.89	1.68, 2.13	0.85	0.72, 1.01
Dependent	1.36	0.09	3.44	2.74, 4.30	1.04	0.76, 1.41
Ob-Com	13.50	0.31	1.53	1.39, 1.69	0.90	0.80, 1.00
Paranoid	9.66	0.21	2.37	2.14, 2.62	0.95	0.82, 1.10
Schizoid	6.44	0.21	2.10	1.89, 2.33	1.01	0.88, 1.16
Histrionic	3.68	0.15	2.10	1.82, 2.43	0.76	0.63, 0.93

§ Missing observations for specific variables: Race – 43, Hispanic origin – 2, age – 13, marital status-4, educational attainment – 70, household income-2544, unemployed – 28, Wave 2 individual suicide related outcomes – 12-18 "unknown" change to "no". Treatment of unknown values in determination of psychiatric diagnosis variables is known only to original NESARC project staff at NIAAA.

*Persons reporting low mood and responding to questions on suicide related outcomes at the NESARC Wave 2 interview.

**SRO (Suicide related outcome: feel like want to die, suicide ideation, suicide attempt; 0=None, 1=any SRO).

Notes: n=7352. Odds Ratios (OR) based on simple regression models estimating Wave 2 SRO as a function of an individual predictor variable. Adjusted Odds Ratios (AOR) based on a multiple logistic regression estimating Wave 2 SRO as a function of age, sex, race/ethnicity, marital status, income, education, unemployed status, Census region, urban residence, smoking status, Axis I and Axis II disorders (as described in text), and lifetime SRO prior to Wave 1.

Table 2: Smoking status change as reported in NESARC Wave 1 and Wave 2 interviews: effects on Wave 2 suicide related outcomes (SRO)*

			Wave 2 SRO*	
Smoking status in Wave 1 to Wave 2	N	Weighted relative frequency (std. err.)	AOR	(95% CI)
1. Nonsmoker to Nonsmoker	3653	47.8 (0.40)	1.00	
2. Former to Former smoker	1185	16.4 (0.26)	1.22	(1.12, 1.34)
3. Current to Former smoker	393	5.3 (0.14)	1.37	(1.16, 1.63)
4. Current to Current smoker	1824	26.3 (0.35)	1.50	(1.35, 1.66)
5. Nonsmoker to Current smoker	194	2.6 (0.10)	1.82	(1.51, 2.19)
6. Former to Current smoker	(S)	< 2.0	3.42	(2.85, 4.11)
	N=7352			

*Includes wish to die, suicide ideation, suicide attempt

Notes: N=7352. AORs are adjusted odds ratios based on multiple logistic regression of Wave 2 SRO as a function of age, sex, race/ethnicity, marital status, income, education, unemployed status, Census region, urban residence, smoking status, Axis I and Axis II disorders (as described in text), and lifetime SRO prior to Wave 1.

The seventh category which consisted of persons who transitioned through a period of smoking to become a former smoker during the last 12 months in Wave 2 produced a sample size that was too small for a valid assessment of risk..

(S)= statistic suppressed to prevent identification of related cell values.

Chi-squared tests for equality of coefficients:

Smoking status change groups	chi-squared stat.	p-value
2 v. 3	1.86	0.17
3 v. 4	1.26	0.26
4 v. 5	4.11 *	0.04
5 v. 6	19.0 *	< .0001
2 v. 4	16.9 *	< .0001
4 v. 6	56.0*	<.0001

*=Statistically significant at 95% confidence level

Table 3: Effect of smoking status and history of SRO[a] reported at NESARC Wave 1 interview on: a) Wave 2 SRO[a], and b) Wave 2 current smoking.

	a) ave 2 SRO[a]		b) ave 2 Current Smoking	
	AOR*	(95% CI)	AOR*	(95% CI)
Current smoker	1.41	(1.28, 1.55)	89.1	(80.3, 98.9)
Former smoker	1.32	(1.21, 1.43)	1.93	(1.72, 2.18)
Wave 1 SRO[a]	3.49	(3.18, 3.84)	0.81	(0.72, 0.90)

[a]SRO includes wish to die, suicidal ideation, suicide attempt.

*Adjusted odds ratio from multiple logistic regression models controlling for demographics and psychiatric history reported at Wave 1 (shown in Table 1)

Table 4 Panel A: Combined AOR* effects of Wave 1 smoking status and Wave 1 SRO[a] upon Wave 2 SRO

	Current smoker, Wave 1		Former smoker, Wave 1		Nonsmoker, Wave 1	
	AOR	95% CI	AOR	95% CI	AOR	95% CI
Wave 1 SRO	4.77	3.70-5.87	4.58	3.60-5.82	4.12	3.65-4.64
No Wave 1 SRO	1.56	1.41, 1.74	1.42	1.28-1.57	1.00	CI=N.A.[b]

Table 4 Panel B: Combined AOR* effects of Wave 1 smoking status and Wave 1 SRO* upon Wave 2 Current smoking

	Current smoker, Wave 1		Former smoker, Wave 1		Nonsmoker, Wave 1	
	AOR	95% CI	AOR	95% CI	AOR	95% CI
Wave 1 SRO	76.98	57.60-104.8	1.15	0.83-1.61	0.70	0.60-0.82
No Wave 1 SRO	82.86	73.7-93.2	2.20	1.77-2.31	1.00	CI=N.A.[b]

[a]SRO includes wish to die, suicidal ideation, suicide attempt
[b]Not applicable

*Adjusted odds ratio from multiple logistic regression models controlling for demographics and psychiatric history reported at Wave 1 (shown in Table 1)

Smoking and suicidal behaviors in a sample of US adults with low mood: a longitudinal analysis

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Smoking and suicidal behaviors in a sample of US adults with low mood: a longitudinal analysis

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ABSTRACT

Objective: To investigate whether: 1) smoking predicts suicide related outcomes (SRO); 2) prior SRO predicts smoking, 3) smoking abstinence affects the risk of SRO, 4) psychiatric comorbidity modifies the relationship between smoking and SRO.

Design: Longitudinal data obtained in Wave 1 (2001-2002) and Wave 2 (2004-2005) of the National Epidemiologic Survey of Alcohol and Related Conditions.

Setting: Face-to-face interviews conducted with persons in the community.

Participants: US adults (N=43,093) aged 18 years or older, interviewed in Wave 1 and re-interviewed (N=34,653) three years later. For the present study, the sample was the subset of persons (N=7,352) who at the Wave 2 interview reported low mood lasting two weeks or more during the past three years and were further queried regarding SRO occurring between Waves 1 and 2.

Outcome measures: SRO composed of any of: 1) want to die, 2) suicidal ideation, 3) suicide attempt, reported at Wave 2. Current smoking reported at Wave 2.

Results: Current and former smoking in Wave 1 predicted increased risk for Wave 2 SRO independently of prior SRO, psychiatric history, and socio-demographic characteristics measured in Wave 1 (Adjusted Odds Ratio (AOR) =1.41, 95% CI=1.28 to 1.55 for current smoking; AOR=1.32, 95% CI=1.21 to 1.43 for former smoking). Prior SRO did not predict current smoking in Wave 2. Compared with persistent never smokers, risk for future SRO was highest among relapsers (AOR=3.42, 95% CI=2.85 to 4.11); next highest among smoking beginners at Wave 2 (AOR=1.82, 95% CI=1.51 to 2.19); and lowest among long-term (four+ years) former smokers (AOR=1.22, 95% CI=1.12 to 1.34). Compared with persistent current

smokers, risk for SRO was lower among long-term (p<0.0001), but not shorter-term (p=0.26) abstinence.

Conclusion: Smoking increased the risk of future SRO independently of psychiatric comorbidity. Abstinence of several years duration reduced that risk.

Word count= 294

Article Summary

Article focus

To investigate longitudinally among persons reporting low mood lasting two weeks or more during the past three years whether:

- smoking predicts suicide related outcomes (want to die, suicidal ideation, suicide attempt); prior suicide related outcomes predict smoking,
- smoking abstinence affects the risk of suicide related outcomes,
- psychiatric comorbidity modifies the relationship between smoking and suicide related outcomes.

Key messages

- Current and former smoking (less than 4 years' reported abstinence) predicted increased risk for suicide related outcomes independently of prior suicide related outcomes, psychiatric history, and socio-demographic characteristics.
- Prior suicide related outcomes did not predict future current smoking.
- Compared with persistent current smokers, risk of suicide related outcomes was reduced with long-term (≥4 years) but not with shorter-term (<4 years) abstinence.

Strengths and limitations

Strengths

- Face-to-face interviews, a longitudinal design, a large sample, a validated diagnostic instrument, a comprehensive range of putative predictors that permitted statistical control of the key background factors and comorbidities.

Limitations

- Only persons with self-reported low mood were questioned about suicide related outcomes, consequently, no generalizability to other populations.
- The sample did not include persons who had completed suicide.
- No assessment of the effects of medical conditions which are possibly causally related to smoking and to suicide related outcomes.
- No information from adolescents, a high risk population for both smoking and suicide related outcomes.

INTRODUCTION

Suicide is a leading cause of death worldwide. Close to one million persons die from suicide each year. The World Health Organization predicts that by 2020 suicide deaths will rise to 1.5 million (1). Completed suicides are largely predicted by the wish to die, thoughts of suicide, and unsuccessful previous suicidal attempts (2), making it important to understand the risks posed by suicide related outcomes (SRO). A history of mental disorders (3-5) and particular demographic characteristics (female gender, younger age, unmarried status, and unemployment) are putative risk factors for suicide and SRO (2). Smoking, long known as a major risk factor for numerous medical illnesses (6), and recently, for psychiatric outcomes as well (7, 8) has received increasing attention for its potential contribution to the risk of completed suicides and SRO (9). Nevertheless, whether the association between smoking and suicidal behaviours is causal or correlational remains unclear.

A link between smoking and suicide was observed as early as 1976 by Doll and Peto in their study of mortality due to smoking in male British doctors (10). Clinical and epidemiological studies that subsequently investigated the issue are in general, but not universal, agreement in finding a significant association between smoking and suicide and suicidal behaviors. Among studies that focused on SRO, three that used cross-sectional epidemiological data found a positive correlational association between smoking and SRO (11-13. Of seven longitudinal studies that also utilized community based data, three (14-16) found that current smoking predicted suicidal behaviors even after controlling for the effects of demographic and psychiatric variables; four studies did not find a positive relationship (17-20).

The effect of smoking abstinence on risk of SRO is also unclear. A study of young adults followed for 10 years found that recent, but not pre-survey, cigarette smoking predicted suicidal

thoughts and attempts (14). Another study showed higher incidence rates of suicidal ideation among former smokers than never smokers (16), but the difference was no longer significant after adjustment with depressive disorder, anxiety symptoms, and alcohol dependence. A study based on Wave 1 data from the National Epidemiological Survey of Alcohol and Related Conditions (NESARC) initially found that longer duration of abstinence decreased risk for SRO, but this effect disappeared upon controlling for psychiatric comorbidity (21).

A further question of theoretical and practical importance is whether prior SRO increases the risk of future smoking. In the single study that has addressed this question, longitudinal data obtained from adolescents showed that smoking predicted suicidal ideation and suicide attempts but prior suicidality was not associated with subsequent smoking (15).

The present study was conducted to address these conundrums of the smoking-suicide relationship: 1) whether prior smoking predicts SRO; 2) whether prior SRO predicts smoking; 3) whether smoking cessation and its corollary, duration of smoking abstinence, affects risk for SRO, and 4) whether these relationships are independent of comorbid psychiatric illness. Also explored were the effects of smoking status changes between the two waves of the NESARC on risk of future SRO. The two-wave format, the large sample, and extensive data on psychiatric comorbidity that characterized the NESARC (22) permitted assessment of these questions.

The survey instrument had asked questions regarding the past occurrence of SRO – want to die, suicidal ideation, and suicide attempt, only of persons reporting low mood. This restriction limits the generalizability of findings to the general population, but the much higher occurrence of suicidal behaviours among persons with low mood (3, 4) provided a more sensitive context for detecting the risk potential of smoking for suicidal behaviours (23).

METHODS

Sample: The NESARC data were collected to obtain a representative national sample of US adults. In Wave 1 (2001-2002), face-to-face interviews were completed with 43,093 persons aged 18 years or older. The overall response rate was 81.0%. The Wave 1 sample was re-interviewed in Wave 2 (2004-2005) three years later (mean interval=36.6 months, s.e.=2.62) with a response rate of 80.4% (N=34,653) based on the Wave 1 sample. The NESARC sample size was chosen to be sufficiently large to produce nationally representative proportions for the study of substance abuse and dependence and mental disorders by demographic group with confidence intervals equal to or smaller than extant studies. The NESARC study used a complex survey design and sampling weights upon responses to adjust for sample selection procedures, non-response from selected households or individuals, oversampling (of young adults, Blacks, and Hispanics), and non-response at the Wave 2 time point. The weights and survey design effects have been incorporated into the following results. Other methodological details of the NESARC have been described in published NESARC Source and Accuracy Statements (24, 25).

Data for the present study were obtained from a subset of persons (N=7,352) who reported low mood at the Wave 2 interview. The latter subsample is referred to herein and in the table as the "at-risk sample". Persons who did not report low mood were skipped out of the SRO sections in Waves 1 and 2. The questions for low mood at the Wave 2 interview were: "Since your LAST interview in (month/year), have you ever had a time when you felt sad, blue, depressed, or down most of the time for at least 2 weeks?" and "Since your LAST interview, have you ever had a time, lasting at least 2 weeks, when you didn't care about the things that you usually cared about, or when you didn't enjoy the things you usually enjoyed?" At the Wave 1 interview, respondents were asked these same questions referenced to their *entire lifetime*.

Variables: The outcome variables for this study were Wave 2 SRO and Wave 2 current smoking. The main covariates were prior SRO and smoking status at Wave 1. The individual SRO questions are: "During that time when (your mood was at its [sic] lowest/you enjoyed or cared the least about things), did you … feel like you wanted to die? think about committing suicide? attempt suicide?" Responses to these items were summed to create the total SRO question and measured as a dichotomous variable (none of the three=0; any of the three=1). Respondents who did not report low mood in Wave 1 and were not asked the SRO questions were assigned a value of 0 for prior SRO.

The questions on tobacco use at Wave 1 are: "In your ENTIRE LIFE, have you ever . . . (a) Smoked at least 100 cigarettes? (b) Smoked at least 50 cigars? (c) Smoked a pipe at least 50 times? (d) Used snuff, such as Skoal, Skoal Bandit [sic] or Copenhagen at least 20 times? (e) Used chewing tobacco, such as Redman, Levi Garrett or Beechnut at least 20 times?" Persons who smoked cigarettes, cigars and/or pipes, comprised (a weighted) 95.9% (3368/3497) of all tobacco users. Following the coding rule of the NESARC, all tobacco users, including the 129 persons who reported using snuff or chewing tobacco only, were labelled as "smokers". A *never smoker* had responded "No" to each of the questions regarding lifetime use of at least 100 cigarettes, at least 50 cigars, smoked a pipe at least 50 times, used snuff at least 20 times, and used chewing tobacco at least 20 times. A *former smoker* was a "Yes" responder to at least one of the prior questions who also reported that he or she had not smoked or used tobacco in the past 12 months. (N.B. Very few, if any, of this latter group would have been experiencing withdrawal; thus, the current study is not an adequate test of post-cessation withdrawal as a predictor of SRO). A *current smoker* was a "Yes" respondent who had smoked or used tobacco

within the past 12 months. At the Wave 2 interview, these same questions on tobacco use were asked with regard to the period since the last interview (month/year).

The smoking status variable (i.e., never, former, current) rather than DSM-IV defined nicotine dependence was selected to assess tobacco use because: 1) the adequacy of the DSM-IV criteria as a valid measure of nicotine dependence remains controversial (26, 27), and 2) response to the single question on smoking status is easier to elicit in the clinical setting, with more validity, than responses to a multi-item measure of tobacco use for which no consensus, stand-alone, instrument yet exists (26, 27). To categorize long-term or recent status as never, former, or current smokers, a change variable was created with the following categories according to their report of smoking at Waves 1 and 2: 1) never smoker to never smoker, 2) former smoker to former smoker, 3) current smoker to former smoker, 4) current smoker to current smoker, 5) never smoker to current smoker, 6) former smoker to current smoker, and 7) never smoker to former smoker.

Other potential confounders or effect modifiers because of their known correlations with smoking and/or SRO, measured at Wave 1, were: demographic characteristics (age, gender, race/ethnicity, marital status, education, employment status, income, urban residence, geographic region), and lifetime measures of DSM-IV Axis I and Axis II disorders. The Axis I disorders were categorized into mood disorders (major depression, dysthymia, bipolar I and bipolar II), anxiety disorders (panic disorder, social phobia, specific phobia, generalized anxiety), alcohol use disorders (alcohol abuse or dependence), and other substance use disorders (drug abuse or dependence). A history of Attention Deficit Hyperactivity Disorder (ADHD), queried only at Wave 2, was used among the Wave 1 predictors, its lifetime quality presumed since the DSM-IV criteria for ADHD include the presence of ADHD symptoms before age seven. All ten of the

Axis II personality disorders measured in AUDADIS-IV (shown in Table 1) were included as well.

Assessment: For both Waves 1 and 2, the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-IV) was administered by interviewers from the U.S. Census Bureau. The reliability and validity of the DSM-IV diagnoses obtained through the AUDADIS-IV have been demonstrated in clinical and general samples in the U.S. and in other countries (28).

Statistical Analysis: Weighted percentages and standard errors measured the distribution of the covariates (demographic characteristics and lifetime psychiatric variables) reported at Wave 1 for the sample with low mood and for the complementary sample of persons with no low mood. Chi-squared tests were used to assess differences between comparison groups, e.g., the at-risk sample and the complementary sample of NESARC participants who did not report low mood. Unadjusted and adjusted odds ratios (OR and AOR) and 95% confidence intervals (CI) were calculated from univariate logistic regressions and multivariate logistic regressions, respectively, to assess prediction of Wave 2 SRO in the sample of persons reporting low mood. respectively. The prevalence rates of SRO at Wave 2 by Wave 1 smoking status, prior SRO at Wave 1, and by all other covariates at Wave 1 were also calculated. The opposite temporal The opposite temporal relationship of prior SRO (reported in Wave 1) on future smoking (reported in Wave 2) was tested using the identical covariates for assessing predictors of Wave 2 SRO, following Granger (29). All models were estimated with the PROC SURVEYLOGISTIC function of SAS statistical software version 9.2, with the results verified through an internal statistical review at the U.S. Census Bureau.

Missing values were replaced through imputation using assignment and allocation methods (24, 25). Sensitivity analyses were performed that included: comparison of the at-risk subsample to the complementary Wave 2 NESARC sample; using different sets of control variables with and without education, Axis II personality disorders, and census region; and including help-seeking behavior controls. These analyses did not change the associations between smoking and SRO reported below.

RESULTS

Wave 1 Characteristics

Table 1 shows weighted percentages by smoking status, SRO taken together and individually, demographic characteristics, and psychiatric disorders (DSM-IV Axis I and Axis II) in the sample of persons reporting low mood at Wave 1 and the rest of the NESARC sample. Current smoking, SRO, and the prevalence of psychiatric disorders were markedly higher among the low mood sample, confirming their at-risk status. Other demographic characteristics previously associated with higher risk of suicide and SROs were also higher in the low mood subsample: more females, more low and fewer high income responders, fewer married, and more separated or never married, and more unemployed individuals. Differences by race/ethnicity, age, urban or rural residence, and geographic area were also observed.

Effects of Wave 1 characteristics on Wave 2 SRO

From here on, reported statistics are for the sample of persons reporting low mood at Wave 2. The overall incidence rate of SRO (occurring between the Wave 1 and Wave 2 interviews) was 28.2% (s.e.=0.33%). Table 2 shows weighted percentages and odds ratios for Wave 2 SRO by smoking history, prior SRO, and the control variables as reported in Wave 1.

Unadjusted odds ratios (OR) and 95% CI for future SRO are shown as reference points. The adjusted odds ratios (AOR) and 95% CI show significantly higher risk of Wave 2 SRO for both Wave 1 current smokers (AOR=1.41, 95% CI= 1.28, 1.55) and former smokers (AOR=1.32, 95% CI=1.21, 1.43) relative to never smokers. The difference in point estimates of risk between current versus former smokers was not significant ($\chi 2=1.95$, $p = 0.16$).

The multivariate model showed that SRO in Wave 1 is the strongest predictor of a Wave 2 SRO (AOR=3.49, 95% CI= 3.18, 3.84). Significant, independent risk of future SRO was also observed for individuals who were female, Hispanic, younger, cohabiting, divorced or separated, of lower income, unemployed, and resided outside the Northeast region. Of the DSM-IV Axis I disorders, only anxiety (AOR= 1.08, 95% CI=1.01, 1.17) and ADHD (AOR=1.56, 95% CI=1.36, 1.79) showed significantly elevated risk of Wave 2 SRO; mood disorder was correlated with reduced Wave 2 SRO risk (AOR=0.77; 95% CI=0.70, 0.84). Three of the DSM-IV Axis II disorders, i.e., borderline personality, schizotypal, and avoidant personality, showed significantly increased risk for Wave 2 SRO.

Smoking status change from Wave 1 to Wave 2

The great majority of the sample (90.5%) did not change their smoking status as never, former, or current smoker, between Waves 1 and 2 (Table 3). Among the remaining 9.5%, over half (5.3%) had shifted from being current smokers to former smokers; more than a fourth (2.6%) were never smokers in Wave 1 who became current smokers in Wave 2; and a smaller proportion (<2%) who were former smokers in Wave 1 relapsed to smoking in Wave 2.

a) *Effects on Wave 2 SRO*. Table 3 shows adjusted odds ratios indicating significant risk for SRO among all categories of ever-smokers relative to the persistent never smokers. The

highest risk was seen for relapsers (former smoker to current smoker) (AOR=3.42, 95% CI=2.85, 4.11); new smokers (never smoker to current smoker) showed the next highest risk (AOR=1.82, 95% CI=1.51, 2.19); and long-term former smokers (during both Wave 1 and 2) showed the least elevated, yet still significant, risk (AOR=1.22, 95% CI=1.12, 1.34). The seventh category consisting of never smokers in Wave 1 who reported former smoker status in Wave 2 was too small for a valid analysis.

b) *Comparative risks by abstinence duration, relapse, and new smoking.* Pair-wise chi-squared tests for equality of coefficients permitted a comparison of risk estimates for Wave 2 SRO (shown in Table 3) between categories of smoking status change. Given the three-year interval between Waves 1 and 2 and the coding requirement that former smoking status is assigned only upon reporting of at least 12 months of abstinence, long-term former smokers (Category 2, Table 3) would have been abstinent for at least four years. Persons who shifted from current smoking in Wave 1 to former smoking in Wave 2 (Category 3, Table 3) would have been abstinent for at least 12 months and a maximum of four years.

The analysis showed that the AOR for Wave 2 SRO among recent former smokers (Category 3) did not differ from persistent current smokers (Category 4) (χ^2 (1) =1.26, p=0.26). However, long-term former smokers (Category 2) showed a significantly lower AOR for Wave 2 SRO than persistent current smokers (χ^2 (1) =16.9, p<0.0001). These data suggest that a reduction in risk for future SRO with past smoking becomes apparent after a considerable period of abstinence. Of additional interest were the risk estimates associated with re-starting (i.e. relapse) and with beginning to smoke in Wave 2. Compared to persistent current smokers, the AOR for Wave 2 SRO was significantly higher for both relapsers (χ^2(1) =56.00, p<0.0001), and

smoking beginners in Wave 2 (χ^2 (1) =4.11, p=0.04). Further, the AOR for Wave 2 SRO was significantly higher among relapsers than beginning smokers (χ^2 (1)=19.0, p<0.0001).

Does prior SRO predict smoking?

A multiple regression model on current smoking in Wave 2 was fit using the identical list of control variables for predicting Wave 2 SRO. This second model did not show a direct effect of prior SRO on Wave 2 current smoking. Persons with Wave 1 SROs were *less* likely to report current smoking status at Wave 2 than were persons who did not experience SRO in Wave 1 (AOR=0.81, 95% CI=0.72, 0.90).

To understand the temporal relationship between smoking and SRO, the effects of the interaction of Wave 1 smoking status (current vs. never smoker and former vs. never smoker) with history of prior SRO were examined. Table 4 shows adjusted odds ratios from separate multiple regression models on SRO and on current smoking in Wave 2 for combined effects of smoking status and prior SRO reported in Wave 1. Never smokers without a prior SRO at Wave 1 were the reference group in each model. These analyses did not fundamentally change the finding that smoking predicts increased risk of SRO and that the reverse relationship does not hold, but indicates nuanced impact of both SRO and smoking history.

The model on Wave 2 SRO (Table 4 section a) shows that, other characteristics (e.g., demographics and psychopathology) being equal: a) all combinations of smoking status and SRO history had statistically significant risks for Wave 2 SRO relative to never smokers without prior SRO; and b) for each smoking category, the risks were considerably greater when the combined group involved a prior SRO. The data also show that former smoking and current smoking, in the absence of prior SRO, are valid predictors of an *initial* SRO. However, once a person has had

a SRO, smoking status history does not change the risk prediction - the risk of *recurrence* is fully predicted by that prior SRO and the other characteristics. The second model, on Wave 2 current smoking (Table 4 section b), shows an expectedly substantial likelihood of being a current smoker in Wave 2 for current smokers in Wave 1, regardless of SRO history. By contrast, prior SRO predicted a *reduction* in the likelihood of smoking uptake in Wave 2 for former smokers and never smokers.

DISCUSSION

The main findings from the present sample of persons reporting low mood are: 1) current and past smoking predicted increased risk for SRO independently of demographics, psychiatric factors, and prior SRO; 2) long-term smoking abstinence was associated with lower risk than persistent smoking; 3) new smoking due to relapse after a period of abstinence or to initiation of smoking by erstwhile never smokers was associated with an increased risk of SRO relative to persistent smoking; 4) prior SRO did not increase the risk of future smoking.

For three Axis I disorders, i.e., mood, alcohol use, and substance use, the adjusted odds ratios indicated either insignificant effects or a decreased risk of future SRO. These results differ from the increased risks yielded in the unadjusted analyses, indicating confounding effects of correlated predictors of SRO, for example, prior SRO and comorbid psychiatric disorders (3-5). In further analysis excluding prior SRO in the multivariate regression model, a positive, predictive effect of mood disorder on future SRO (AOR=2.05, 95% CI=1.92,2.17) was observed, contrary to the reduced effect of mood disorder in the full model that adjusted for prior SRO (results available upon request). This finding exemplifies an instance when collinearity with a stronger predictor (e.g., Wave 1 SRO) overwhelmed the explanatory power of other predictors

with weaker relationships. It is thus remarkable that significant effects of smoking on risk of SRO remained despite the evidence of effect suppression due to confounding. Ranked in decreasing order, the significant predictors of SRO risk in the present sample were: prior SRO, borderline personality disorder, ADHD, schizotypal disorder, current smoking, former smoking, avoidant personality disorder, and selected demographic characteristics.

Other than the present one, there have been seven longitudinal epidemiological studies of smoking and SRO (14-20). The positive effect of current smoking on future SRO reported here was also observed in three studies (14-16). Problems of recall due to the long, ten year, interval between data time points could explain the negative finding of the study by Kessler et al (17); while the younger age of the samples in two studies (19-20) could have masked a future effect. Of clinical and public health importance is the finding, first reported here, that longer abstinence from smoking decreased the risk for SRO. The latter observation, not considered in two negative studies regarding past smoking (14, 16), could account for the inconsistent findings. Notably, the divergence according to longevity of abstinence is consistent with evidence for lung cancer and other smoking-related disorders that risk reduction from stopping smoking occurs only after multiple years of abstinence (31, 32). The worrisome observation that relapsers and new smokers are at even higher risk of future SRO than persistent smokers suggests particular targets for increased therapeutic attention. Finally, the data negated a reverse temporal relationship of SRO on smoking, as also seen in a study of adolescents (15). Instead, a reduction in risk for future smoking was observed among former and never smokers with prior SRO in Wave 1 compared to their counterparts without prior SRO. Perhaps among those former and never smokers, already inclined towards the pro-health behaviour of not currently smoking, was a subset spurred by the prior SRO to undertake further health-promoting and therapeutic actions,

which immunized them against future smoking. Their counterparts who did not experience a prior SRO were less likely to be as self-protective or to seek counselling and similar treatments, and were less immunized against resorting to new smoking. The serendipitous observation from the present sample that prior SRO and treatment seeking were well-correlated (r=0.43, p=0.0001) is consistent with that conjecture.

Strengths and limitations of the study are noted. An important strength is the concomitance of rigorous methods and materials not found in prior work on the smoking-suicide question – face-to-face interviews, a longitudinal design, a large sample, a validated instrument, and a comprehensive range of putative predictors that permitted statistical control of the key background factors and comorbidities. A further strength is the use of a simple yet meaningful measure of smoking status (i.e., never, former or current smoking), that is easy for a questioner to administer and for the respondent to recall and understand. Even so, study limitations call for cautious interpretation of the findings. The present sample comprised the subgroup (22%) of Wave 2 participants (N=34,653) who self-reported low mood during the three-year interval between the interviews. This selectivity yields findings relevant to mental health settings that are likely to serve persons experiencing mood problems; however, they may not generalize to the rest of the NESARC sample or to the national population. Second, the sample did not include persons who had completed suicide attempts. Using the U.S. rate of 11.1 per 100,000 population per year (30), the Wave 1 sample of 43,093 could be expected to include about 14 persons with completed suicides before Wave 2 (95% CI= 6.8, 21.6), introducing a non-trivial, although likely small, selection bias. Third, the present study did not assess the effects of medical conditions which are possibly causally related, albeit in different directions, to smoking and to SRO. Fourth, the NESARC did not obtain information from adolescents, a subgroup with a known high risk

for SRO (2). Finally, in exploratory, unadjusted, analyses, predictive effects of current smoking were observed across the individual SRO whereas past smoking predicted want to die and suicidal ideation, but not suicide attempt. Validation and articulation of these preliminary observations need to be accomplished in future work.

The rigorous methodology employed in the NESARC gives eminent credence to the central findings of this analysis - an independent effect of smoking on SRO and the absence of a positive influence of prior SRO on future smoking. These results are consistent with the hypothesis that smoking exerts a contributing, and not simply a correlational, effect on risk of SRO. By contrast, these results are inconsistent with the hypothesis that SRO causes smoking or that a third factor causes both smoking and SRO. The neurobiological, genetic, psychiatric and psychological underpinnings of these associations warrant further investigation. The knowledge gained could advance prevention and treatment options for reducing the prevalence of tobacco use and suicide.

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spouses of the authors had financial relationships that may be relevant to the submitted work; 6) none of the authors had a non-financial interest that may be relevant to the submitted work.

Lirio Covey and Ivan Berlin conceptualized this study and, with Mei-Chen Hu, designed the analysis. Jahn Hakes had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Lirio Covey was the lead writer of the manuscript. All authors participated in the interpretation of findings and writing of the manuscript. All authors had full access to the statistical reports, tables, and the manuscript; and take responsibility for the integrity of the data and the accuracy of the data analysis. The U.S. Census Bureau, NIAAA, and other employers of the authors had no role in the study design, implementation of the study, analysis and interpretation of data, in the writing of the report, and the decision to submit the article for publication.

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The study is a secondary analysis of data collected by the National Institute of Health-National Institute of Alcohol and Alcohol Abuse of the US government. Before data collection, each respondent was informed of the nature of the survey and its potential uses, ensured of confidentiality, and told that participation was voluntary. All participants signed a consent form prior to participating in the interviews. The US Census Bureau and the US Office of Management and Budget reviewed and approved the ethics protocol. Individual data files are de-identified to prevent full anonymity of participants. Approval for conducting this secondary analysis of previously collected data was not required.

In order to safeguard sensitive personal information, NESARC data are not available for public use. The restricted use data sets are maintained by the U.S. Census Bureau on behalf of NIAAA, and any requests to use NESARC data for replication or other purposes may be directed to the NIAAA coordinator for NESARC, Aaron White (whitea4@mail.nih.gov).

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Table 1: Wave 1 characteristics of the low mood sample and the rest of the NESARC Wave 2 sample. Weighted percentages[a] (%) and standard error (s.e)

Variable	Total Wave 2 sample %	s.e.	Low mood Sample[b] %	s.e.	Rest of sample[c] %	s.e.
Total n	34,653		7,352		27,301	
Smoking status						
Current smoker	27.02	0.17	31.65	0.38	25.85	0.19
Former smoker	19.58	0.16	17.84	0.28	20.02	0.17
Never smoker	53.40	0.19	50.51	0.42	54.13	0.20
Wave 1 Suicide related outcomes (SRO)	11.42	0.10	25.55	0.27	7.84	0.10
Want to die	10.17	0.10	23.35	0.26	6.82	0.10
Suicidal ideation	8.42	0.09	19.27	0.27	5.66	0.09
Suicide attempt	2.35	0.04	6.09	0.17	1.40	0.04
Demographics						
Gender						
Female	52.08	0.16	64.13	0.40	49.02	0.17
Male	47.92	0.16	35.87	0.40	50.98	0.17
Race/Ethnicity						
White	70.93	0.24	71.39	0.40	70.81	0.25
Black	10.75	0.20	10.61	0.22	10.79	0.21
Hispanic	11.56	0.10	11.20	0.15	11.65	0.12
Asian/Pac. Islander	4.36	0.06	3.50	0.10	4.58	0.06
Amer. Indian/Alaska Native	2.40	0.11	3.29	0.20	2.17	0.11
Age: 18-19	4.02	0.07	4.47	0.15	3.91	0.08
20-29	17.78	0.14	19.28	0.30	17.40	0.15
30-44	30.90	0.17	32.28	0.29	30.54	0.18
45-64	31.08	0.15	31.64	0.24	30.94	0.17
65and over	16.22	0.10	12.32	0.25	17.21	0.12
Household Income:						
Less than $20,000	20.35	0.17	25.07	0.32	19.15	0.19
$20,000 to $34,999	19.62	0.13	20.84	0.27	19.31	0.15
$35,000 to $59,999	26.27	0.16	24.85	0.31	26.63	0.17
$60,000 and over	33.76	0.16	29.24	0.33	34.91	0.17
Marital status:						
Married	59.81	0.17	54.75	0.35	61.10	0.17
Cohabiting	3.25	0.06	3.60	0.11	3.16	0.07
Widowed	6.04	0.07	5.37	0.12	6.21	0.08
Divorced	8.45	0.06	10.73	0.19	7.87	0.07
Separated	1.98	0.04	2.98	0.12	1.73	0.04
Never Married	20.46	0.17	22.57	0.33	19.93	0.17

Education:						
Less than HS	14.65	0.13	16.25	0.26	14.24	0.14
High School diploma	29.03	0.18	29.35	0.35	28.95	0.20
College	56.32	0.22	54.40	0.38	56.81	0.23
Unemployed	7.16	0.09	12.31	0.25	5.85	0.09
Not unemployed	92.84	0.09	87.69	0.25	94.15	0.09
Urban	28.89	0.26	30.59	0.41	28.46	0.25
Rural/Not in Central City	71.11	0.26	69.41	0.41	71.54	0.25
Northeast	19.67	0.08	18.57	0.15	19.95	0.10
Midwest	23.15	0.16	23.52	0.32	23.05	0.21
South	35.21	0.15	34.89	0.39	35.29	0.19
West	21.97	0.11	23.02	0.23	21.71	0.15
Lifetime Psychiatric Disorders						
Axis I Disorders						
Alcohol Use	30.43	0.20	33.57	0.39	29.63	0.20
Substance Use	10.42	0.11	15.06	0.26	9.25	0.11
Nicotine Dependence	17.47	0.13	24.33	0.37	15.73	0.13
Anxiety disorder	17.88	0.17	31.00	0.34	14.55	0.17
Mood disorder	21.09	0.13	41.82	0.33	15.82	0.13
Attention Deficit/Hyperactivity	2.51	0.06	5.82	0.19	1.67	0.05
Axis II Disorders						
Borderline	5.89	0.08	18.44	0.28	2.70	0.07
Schizotypal	3.93	0.06	11.20	0.24	2.09	0.05
Narcissistic	6.18	0.08	11.88	0.23	4.74	0.08
Avoidant	2.32	0.05	6.14	0.17	1.36	0.05
Antisocial	3.63	0.07	5.86	0.21	3.07	0.07
Dependent	0.43	0.02	1.36	0.09	0.19	0.01
Obsessive-Compulsive	8.07	0.10	13.50	0.31	6.69	0.09
Paranoid	4.33	0.07	9.66	0.21	2.98	0.06
Schizoid	3.06	0.06	6.44	0.21	2.21	0.05
Histrionic	1.80	0.04	3.68	0.15	1.32	0.04

[a]The sampling weight variable in Wave 2 was used.

[b]Respondents in NESARC Wave 2 who reported low mood lasting two weeks or more during the three-year interval covered in the Wave 2 NESARC and were asked the three suicidal behavior questions.

[c]Respondents in NESARC Wave 2 who did not report low mood and were not asked the three suicidal questions.

Table 2: Percentage of suicide related outcomes (SRO)[a] reported in Wave 2 by Wave 1 characteristics, and unadjusted and adjusted odds ratios for risk of Wave 2 SRO among persons reporting low mood at the NESARC Wave 2 interview. (N=7352)[b]

Variable	% of Wave 2 SRO	Standard error	OR[c]	95% CI	AOR[d]	95% CI
Smoking history						
Current smoker in Wave 1	35.73	0.64	1.77	1.64, 1.90	1.41	1.28, 1.55
Former Smoker in Wave 1	26.68	0.67	1.16	1.07, 1.25	1.32	1.21, 1.43
Never Smoker in Wave 1	23.94	0.43	1.00		1.00	
SRO in Wave 1	50.01	0.76	3.84	3.60, 4.10	3.49	3.18, 3.84
Demographics						
Female	28.51	0.36	1.05	0.98, 1.12	1.13	1.04, 1.22
Male	27.54	0.59	1.00		1.00	
White	28.38	0.36	1.00		1.00	
Black	26.53	0.70	0.91	0.84, 0.99	0.84	0.76, 0.92
Hispanic	30.33	0.52	1.10	1.04, 1.17	1.26	1.16, 1.36
Asian/Pacific Islander	22.68	0.84	0.74	0.67, 0.82	0.93	0.82, 1.06
American Indian	27.18	2.81	0.94	0.71, 1.25	0.69	0.51, 0.92
Age 18-19	36.65	1.73	1.00		1.00	
Age 20-29	31.40	0.67	0.83	0.69, 0.98	0.77	0.63, 0.94
Age 30-44	29.32	0.62	0.75	0.64, 0.88	0.73	0.60, 0.90
Age 45-64	26.82	0.63	0.66	0.56, 0.78	0.69	0.56, 0.84
Age 65 and over	20.90	0.93	0.47	0.39, 0.57	0.68	0.54, 0.86
Married	24.87	0.49	1.00		1.00	
Cohabiting	35.58	1.67	1.67	1.42, 1.96	1.27	1.07, 1.51
Widowed	24.26	1.09	0.97	0.85, 1.10	0.92	0.78, 1.07
Divorced	36.01	0.84	1.70	1.57, 1.84	1.20	1.10, 1.32
Separated	37.93	1.78	1.85	1.58, 2.15	1.29	1.06, 1.56
Never married	30.87	0.69	1.35	1.24, 1.46	0.97	0.87, 1.09
Less than High School	31.58	0.92	1.17	1.04, 1.32	1.09	0.95, 1.25
High School Diploma	28.27	0.74	1.00		1.00	
Some College or more	27.08	0.35	0.94	0.87, 1.02	1.08	1.00, 1.17
Unemployed	39.93	1.17	1.84	1.68, 2.03	1.28	1.13,1.45
Not unemployed	26.51	0.32	1.00		1.00	

Urban	29.30	0.38	1.08		1.03	0.97, 1.10
Rural	27.66	0.46	1.00	1.02, 1.15	1.00	
Lifetime Psychiatric Disorders						
Axis I Disorders						
Alcohol Use	32.74	0.60	1.40	1.31, 1.49	0.95	0.87, 1.04
Substance Use	38.42	0.94	1.75	1.61, 1.89	0.98	0.88, 1.09
Anxiety	37.57	0.60	1.72	1.62, 1.83	1.08	1.01, 1.17
Mood	36.62	0.48	2.04	1.92, 2.17	0.77	0.70, 0.84
Attention Deficit Hyperactivity Disorder	51.14	1.42	2.87	2.56, 3.22	1.56	1.36, 1.79
Axis II Disorders						
Borderline	55.75	0.79	4.49	4.22, 4.77	2.91	2.69, 3.16
Schizotypal	53.41	1.26	3.44	3.09, 3.84	1.50	1.31, 1.72
Narcissistic	42.49	1.01	2.08	1.89, 2.29	1.03	0.92, 1.14
Avoidant	51.87	1.37	2.97	2.66, 3.32	1.29	1.05, 1.58
Antisocial	41.55	1.39	1.89	1.68, 2.13	0.85	0.72, 1.01
Dependent	56.90	2.90	3.44	2.74, 4.30	1.04	0.76, 1.41
Ob-Com	36.07	1.05	1.53	1.39, 1.69	0.90	0.80, 1.00
Paranoid	45.74	1.16	2.37	2.14, 2.62	0.95	0.82, 1.10
Schizoid	43.81	1.26	2.10	1.89, 2.33	1.01	0.88, 1.16
Histrionic	44.42	1.83	2.10	1.82, 2.43	0.76	0.63, 0.93

[a]SRO (Suicide related outcome: feel like want to die, suicide ideation, suicide attempt; 0=None, 1=any SRO).

[b]Missing observations for specific variables: Race – 43, Hispanic origin – 2, age – 13, marital status-4, educational attainment – 70, household income-2544, unemployed – 28, Wave 2 individual suicide related outcomes – 12-18 "unknown" changed to "no". Treatment of unknown values in determination of psychiatric diagnosis variables is known only to original NESARC project staff at NIAAA.

[c]Odds Ratios (OR) and 95% confidence intervals (CI) based on simple regression models estimating Wave 2 SRO as a function of an individual predictor variable.

[d]Adjusted Odds Ratios (AOR) and 95% CI based on a multiple logistic regression estimating Wave 2 SRO as a function of age, sex, race/ethnicity, marital status, income, education, unemployed status, Census region, urban residence, smoking status, Axis I and Axis II disorders (as described in text), and lifetime SRO prior to Wave 1.

Table 3: Effects on Wave 2 suicide related outcomes (SRO) according to smoking status change as reported in NESARC Wave 1 and Wave 2 interviews.

			Wave 2 SRO[a]	
Smoking status in Wave 1 to Wave 2	N	Weighted percentage[b] (standard error)	AOR[c]	(95% CI)
1. Consistent never smoker (in Wave 1 and Wave 2)	3653	47.8 (0.40)	1.00	
2.Long-term former smoker (in Wave 1 and Wave 2)	1185	16.4 (0.26)	1.22	(1.12, 1.34)
3. Recent former smoker (current smoker in Wave 1, former smoker in Wave 2)	393	5.3 (0.14)	1.37	(1.16, 1.63)
4. Persistent current smoker (in Wave 1 and Wave 2)	1824	26.3 (0.35)	1.50	(1.35, 1.66)
5. New current smoker (never smoker in Wave 1, current smoker in Wave 2)	194	2.6 (0.10)	1.82	(1.51, 2.19)
6. Relapser (former smoker in Wave 1, current smoker in Wave 2)	95	1.5 (0.08)	3.42	(2.85, 4.11)
	N=7352[d]			

[a]Any of three items: want to die, suicidal ideation, suicide attempt

[b]The sampling weight variable in Wave 2 was used.

[c]AORs are adjusted odds ratio with 95% confidence intervals (CI) based on multiple logistic regression of Wave 2 SRO as a function of age, sex, race/ethnicity, marital status, income, education, unemployed status, Census region, urban residence, smoking status, Axis I and Axis II disorders (as described in text), and lifetime SRO reported in Wave 1.

[d]The seventh group (n=8), which consisted of persons who were never smokers in Wave 1, began to smoke and then stopped smoking in Wave 2, was too small for a valid assessment of risk.

Table 4: Combined effects of smoking status and prior SRO[a] reported in Wave 1 on a) Wave 2 SRO and b) Wave 2 current smoking

Wave 1 Smoking status and Wave 1 SRO	Frequency/ N	Weighted percentages (standard error)	AOR[b]	95% CI
a) Effect on Wave 2 SRO				
Never smoker - No prior SRO (referent)	550 /2978	17.5 (0.4)	1.00	N.A.[c]
Never smoker - Prior SRO	431 / 877	46.8 (1.0)	4.12	3.65,4.64
Former smoker - No prior SRO	187 / 968	20.6 (0.8)	1.42	1.28,1.57
Former smoker - Prior SRO	152 / 312	48.2 (1.6)	4.58	3.60,5.82
Current smoker - No prior SRO	383 /1466	26.6 (0.7)	1.56	1.41,1.74
Current smoker - Prior SRO	426 / 751	54.1 (1.2)	4.77	3.70,5.87
b) Effect on Wave 2 Current smoking				
Never smoker – No prior SRO (referent)	166 /2978	5.3 (0.2)	1.00	N.A.[c]
Never smoker –Prior SRO	28 / 877	4.3 (0.4)	0.70	0.60-0.82
Former smoker – No prior SRO	71 / 968	8.6 (0.5)	2.20	1.77-2.31
Former smoker – Prior SRO	24 / 312	6.9 (0.6)	1.15	0.83-1.61
Current smoker – No prior SRO	1204 /1466	82.7 (0.5)	82.9	73.7-93.2
Current smoker – Prior SRO	620 / 751	84.2 (0.8)	77.0	57.6-104.8

[a]Any of three items: want to die, suicidal ideation, suicide attempt

[b]AORs are adjusted odds ratios with 95% confidence intervals (CI) based on multiple logistic regression models controlling for demographics and psychiatric history at Wave 1 (shown in Table 1).

[c]Not applicable

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Smoking and suicidal behaviors in a sample of US adults with low mood: a retrospective analysis of longitudinal data

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Smoking and suicidal behaviors in a sample of US adults with low mood: a retrospective analysis of longitudinal data

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ABSTRACT

Objective: To investigate whether: 1) smoking predicts suicide related outcomes (SRO); 2) prior SRO predicts smoking, 3) smoking abstinence affects the risk of SRO, 4) psychiatric comorbidity modifies the relationship between smoking and SRO.

Design: Retrospective analysis of longitudinal data obtained in Wave 1 (2001-2002) and Wave 2 (2004-2005) of the National Epidemiologic Survey of Alcohol and Related Conditions.

Setting: Face-to-face interviews conducted with persons in the community.

Participants: US adults (N=43,093) aged 18 years or older were interviewed in Wave 1 and re-interviewed (N=34,653) three years later. For the present study, the sample was the subset of persons (N=7,352) who at the Wave 2 interview reported low mood lasting two weeks or more during the past three years and were further queried regarding SRO occurring between Waves 1 and 2.

Outcome measures: SRO composed of any of: 1) want to die, 2) suicidal ideation, 3) suicide attempt, reported at Wave 2. Current smoking reported at Wave 2.

Results: Current and former smoking in Wave 1 predicted increased risk for Wave 2 SRO independently of prior SRO, psychiatric history, and socio-demographic characteristics measured in Wave 1 (Adjusted Odds Ratio (AOR) =1.41, 95% CI=1.28 to 1.55 for current smoking; AOR=1.32, 95% CI=1.21 to 1.43 for former smoking). Prior SRO did not predict current smoking in Wave 2. Compared with persistent never smokers, risk for future SRO was highest among relapsers (AOR=3.42, 95% CI=2.85 to 4.11); next highest among smoking beginners at Wave 2 (AOR=1.82, 95% CI=1.51 to 2.19); and lowest among long-term (four+ years) former smokers (AOR=1.22, 95% CI=1.12 to 1.34). Compared with persistent current

smokers, risk for SRO was lower among long-term (p<0.0001), but not shorter-term (p=0.26) abstainers.

Conclusion: Smoking increased the risk of future SRO independently of psychiatric comorbidity. Abstinence of several years duration reduced that risk.

Word count= 298

Article Summary

Article focus

To investigate among persons reporting low mood lasting two weeks or more during the past three years whether:

- smoking predicts suicide related outcomes (want to die, suicidal ideation, suicide attempt); prior suicide related outcomes predict smoking,
- smoking abstinence affects the risk of suicide related outcomes,
- psychiatric comorbidity modifies the relationship between smoking and suicide related outcomes.

Key messages

- Current and former smoking (less than 4 years' reported abstinence) predicted increased risk for suicide related outcomes independently of prior suicide related outcomes, psychiatric history, and socio-demographic characteristics.
- Prior suicide related outcomes did not predict future current smoking.
- Compared with persistent current smokers, risk of suicide related outcomes was reduced with long-term (≥4 years) but not with shorter-term (<4 years) abstinence.

Strengths and limitations

Strengths

- Face-to-face interviews, a longitudinal design, a large representative sample, a validated diagnostic instrument, a comprehensive range of putative predictors that permitted statistical control of the key background factors and comorbidities.

Limitations

- Only persons with self-reported low mood were questioned about suicide related outcomes; consequently, no generalizability to other populations.
- The sample did not include persons who had completed suicide.
- No assessment of the effects of medical conditions which are possibly causally related to smoking and to suicide related outcomes.
- No information from adolescents, a high risk population for both smoking and suicide related outcomes.

INTRODUCTION

Suicide is a leading cause of death worldwide. Close to one million persons die from suicide each year. The World Health Organization predicts that by 2020 suicide deaths will rise to 1.5 million (1). Completed suicides are largely predicted by the wish to die, thoughts of suicide, and unsuccessful previous suicidal attempts (2), making it important to understand the risks posed by suicide related outcomes (SRO). A history of mental disorders (3-5) and particular demographic characteristics (female gender, younger age, unmarried status, and unemployment) are putative risk factors for suicide and SRO (2). Smoking, long known as a major risk factor for numerous medical illnesses (6), and recently, for psychiatric outcomes as well (7, 8) has received increasing attention for its potential contribution to the risk of completed suicides and SRO (9). Nevertheless, whether the association between smoking and suicidal behaviours is causal or correlational remains unclear.

A link between smoking and suicide was observed as early as 1976 by Doll and Peto in their study of mortality due to smoking in male British doctors (10). Clinical and epidemiological studies that subsequently investigated the issue are in general, but not universal, agreement in finding a significant association between smoking and suicide and suicidal behaviors. Among studies that focused on SRO, three that used cross-sectional epidemiological data found a positive correlational association between smoking and SRO (11-13). Of seven longitudinal studies that also utilized community-based data, three (14-16) found that current smoking predicted suicidal behaviors even after controlling for the effects of demographic and psychiatric variables; four studies did not find a positive relationship (17-20).

The effect of smoking abstinence on risk of SRO is also unclear. A study of young adults followed for 10 years found that recent, but not pre-survey, cigarette smoking predicted suicidal

thoughts and attempts (14). Another study showed higher incidence rates of suicidal ideation among former smokers than never smokers, but the difference was no longer significant after adjustment with depressive disorder, anxiety symptoms, and alcohol dependence (16). A study based on Wave 1 data from the National Epidemiological Survey of Alcohol and Related Conditions (NESARC) initially found that longer duration of abstinence decreased risk for SRO, but this effect disappeared upon controlling for psychiatric comorbidity (21).

A further question of theoretical and practical importance is whether prior SRO increases the risk of future smoking. In the single study that has addressed this question, longitudinal data obtained from adolescents showed that smoking predicted suicidal ideation and suicide attempts but prior suicidality was not associated with subsequent smoking (15).

The present study was conducted to address these conundrums of the smoking-suicide relationship: 1) whether prior smoking predicts SRO; 2) whether prior SRO predicts smoking; 3) whether smoking cessation and its corollary, duration of smoking abstinence, affects risk for SRO, and 4) whether these relationships are independent of comorbid psychiatric illness. Also explored were the effects of smoking status changes between the two waves of the NESARC on risk of future SRO. The two-wave format, the large sample, and extensive data on psychiatric comorbidity that characterized the NESARC (22) permitted assessment of these questions.

The survey instrument had asked questions regarding the past occurrence of SRO – want to die, suicidal ideation, and suicide attempt, only of persons reporting low mood. This restriction limits the generalizability of findings to the general population, but the much higher occurrence of suicidal behaviours among persons with low mood (3, 4) provided a more sensitive context for detecting the risk potential of smoking for suicidal behaviours (23).

METHODS

Sample: The NESARC data were collected to obtain a representative national sample of US adults. In Wave 1 (2001-2002), face-to-face interviews were completed with 43,093 persons aged 18 years or older. The overall response rate was 81.0%. The Wave 1 sample was re-interviewed in Wave 2 (2004-2005) three years later (mean interval=36.6 months, s.e.=2.62) with a response rate of 80.4% (N=34,653) based on the Wave 1 sample. The NESARC sample size was chosen to be sufficiently large to produce nationally representative proportions for the study of substance abuse and dependence and mental disorders by demographic group with confidence intervals equal to or smaller than extant studies. The NESARC study used a complex survey design and sampling weights upon responses to adjust for sample selection procedures, non-response from selected households or individuals, oversampling (of young adults, Blacks, and Hispanics), and non-response at the Wave 2 time point. Those weights and survey design effects, employed in other studies based on NESARC data, as well as other methodological details of Waves 1 and 2 are described in published NESARC Source and Accuracy Statements (24, 25).

Data for the present study were obtained from a subset of persons (N=7,352) who reported low mood at the Wave 2 interview, irrespective of low mood in Wave 1. This subsample was selected for the present analysis because it produced the largest number of persons from whom evaluable information for predicting Wave 2 SRO was available. The latter subsample is also referred to herein as the "at-risk sample". Persons who did not report low mood were skipped out of the SRO sections in Waves 1 and 2. The questions for low mood at the Wave 2 interview were: "Since your LAST interview in (month/year), have you ever had a time when you felt sad, blue, depressed, or down most of the time for at least 2 weeks?" and "Since

your LAST interview, have you ever had a time, lasting at least 2 weeks, when you didn't care about the things that you usually cared about, or when you didn't enjoy the things you usually enjoyed?" At the Wave 1 interview, respondents were asked these same questions referenced to their *entire lifetime*.

Variables: The outcome variables for this study were Wave 2 SRO and Wave 2 current smoking. The main covariates were prior SRO and smoking status at Wave 1. The individual SRO questions are: "During that time when (your mood was at its [sic] lowest/you enjoyed or cared the least about things), did you … feel like you wanted to die? think about committing suicide? attempt suicide?" Responses to these items were summed to create the total SRO question and measured as a dichotomous variable (none of the three=0; any of the three=1). Respondents who did not report low mood in Wave 1 and were not asked the SRO questions were assigned a value of 0 for prior SRO.

The questions on tobacco use at Wave 1 are: "In your ENTIRE LIFE, have you ever . . . (a) Smoked at least 100 cigarettes? (b) Smoked at least 50 cigars? (c) Smoked a pipe at least 50 times? (d) Used snuff, such as Skoal, Skoal Bandit [sic] or Copenhagen at least 20 times? (e) Used chewing tobacco, such as Redman, Levi Garrett or Beechnut at least 20 times?" Persons who smoked cigarettes, cigars and/or pipes, comprised (a weighted) 95.9% (3368/3497) of all tobacco users. Following the coding rule of the NESARC, all tobacco users, including the 129 persons who reported using snuff or chewing tobacco only, were labelled as "smokers". A *never smoker* had responded "No" to each of the questions regarding lifetime use of at least 100 cigarettes, at least 50 cigars, smoked a pipe at least 50 times, used snuff at least 20 times, and used chewing tobacco at least 20 times. A *former smoker* was a "Yes" responder to at least one of the prior questions who also reported that he or she had not smoked or used tobacco in the

past 12 months. (N.B. Very few, if any, of this latter group would have been experiencing withdrawal; thus, the current study is not an adequate test of post-cessation withdrawal as a predictor of SRO). A *current smoker* was a "Yes" respondent who had smoked or used tobacco within the past 12 months. At the Wave 2 interview, these same questions on tobacco use were asked with regard to the period since the last interview (month/year).

The smoking status variable (i.e., never, former, current) rather than DSM-IV defined nicotine dependence was selected to assess tobacco use because: 1) the adequacy of the DSM-IV criteria as a valid measure of nicotine dependence remains controversial (26, 27), and 2) response to the single question on smoking status is easier to elicit in the clinical setting, with more validity, than responses to a multi-item measure of tobacco use for which no consensus, stand-alone, instrument yet exists (26, 27). To categorize long-term or recent status as never, former, or current smokers, a change variable was created with the following categories according to their report of smoking at Waves 1 and 2: 1) never smoker to never smoker, 2) former smoker to former smoker, 3) current smoker to former smoker, 4) current smoker to current smoker, 5) never smoker to current smoker, 6) former smoker to current smoker, and 7) never smoker to former smoker.

Other potential confounders or effect modifiers because of their known correlations with smoking and/or SRO, measured at Wave 1, were: demographic characteristics (age, gender, race/ethnicity, marital status, education, employment status, income, urban residence, geographic region), and lifetime measures of DSM-IV Axis I and Axis II disorders. The Axis I disorders were categorized into mood disorders (major depression, dysthymia, bipolar I and bipolar II), anxiety disorders (panic disorder, social phobia, specific phobia, generalized anxiety), alcohol use disorders (alcohol abuse or dependence), and other substance use disorders (drug abuse or

dependence). A history of Attention Deficit Hyperactivity Disorder (ADHD), queried only at Wave 2, was used among the Wave 1 predictors, its lifetime quality presumed since the DSM-IV criteria for ADHD include the presence of ADHD symptoms before age seven. All ten of the Axis II personality disorders measured in AUDADIS-IV (shown in Table 1), measured at Wave 1, were included as well.

Assessment: For both Waves 1 and 2, the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-IV) was administered by interviewers from the U.S. Census Bureau. The reliability and validity of the DSM-IV diagnoses obtained through the AUDADIS-IV have been demonstrated in clinical and general samples in the U.S. and in other countries (28).

Statistical Analysis: Weighted percentages and standard errors measured the distribution of the covariates (demographic characteristics and lifetime psychiatric variables) reported at Wave 1 for the sample with low mood and for the complementary sample of persons with no low mood. Chi-squared tests were used to assess differences between comparison groups, e.g., the at-risk sample and the complementary sample of NESARC participants who did not report low mood. Unadjusted and adjusted odds ratios (OR and AOR) and 95% confidence intervals (CI) were calculated from univariate logistic regressions and multivariate logistic regressions, respectively, to assess prediction of Wave 2 SRO in the sample of persons reporting low mood. respectively. The incidence of SRO at Wave 2 (since the Wave 1 interview) by smoking status, prior SRO, and all other covariates at Wave 1, were also calculated. The opposite temporal relationship of prior SRO (reported in Wave 1) on future current smoking (reported in Wave 2) was tested using the identical covariates for assessing predictors of Wave 2 SRO, following Granger (29). All models were estimated with the PROC SURVEYLOGISTIC function of SAS

statistical software version 9.2, with the results verified through an internal statistical review at the U.S. Census Bureau.

Missing values were replaced through imputation using assignment and allocation methods as described in the NESARC Source and Accuracy Statements (24, 25). Sensitivity analyses were performed that included: comparison of the at-risk subsample to the complementary Wave 2 NESARC sample; using different sets of control variables with and without education, and census region; and including help-seeking behavior controls. These analyses did not change the associations between smoking and SRO reported below.

RESULTS

Wave 1 Characteristics

Table 1 shows weighted percentages by smoking status, SRO taken together and individually, demographic characteristics, and psychiatric disorders (DSM-IV Axis I and Axis II) in the sample of persons reporting low mood at Wave 1 and the rest of the NESARC sample. Current smoking, SRO, and the prevalence of psychiatric disorders were markedly higher among the low mood sample, confirming their at-risk status. Other demographic characteristics previously associated with higher risk of suicide and SROs were also higher in the low mood subsample: more females, more low and fewer high income responders, fewer married, and more separated or never married, and more unemployed individuals. Differences by race/ethnicity, age, urban or rural residence, and geographic area were also observed.

Effects of Wave 1 characteristics on Wave 2 SRO

From here on, reported statistics are for the sample of persons reporting low mood at Wave 2. The overall incidence rate of SRO (occurring between the Wave 1 and Wave 2 interviews) was 28.2% (s.e.=0.33%). Table 2 shows weighted percentages and odds ratios for Wave 2 SRO by smoking history, prior SRO, and the control variables as reported in Wave 1. Unadjusted odds ratios (OR) and 95% CI for future SRO are shown as reference points. The adjusted odds ratios (AOR) and 95% CI show significantly higher risk of Wave 2 SRO for both Wave 1 current smokers (AOR=1.41, 95% CI= 1.28, 1.55) and former smokers (AOR=1.32, 95% CI=1.21, 1.43) relative to never smokers. The difference in point estimates of risk between current versus former smokers was not significant ($\chi 2=1.95$, $p = 0.16$).

The multivariate model showed that SRO in Wave 1 is the strongest predictor of a Wave 2 SRO (AOR=3.49, 95% CI= 3.18, 3.84). Significant, independent risk of future SRO was also observed for individuals who were female, Hispanic, younger, cohabiting, divorced or separated, of lower income, unemployed, and resided outside the Northeast region. Of the DSM-IV Axis I disorders, only anxiety (AOR= 1.08, 95% CI=1.01, 1.17) and ADHD (AOR=1.56, 95% CI=1.36, 1.79) showed significantly elevated risk of Wave 2 SRO; mood disorder was correlated with reduced Wave 2 SRO risk (AOR=0.77; 95% CI=0.70, 0.84). Three of the DSM-IV Axis II disorders, i.e., borderline personality, schizotypal, and avoidant personality, showed significantly increased risk for Wave 2 SRO.

Smoking status change from Wave 1 to Wave 2

The great majority of the sample (90.5%) did not change their smoking status as never, former, or current smoker, between Waves 1 and 2 (Table 3). Among the remaining 9.5%, over half (5.3%) had shifted from being current smokers to former smokers; more than a fourth

(2.6%) were never smokers in Wave 1 who became current smokers in Wave 2; and a smaller proportion (<2%) who were former smokers in Wave 1 relapsed to smoking in Wave 2.

a) *Effects on Wave 2 SRO*. Table 3 shows adjusted odds ratios indicating significant risk for SRO among all categories of ever-smokers relative to the persistent never smokers. The highest risk was seen for relapsers (former smoker to current smoker) (AOR=3.42, 95% CI=2.85, 4.11); new smokers (never smoker to current smoker) showed the next highest risk (AOR=1.82, 95% CI=1.51, 2.19); and long-term former smokers (during both Wave 1 and 2) showed the least elevated, yet still significant, risk (AOR=1.22, 95% CI=1.12, 1.34). The seventh category consisting of never smokers in Wave 1 who reported former smoker status in Wave 2 was too small for a valid analysis.

b) *Comparative risks by abstinence duration, relapse, and new smoking.* Pair-wise chi-squared tests for equality of coefficients permitted a comparison of risk estimates for Wave 2 SRO (shown in Table 3) between categories of smoking status change. Given the three-year interval between Waves 1 and 2 and the coding requirement that former smoking status is assigned only upon reporting of at least 12 months of abstinence, long-term former smokers (Category 2, Table 3) would have been abstinent for at least four years. Persons who shifted from current smoking in Wave 1 to former smoking in Wave 2 (Category 3, Table 3) would have been abstinent for at least 12 months and a maximum of four years.

The analysis showed that the AOR for Wave 2 SRO among recent former smokers (Category 3) did not differ from persistent current smokers (Category 4) (χ^2 (1) =1.26, p=0.26). However, long-term former smokers (Category 2) showed a significantly lower AOR for Wave 2 SRO than persistent current smokers (χ^2 (1) =16.9, p<0.0001). These data suggest that a reduction in risk for future SRO with past smoking becomes apparent after a considerable period

of abstinence. Of additional interest were the risk estimates associated with re-starting (i.e. relapse) and with beginning to smoke in Wave 2. Compared to persistent current smokers, the AOR for Wave 2 SRO was significantly higher for both relapsers ($\chi^2(1) = 56.00$, $p<0.0001$), and smoking beginners in Wave 2 ($\chi^2(1) = 4.11$, $p=0.04$). Further, the AOR for Wave 2 SRO was significantly higher among relapsers than beginning smokers ($\chi^2(1) = 19.0$, $p<0.0001$).

Does prior SRO predict smoking?

A multiple regression model on current smoking in Wave 2 was fit using the identical list of control variables for predicting Wave 2 SRO. This second model did not show a direct effect of prior SRO on Wave 2 current smoking. Persons with Wave 1 SROs were *less* likely to report current smoking status at Wave 2 than were persons who did not experience SRO in Wave 1 (AOR=0.81, 95% CI=0.72, 0.90).

To understand the temporal relationship between smoking and SRO, the effects of the interaction of Wave 1 smoking status (current vs. never smoker and former vs. never smoker) with history of prior SRO were examined. Table 4 shows adjusted odds ratios from separate multiple regression models on SRO and on current smoking in Wave 2 for combined effects of smoking status and prior SRO reported in Wave 1. Never smokers without a prior SRO at Wave 1 comprised the reference group in each model. These analyses did not fundamentally change the finding that smoking predicts increased risk of SRO and that the reverse relationship does not hold, but indicates nuanced impact of both SRO and smoking history.

The model on Wave 2 SRO (Table 4 section a) shows that, other characteristics (e.g., demographics and psychopathology) being equal: a) all combinations of smoking status and SRO history had statistically significant risks for Wave 2 SRO relative to never smokers without prior

SRO; and b) for each smoking category, the risks were considerably greater when the combined group involved a prior SRO. The data also show that former smoking and current smoking, in the absence of prior SRO, are valid predictors of an *initial* SRO. However, once a person has had a SRO, smoking status history does not change the risk prediction - the risk of *recurrence* is fully predicted by that prior SRO and the other characteristics. The second model, on Wave 2 current smoking (Table 4 section b), shows an expectedly substantial likelihood of being a current smoker in Wave 2 for current smokers in Wave 1, regardless of SRO history. Of interest, prior SRO predicted a contrasting *reduction* in the likelihood of smoking uptake in Wave 2 for former smokers and never smokers.

DISCUSSION

The main findings from the present sample of persons reporting low mood are: 1) current and past smoking predicted increased risk for SRO independently of demographics, psychiatric factors, and prior SRO; 2) long-term smoking abstinence was associated with lower risk than persistent smoking; 3) new smoking due to relapse after a period of abstinence or to initiation of smoking by erstwhile never smokers was associated with an increased risk of SRO relative to persistent smoking; 4) prior SRO did not increase the risk of future smoking.

For three Axis I disorders, i.e., mood, alcohol use, and substance use, the adjusted odds ratios indicated either insignificant effects or a decreased risk of future SRO. These results differ from the increased risks found in the unadjusted analyses, indicating confounding effects of correlated predictors of SRO, for example, prior SRO and comorbid psychiatric disorders (3-5). In further analysis that excluded prior SRO in the multivariate model, a positive, predictive effect of mood disorder on future SRO (AOR=2.05, 95% CI=1.92,2.17) was observed, contrary to the

reduced effect of mood disorder in the full model that adjusted for prior SRO (results available upon request). This finding exemplifies an instance when collinearity with a stronger predictor (e.g., Wave 1 SRO) overwhelmed the explanatory power of other predictors with weaker relationships. It is thus remarkable that significant effects of smoking on risk of SRO remained despite the evidence of effect suppression due to confounding. Ranked in decreasing order, the significant predictors of SRO risk in the present sample were: prior SRO, borderline personality disorder, ADHD, schizotypal disorder, current smoking, former smoking, avoidant personality disorder, and selected demographic characteristics.

Other than the present one, there have been seven longitudinal epidemiological studies of smoking and SRO (14-20). The positive effect of current smoking on future SRO reported here was also observed in three studies (14-16). Problems of recall due to the long, ten year, interval between data time points could explain the negative finding of the study by Kessler et al (17); while the younger age of the samples in two studies (19-20) could have masked a future effect. Of clinical and public health importance is the finding, first reported here, that longer abstinence from smoking decreased the risk for SRO. The latter observation, not considered in two negative studies regarding past smoking (14, 16), could account for the inconsistent findings. Notably, the divergence according to longevity of abstinence is consistent with evidence for lung cancer and other smoking-related disorders that risk reduction from stopping smoking occurs only after multiple years of abstinence (31, 32). The worrisome observation that relapsers and new smokers are at even higher risk of future SRO than persistent smokers suggests particular targets for increased therapeutic attention. Finally, the data negated a reverse temporal relationship of SRO on smoking, as also seen in a study of adolescents (15). Instead, a reduction in risk for future smoking was observed among former and never smokers with prior SRO in Wave 1

compared to their counterparts without prior SRO. Perhaps among those former and never smokers, already inclined towards the pro-health behaviour of not currently smoking, was a subset spurred by the prior SRO to undertake further health-promoting and therapeutic actions, which immunized them against future smoking. Their counterparts who did not experience a prior SRO were less likely to be as self-protective or to seek counselling and similar treatments, and were less immunized against resorting to new smoking. The serendipitous observation from the present sample that prior SRO and treatment seeking were well-correlated (r=0.43, p=0.0001) is consistent with that conjecture.

Strengths and limitations of the study are noted. An important strength is the concomitance of rigorous methods and materials not found in prior work on the smoking-suicide question – face-to-face interviews, a longitudinal design, a large sample, a validated instrument, and a comprehensive range of putative predictors that permitted statistical control of key background factors and comorbidities. A further strength is the use of a simple yet meaningful measure of smoking status (i.e., never, former or current smoking), that is easy for a questioner to administer and for the respondent to recall and understand. Even so, study limitations call for cautious interpretation of the findings. The present sample comprised the subgroup (22%) of Wave 2 participants (N=34,653) who self-reported low mood during the three-year interval between the interviews. This selectivity yields findings relevant to mental health settings that are likely to serve persons experiencing mood problems; however, they may not generalize to the rest of the NESARC sample or to the national population. Second, the sample did not include persons who had completed suicide attempts. Using the U.S. rate of 11.1 per 100,000 population per year (30), the Wave 1 sample of 43,093 could be expected to include about 14 persons with completed suicides before Wave 2 (95% CI= 6.8, 21.6), introducing a non-trivial, although likely

small, selection bias. Third, the present study did not assess the effects of medical conditions which are possibly causally related, albeit in different directions, to smoking and to SRO. Fourth, the NESARC did not obtain information from adolescents, a subgroup with a known high risk for SRO (2). Finally, in exploratory, unadjusted, analyses, predictive effects of current smoking were observed across the individual SRO whereas past smoking predicted want to die and suicidal ideation, but not suicide attempt. Validation and articulation of these preliminary observations need to be accomplished in future work.

The rigorous methodology employed in the NESARC gives eminent credence to the central findings of this analysis - an independent effect of smoking on SRO and the absence of a positive influence of prior SRO on future smoking. These results are consistent with the hypothesis that smoking exerts a contributing, and not simply a correlational, effect on risk of SRO. By contrast, these results are inconsistent with the hypothesis that SRO causes smoking or that a third factor causes both smoking and SRO. The neurobiological, genetic, psychiatric and psychological underpinnings of these associations warrant further investigation. The knowledge gained could advance prevention and treatment options for reducing the prevalence of tobacco use and suicide.

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Lirio Covey and Ivan Berlin conceptualized this study and, with Mei-Chen Hu, designed the analysis. Jahn Hakes had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Lirio Covey was the lead writer of the manuscript. All authors participated in the interpretation of findings and writing of the manuscript. All authors had full access to the statistical reports, tables, and the manuscript; and take responsibility for the integrity of the data and the accuracy of the data analysis. The U.S. Census Bureau, NIAAA, and other employers of the authors had no role in the study design, implementation of the study, analysis and interpretation of data, in the writing of the report, and the decision to submit the article for publication.

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In order to safeguard sensitive personal information, NESARC data are not available for public use. The restricted use data sets are maintained by the U.S. Census Bureau on behalf of NIAAA, and any requests to use NESARC data for replication or other purposes may be directed to the NIAAA coordinator for NESARC, Aaron White (whitea4@mail.nih.gov).

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Table 1: Wave 1 characteristics of the low mood sample and the rest of the NESARC Wave 2 sample. Weighted percentages[a] (%) and standard error (s.e)

Variable	Total Wave 2 sample %	s.e.	Low mood sample[b] %	s.e.	Rest of sample[c] %	s.e.
Sample size	34,653		7,352		27,301	
Smoking status						
Current smoker	27.02	0.17	31.65	0.38	25.85	0.19
Former smoker	19.58	0.16	17.84	0.28	20.02	0.17
Never smoker	53.40	0.19	50.51	0.42	54.13	0.20
Wave 1 Suicide related outcomes (SRO)	11.42	0.10	25.55	0.27	7.84	0.10
Want to die	10.17	0.10	23.35	0.26	6.82	0.10
Suicidal ideation	8.42	0.09	19.27	0.27	5.66	0.09
Suicide attempt	2.35	0.04	6.09	0.17	1.40	0.04
Demographics						
Gender						
Female	52.08	0.16	64.13	0.40	49.02	0.17
Male	47.92	0.16	35.87	0.40	50.98	0.17
Race/Ethnicity						
White	70.93	0.24	71.39	0.40	70.81	0.25
Black	10.75	0.20	10.61	0.22	10.79	0.21
Hispanic	11.56	0.10	11.20	0.15	11.65	0.12
Asian/Pac. Islander	4.36	0.06	3.50	0.10	4.58	0.06
Amer. Indian/Alaska Native	2.40	0.11	3.29	0.20	2.17	0.11
Age: 18-19	4.02	0.07	4.47	0.15	3.91	0.08
20-29	17.78	0.14	19.28	0.30	17.40	0.15
30-44	30.90	0.17	32.28	0.29	30.54	0.18
45-64	31.08	0.15	31.64	0.24	30.94	0.17
65and over	16.22	0.10	12.32	0.25	17.21	0.12
Household Income:						
Less than $20,000	20.35	0.17	25.07	0.32	19.15	0.19
$20,000 to $34,999	19.62	0.13	20.84	0.27	19.31	0.15
$35,000 to $59,999	26.27	0.16	24.85	0.31	26.63	0.17
$60,000 and over	33.76	0.16	29.24	0.33	34.91	0.17
Marital status:						
Married	59.81	0.17	54.75	0.35	61.10	0.17
Cohabiting	3.25	0.06	3.60	0.11	3.16	0.07
Widowed	6.04	0.07	5.37	0.12	6.21	0.08
Divorced	8.45	0.06	10.73	0.19	7.87	0.07
Separated	1.98	0.04	2.98	0.12	1.73	0.04
Never Married	20.46	0.17	22.57	0.33	19.93	0.17

Education:						
Less than HS	14.65	0.13	16.25	0.26	14.24	0.14
High School diploma	29.03	0.18	29.35	0.35	28.95	0.20
College	56.32	0.22	54.40	0.38	56.81	0.23
Unemployed	7.16	0.09	12.31	0.25	5.85	0.09
Not unemployed	92.84	0.09	87.69	0.25	94.15	0.09
Urban	28.89	0.26	30.59	0.41	28.46	0.25
Rural/Not in Central City	71.11	0.26	69.41	0.41	71.54	0.25
Northeast	19.67	0.08	18.57	0.15	19.95	0.10
Midwest	23.15	0.16	23.52	0.32	23.05	0.21
South	35.21	0.15	34.89	0.39	35.29	0.19
West	21.97	0.11	23.02	0.23	21.71	0.15
Lifetime Psychiatric Disorders						
Axis I Disorders						
Alcohol Use	30.43	0.20	33.57	0.39	29.63	0.20
Substance Use	10.42	0.11	15.06	0.26	9.25	0.11
Nicotine Dependence	17.47	0.13	24.33	0.37	15.73	0.13
Anxiety disorder	17.88	0.17	31.00	0.34	14.55	0.17
Mood disorder	21.09	0.13	41.82	0.33	15.82	0.13
Attention Deficit/Hyperactivity	2.51	0.06	5.82	0.19	1.67	0.05
Axis II Disorders						
Borderline	5.89	0.08	18.44	0.28	2.70	0.07
Schizotypal	3.93	0.06	11.20	0.24	2.09	0.05
Narcissistic	6.18	0.08	11.88	0.23	4.74	0.08
Avoidant	2.32	0.05	6.14	0.17	1.36	0.05
Antisocial	3.63	0.07	5.86	0.21	3.07	0.07
Dependent	0.43	0.02	1.36	0.09	0.19	0.01
Obsessive-Compulsive	8.07	0.10	13.50	0.31	6.69	0.09
Paranoid	4.33	0.07	9.66	0.21	2.98	0.06
Schizoid	3.06	0.06	6.44	0.21	2.21	0.05
Histrionic	1.80	0.04	3.68	0.15	1.32	0.04

[a]The sampling weight variable in Wave 2 was used.
[b]Respondents in NESARC Wave 2 who reported low mood lasting two weeks or more during the three-year interval covered in the Wave 2 NESARC and were asked the three suicidal behavior questions.
[c]Respondents in NESARC Wave 2 who did not report low mood and were not asked the three suicidal questions.

Table 2: Weighted percentage of suicide related outcomes (SRO)[a] reported in Wave 2 by Wave 1 characteristics, and unadjusted and adjusted odds ratios for risk of Wave 2 SRO among persons reporting low mood at the NESARC Wave 2 interview. (N=7352)[b]

Variable	n/N	Weighted percentage of Wave 2 SRO	Standard error	OR[c]	95% CI	AOR[d]	95% CI
Smoking history							
Current smoker in Wave 1	809/2217	35.73	0.64	1.77	1.64, 1.90	1.41	1.28, 1.55
Former Smoker in Wave 1	339/1280	26.68	0.67	1.16	1.07, 1.25	1.32	1.21, 1.43
Never Smoker in Wave 1	981/3855	23.94	0.43	1.00		1.00	
SRO in Wave 1	1009/1940	50.01	0.76	3.84	3.60, 4.10	3.49	3.18, 3.84
Demographics							
Female	1488/5090	28.51	0.36	1.05	0.98, 1.12	1.13	1.04, 1.22
Male	641/2262	27.54	0.59	1.00		1.00	
White	1253/4295	28.38	0.36	1.00		1.00	
Black	333/1352	26.53	0.70	0.91	0.84, 0.99	0.84	0.76, 0.92
Hispanic	438/1342	30.33	0.52	1.10	1.04, 1.17	1.26	1.16, 1.36
Asian/Pacific Islander	47/ 169	22.68	0.84	0.74	0.67, 0.82	0.93	0.82, 1.06
American Indian	58/ 194	27.18	2.81	0.94	0.71, 1.25	0.69	0.51, 0.92
Age 18-19	94/ 264	36.65	1.73	1.00		1.00	
Age 20-29	410/1287	31.40	0.67	0.83	0.69, 0.98	0.77	0.63, 0.94
Age 30-44	750/2438	29.32	0.62	0.75	0.64, 0.88	0.73	0.60, 0.90
Age 45-64	679/2395	26.82	0.63	0.66	0.56, 0.78	0.69	0.56, 0.84
Age 65 and over	196/ 968	20.90	0.93	0.47	0.39, 0.57	0.68	0.54, 0.86
Married	836/3309	24.87	0.49	1.00		1.00	
Cohabiting	86/ 230	35.58	1.67	1.67	1.42, 1.96	1.27	1.07, 1.51
Widowed	128/ 562	24.26	1.09	0.97	0.85, 1.10	0.92	0.78, 1.07
Divorced	390/1104	36.01	0.84	1.70	1.57, 1.84	1.20	1.10, 1.32
Separated	130/ 338	37.93	1.78	1.85	1.58, 2.15	1.29	1.06, 1.56
Never married	559/2129	30.87	0.69	1.35	1.24, 1.46	0.97	0.87, 1.09
Less than High School	440/1358	31.58	0.92	1.17	1.04, 1.32	1.09	0.95, 1.25
High School Diploma	606/2111	28.27	0.74	1.00		1.00	
Some College or more	1083/3883	27.08	0.35	0.94	0.87, 1.02	1.08	1.00, 1.17
Lifetime Psychiatric Disorder							
Axis I Disorders							
Alcohol Use	811/2350	32.74	0.60	1.40	1.31, 1.49	0.95	0.87, 1.04
Substance Use	427/1033	38.42	0.94	1.75	1.61, 1.89	0.98	0.88, 1.09

Anxiety	843/2278	37.57	0.60	1.72	1.62, 1.83	1.08	1.01, 1.17
Mood	1217/3151	36.62	0.48	2.04	1.92, 2.17	0.77	0.70, 0.84
Attention Deficit Hyperactivity Disorder	208/ 394	51.14	1.42	2.87	2.56, 3.22	1.56	1.36, 1.79
Axis II Disorders							
Borderline	821/1433	55.75	0.79	4.49	4.22, 4.77	2.91	2.69, 3.16
Schizotypal	485/ 886	53.41	1.26	3.44	3.09, 3.84	1.50	1.31, 1.72
Narcissistic	443/ 993	42.49	1.01	2.08	1.89, 2.29	1.03	0.92, 1.14
Avoidant	245/ 446	51.87	1.37	2.97	2.66, 3.32	1.29	1.05, 1.58
Antisocial	188/ 395	41.55	1.39	1.89	1.68, 2.13	0.85	0.72, 1.01
Dependent	58/ 90	56.90	2.90	3.44	2.74, 4.30	1.04	0.76, 1.41
Ob-Com	377/ 961	36.07	1.05	1.53	1.39, 1.69	0.90	0.80, 1.00
Paranoid	364/ 756	45.74	1.16	2.37	2.14, 2.62	0.95	0.82, 1.10
Schizoid	210/ 473	43.81	1.26	2.10	1.89, 2.33	1.01	0.88, 1.16
Histrionic	129/ 266	44.42	1.83	2.10	1.82, 2.43	0.76	0.63, 0.93

[a]SRO (Suicide related outcome: feel like want to die, suicide ideation, suicide attempt; 0=None, 1=any SRO).

[b]Missing observations for specific variables: Race – 43, Hispanic origin – 2, age – 13, marital status-4, educational attainment – 70, household income-2544, unemployed – 28, Wave 2 individual suicide related outcomes – 12-18 "unknown" changed to "no". Treatment of unknown values in determination of psychiatric diagnosis variables is known only to original NESARC project staff at NIAAA.

[c]Odds Ratios (OR) and 95% confidence intervals (CI) based on simple regression models estimating Wave 2 SRO as a function of an individual predictor variable.

[d]Adjusted Odds Ratios (AOR) and 95% CI based on a multiple logistic regression estimating Wave 2 SRO as a function of age, sex, race/ethnicity, marital status, income, education, unemployed status, Census region, urban residence, smoking status, Axis I and Axis II disorders (as described in text), and lifetime SRO prior to Wave 1.

Table 3: Effects on Wave 2 suicide related outcomes (SRO) according to smoking status change as reported in NESARC Wave 1 and Wave 2 interviews.

			Wave 2 SRO[a]	
Smoking status in Wave 1 to Wave 2	n/N	Weighted percentage[b] (standard error)	AOR[c]	95% CI
1. Consistent never smoker (in Wave 1 and Wave 2)	897/3653	47.8 (0.40)	1.00	
2.Long-term former smoker (in Wave 1 and Wave 2)	293/1185	16.4 (0.26)	1.22	1.12, 1.34
3. Recent former smoker (current smoker in Wave 1, former smoker in Wave 2)	126/393	5.3 (0.14)	1.37	1.16, 1.63
4. Persistent current smoker (in Wave 1 and Wave 2)	683/1824	26.3 (0.35)	1.50	1.35, 1.66
5. New current smoker (never smoker in Wave 1, current smoker in Wave 2)	82/194	2.6 (0.10)	1.82	1.51, 2.19
6. Relapser (former smoker in Wave 1, current smoker in Wave 2)	46/95	1.5 (0.08)	3.42	2.85, 4.11
	N=7352[d]			

[a]Any of three items: want to die, suicidal ideation, suicide attempt

[b]The sampling weight variable in Wave 2 was used.

[c]AORs are adjusted odds ratio with 95% confidence intervals (CI) based on multiple logistic regression of Wave 2 SRO as a function of age, sex, race/ethnicity, marital status, income, education, unemployed status, Census region, urban residence, smoking status, Axis I and Axis II disorders (as described in text), and lifetime SRO reported in Wave 1.

[d]The seventh group (n=8), which consisted of persons who were never smokers in Wave 1, began to smoke and then stopped smoking in Wave 2, was too small for a valid assessment of risk.

Table 4: Combined effects of smoking status and prior SRO[a] reported in Wave 1 on a) Wave 2 SRO and b) Wave 2 current smoking

Wave 1 Smoking status and Wave 1 SRO	n/N	Weighted percentages (standard error)	AOR[b]	95% CI
a) Effect on Wave 2 SRO				
Never smoker - No prior SRO (referent)	550 /2978	17.5 (0.4)	1.00	N.A.[c]
Never smoker - Prior SRO	431 / 877	46.8 (1.0)	4.12	3.65, 4.64
Former smoker - No prior SRO	187 / 968	20.6 (0.8)	1.42	1.28, 1.57
Former smoker - Prior SRO	152 / 312	48.2 (1.6)	4.58	3.60, 5.82
Current smoker - No prior SRO	383 /1466	26.6 (0.7)	1.56	1.41, 1.74
Current smoker - Prior SRO	426 / 751	54.1 (1.2)	4.77	3.70, 5.87
b) Effect on Wave 2 Current smoking				
Never smoker – No prior SRO (referent)	166 /2978	5.3 (0.2)	1.00	N.A.[c]
Never smoker –Prior SRO	28 / 877	4.3 (0.4)	0.70	0.60, 0.82
Former smoker – No prior SRO	71 / 968	8.6 (0.5)	2.20	1.77, 2.31
Former smoker – Prior SRO	24 / 312	6.9 (0.6)	1.15	0.83, 1.61
Current smoker – No prior SRO	1204 /1466	82.7 (0.5)	82.9	73.7, 93.2
Current smoker – Prior SRO	620 / 751	84.2 (0.8)	77.0	57.6,104.8

[a]Any of three items: want to die, suicidal ideation, suicide attempt

[b]AORs are adjusted odds ratios with 95% confidence intervals (CI) based on multiple logistic regression models controlling for demographics and psychiatric history at Wave 1 (shown in Table 1).

[c]Not applicable

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Smoking and suicidal behaviors in a sample of US adults with low mood: a retrospective analysis of longitudinal data

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Smoking and suicidal behaviors in a sample of US adults with low mood: a retrospective analysis of longitudinal data

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ABSTRACT

Objective: To investigate whether: 1) smoking predicts suicide related outcomes (SRO); 2) prior SRO predicts smoking, 3) smoking abstinence affects the risk of SRO, 4) psychiatric comorbidity modifies the relationship between smoking and SRO.

Design: Retrospective analysis of longitudinal data obtained in Wave 1 (2001-2002) and Wave 2 (2004-2005) of the National Epidemiologic Survey of Alcohol and Related Conditions.

Setting: Face-to-face interviews conducted with persons in the community.

Participants: US adults (N=43,093) aged 18 years or older were interviewed in Wave 1 and re-interviewed (N=34,653) three years later. For the present study, the sample was the subset of persons (N=7,352) who at the Wave 2 interview reported low mood lasting two weeks or more during the past three years and were further queried regarding SRO occurring between Waves 1 and 2.

Outcome measures: SRO composed of any of: 1) want to die, 2) suicidal ideation, 3) suicide attempt, reported at Wave 2. Current smoking reported at Wave 2.

Results: Current and former smoking in Wave 1 predicted increased risk for Wave 2 SRO independently of prior SRO, psychiatric history, and socio-demographic characteristics measured in Wave 1 (Adjusted Odds Ratio (AOR) =1.41, 95% CI=1.28 to 1.55 for current smoking; AOR=1.32, 95% CI=1.21 to 1.43 for former smoking). Prior SRO did not predict current smoking in Wave 2. Compared with persistent never smokers, risk for future SRO was highest among relapsers (AOR=3.42, 95% CI=2.85 to 4.11); next highest among smoking beginners at Wave 2 (AOR=1.82, 95% CI=1.51 to 2.19); and lowest among long-term (four+ years) former smokers (AOR=1.22, 95% CI=1.12 to 1.34). Compared with persistent current

smokers, risk for SRO was lower among long-term (p<0.0001), but not shorter-term (p=0.26) abstainers.

Conclusion: Smoking increased the risk of future SRO independently of psychiatric comorbidity. Abstinence of several years duration reduced that risk.

Word count= 298

Article Summary

Article focus

To investigate among persons reporting low mood lasting two weeks or more during the past three years whether:

- smoking predicts suicide related outcomes (want to die, suicidal ideation, suicide attempt); prior suicide related outcomes predict smoking,
- smoking abstinence affects the risk of suicide related outcomes,
- psychiatric comorbidity modifies the relationship between smoking and suicide related outcomes.

Key messages

- Current and former smoking (less than 4 years' reported abstinence) predicted increased risk for suicide related outcomes independently of prior suicide related outcomes, psychiatric history, and socio-demographic characteristics.
- Prior suicide related outcomes did not predict future current smoking.
- Compared with persistent current smokers, risk of suicide related outcomes was reduced with long-term (≥4 years) but not with shorter-term (<4 years) abstinence.

Strengths and limitations

Strengths

- Face-to-face interviews, a longitudinal design, a large representative sample, a validated diagnostic instrument, a comprehensive range of putative predictors that permitted statistical control of the key background factors and comorbidities.

Limitations

- Only persons with self-reported low mood were questioned about suicide related outcomes; consequently, no generalizability to other populations.
- The sample did not include persons who had completed suicide.
- No assessment of the effects of medical conditions which are possibly causally related to smoking and to suicide related outcomes.
- Smoking information was self-reported, not biologically verified.
- No information from adolescents, a high risk population for both smoking and suicide related outcomes.

INTRODUCTION

Suicide is a leading cause of death worldwide. Close to one million persons die from suicide each year. The World Health Organization predicts that by 2020 suicide deaths will rise to 1.5 million (1). Completed suicides are largely predicted by the wish to die, thoughts of suicide, and unsuccessful previous suicidal attempts (2), making it important to understand the risks posed by suicide related outcomes (SRO). A history of mental disorders (3-5) and particular demographic characteristics (female gender, younger age, unmarried status, and unemployment) are putative risk factors for suicide and SRO (2). Smoking, long known as a major risk factor for numerous medical illnesses (6), and recently, for psychiatric outcomes as well (7, 8) has received increasing attention for its potential contribution to the risk of completed suicides and SRO (9). Nevertheless, whether the association between smoking and suicidal behaviours is causal or correlational remains unclear.

A link between smoking and suicide was observed as early as 1976 by Doll and Peto in their study of mortality due to smoking in male British doctors (10). Clinical and epidemiological studies that subsequently investigated the issue are in general, but not universal, agreement in finding a significant association between smoking and suicide and suicidal behaviors. Among studies that focused on SRO, three that used cross-sectional epidemiological data found a positive correlational association between smoking and SRO (11-13). Of seven longitudinal studies that also utilized community-based data, three (14-16) found that current smoking predicted suicidal behaviors even after controlling for the effects of demographic and psychiatric variables; four studies did not find a positive relationship (17-20).

The effect of smoking abstinence on risk of SRO is also unclear. A study of young adults followed for 10 years found that recent, but not pre-survey, cigarette smoking predicted suicidal thoughts and attempts (14). Another study showed higher incidence rates of suicidal ideation among former smokers than never smokers, but the difference was no longer significant after adjustment with depressive disorder, anxiety symptoms, and alcohol dependence (16). A study based on Wave 1 data from the National Epidemiological Survey of Alcohol and Related Conditions (NESARC) initially found that longer duration of abstinence decreased risk for SRO, but this effect disappeared upon controlling for psychiatric comorbidity (21).

A further question of theoretical and practical importance is whether prior SRO increases the risk of future smoking. In the single study that has addressed this question, longitudinal data obtained from adolescents showed that smoking predicted suicidal ideation and suicide attempts but prior suicidality was not associated with subsequent smoking (15).

The present study was conducted to address these conundrums of the smoking-suicide relationship: 1) whether prior smoking predicts SRO; 2) whether prior SRO predicts smoking; 3) whether smoking cessation and its corollary, duration of smoking abstinence, affects risk for SRO, and 4) whether these relationships are independent of comorbid psychiatric illness. Also explored were the effects of smoking status changes between the two waves of the NESARC on risk of future SRO. The two-wave format, the large sample, and extensive data on psychiatric comorbidity that characterized the NESARC (22) permitted assessment of these questions.

The survey instrument had asked questions regarding the past occurrence of SRO – want to die, suicidal ideation, and suicide attempt, only of persons reporting low mood. This restriction limits the generalizability of findings to the general population, but the much higher

occurrence of suicidal behaviours among persons with low mood (3, 4) provided a more sensitive context for detecting the risk potential of smoking for suicidal behaviours (23).

METHODS

Sample: The NESARC data were collected to obtain a representative national sample of US adults. In Wave 1 (2001-2002), face-to-face interviews were completed with 43,093 persons aged 18 years or older. The overall response rate was 81.0%. The Wave 1 sample was re-interviewed in Wave 2 (2004-2005) three years later (mean interval=36.6 months, s.e.=2.62) with a response rate of 80.4% (N=34,653) based on the Wave 1 sample. The NESARC sample size was chosen to be sufficiently large to produce nationally representative proportions for the study of substance abuse and dependence and mental disorders by demographic group with confidence intervals equal to or smaller than extant studies. Following NESARC guidelines (24, 25), the original NESARC data set was transformed to account for survey design effects and sampling weights upon responses in order to adjust for sample selection procedures, non-response from selected households or individuals, oversampling (of young adults, Blacks, and Hispanics), and non-response at the Wave 2 time point. Those weights and survey design effects, employed in other studies based on NESARC data, as well as other methodological details of Waves 1 and 2 are described in published NESARC Source and Accuracy Statements (24, 25).

Data for the present study were obtained from a subset of persons (N=7,352) who reported low mood at the Wave 2 interview, irrespective of low mood in Wave 1. This subsample was selected for the present analysis because it produced the largest number of persons from whom evaluable information for predicting Wave 2 SRO was available. The latter subsample is also referred to herein as the "at-risk sample". Persons who did not report low

mood were skipped out of the SRO sections in Waves 1 and 2. The questions for low mood at the Wave 2 interview were: "Since your LAST interview in (month/year), have you ever had a time when you felt sad, blue, depressed, or down most of the time for at least 2 weeks?" and "Since your LAST interview, have you ever had a time, lasting at least 2 weeks, when you didn't care about the things that you usually cared about, or when you didn't enjoy the things you usually enjoyed?" At the Wave 1 interview, respondents were asked these same questions referenced to their *entire lifetime*.

Variables: The outcome variables for this study were Wave 2 SRO and Wave 2 current smoking. The main covariates were prior SRO and smoking status at Wave 1. The individual SRO questions are: "During that time when (your mood was at its [sic] lowest/you enjoyed or cared the least about things), did you … feel like you wanted to die? think about committing suicide? attempt suicide?" Responses to these items were summed to create the total SRO question and measured as a dichotomous variable (none of the three=0; any of the three=1). Respondents who did not report low mood in Wave 1 and were not asked the SRO questions were assigned a value of 0 for prior SRO.

The questions on tobacco use at Wave 1 are: "In your ENTIRE LIFE, have you ever . . . (a) Smoked at least 100 cigarettes? (b) Smoked at least 50 cigars? (c) Smoked a pipe at least 50 times? (d) Used snuff, such as Skoal, Skoal Bandit [sic] or Copenhagen at least 20 times? (e) Used chewing tobacco, such as Redman, Levi Garrett or Beechnut at least 20 times?" Persons who smoked cigarettes, cigars and/or pipes, comprised (a weighted) 95.9% (3368/3497) of all tobacco users. Following the coding rule of the NESARC, all tobacco users, including the 129 persons who reported using snuff or chewing tobacco only, were labelled as "smokers". A *never smoker* had responded "No" to each of the questions regarding lifetime use of at least 100

cigarettes, at least 50 cigars, smoked a pipe at least 50 times, used snuff at least 20 times, and used chewing tobacco at least 20 times. A *former smoker* was a "Yes" responder to at least one of the prior questions who also reported that he or she had not smoked or used tobacco in the past 12 months. (N.B. Very few, if any, of this latter group would have been experiencing withdrawal; thus, the current study is not an adequate test of post-cessation withdrawal as a predictor of SRO). A *current smoker* was a "Yes" respondent who had smoked or used tobacco within the past 12 months. At the Wave 2 interview, these same questions on tobacco use were asked with regard to the period since the last interview (month/year).

The smoking status variable (i.e., never, former, current) rather than DSM-IV defined nicotine dependence was selected to assess tobacco use because: 1) the adequacy of the DSM-IV criteria as a valid measure of nicotine dependence remains controversial (26, 27), and 2) response to the single question on smoking status is easier to elicit in the clinical setting, with more validity, than responses to a multi-item measure of tobacco use for which no consensus, stand-alone, instrument yet exists (26, 27). To categorize long-term or recent status as never, former, or current smokers, a change variable was created with the following categories according to their report of smoking at Waves 1 and 2: 1) never smoker to never smoker, 2) former smoker to former smoker, 3) current smoker to former smoker, 4) current smoker to current smoker, 5) never smoker to current smoker, 6) former smoker to current smoker, and 7) never smoker to former smoker.

Other potential confounders or effect modifiers because of their known correlations with smoking and/or SRO, measured at Wave 1, were: demographic characteristics (age, gender, race/ethnicity, marital status, education, employment status, income, urban residence, geographic region), and lifetime measures of DSM-IV Axis I and Axis II disorders. The Axis I disorders

were categorized into mood disorders (major depression, dysthymia, bipolar I and bipolar II), anxiety disorders (panic disorder, social phobia, specific phobia, generalized anxiety), alcohol use disorders (alcohol abuse or dependence), and other substance use disorders (drug abuse or dependence). A history of Attention Deficit Hyperactivity Disorder (ADHD), queried only at Wave 2, was used among the Wave 1 predictors, its lifetime quality presumed since the DSM-IV criteria for ADHD include the presence of ADHD symptoms before age seven. All ten of the Axis II personality disorders measured in AUDADIS-IV (shown in Table 1), measured at Wave 1, were included as well.

Assessment: For both Waves 1 and 2, the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-IV) was administered by interviewers from the U.S. Census Bureau. The reliability and validity of the DSM-IV diagnoses obtained through the AUDADIS-IV have been demonstrated in clinical and general samples in the U.S. and in other countries (28).

Statistical Analysis: Weighted percentages and standard errors measured the distribution of the covariates (demographic characteristics and lifetime psychiatric variables) reported at Wave 1 for the sample with low mood and for the complementary sample of persons with no low mood. Chi-squared tests were used to assess differences between comparison groups, e.g., the at-risk sample and the complementary sample of NESARC participants who did not report low mood. Unadjusted and adjusted odds ratios (OR and AOR) and 95% confidence intervals (CI) were calculated from univariate logistic regressions and multivariate logistic regressions, respectively, to assess prediction of Wave 2 SRO in the sample of persons reporting low mood. respectively. The incidence of SRO at Wave 2 (since the Wave 1 interview) by smoking status, prior SRO, and all other covariates at Wave 1, were also calculated. The opposite temporal

relationship of prior SRO (reported in Wave 1) on future current smoking (reported in Wave 2) was tested using the identical covariates for assessing predictors of Wave 2 SRO, following Granger (29). All models were estimated with the PROC SURVEYLOGISTIC function of SAS statistical software version 9.2, with the results verified through an internal statistical review at the U.S. Census Bureau.

Missing values were replaced through imputation using assignment and allocation methods as described in the NESARC Source and Accuracy Statements (24, 25). Sensitivity analyses were performed that included: comparison of the at-risk subsample to the complementary Wave 2 NESARC sample; using different sets of control variables with and without education, and census region; and including help-seeking behavior controls. In response to reviewer concerns, we performed the multiple logistic regression models for assessing prediction of Wave 2 SRO and of Wave 2 current smoking based on the unweighted data adjusted for design effects. These various sensitivity analyses did not alter the associations between smoking and SRO reported below.

RESULTS

Wave 1 Characteristics

Table 1 shows weighted percentages by smoking status, SRO taken together and individually, demographic characteristics, and psychiatric disorders (DSM-IV Axis I and Axis II) in the sample of persons reporting low mood at Wave 1 and the rest of the NESARC sample. Current smoking, SRO, and the prevalence of psychiatric disorders were markedly higher among the low mood sample, confirming their at-risk status. Other demographic characteristics previously associated with higher risk of suicide and SROs were also higher in the low mood

subsample: more females, more low and fewer high income responders, fewer married, and more separated or never married, and more unemployed individuals. Differences by race/ethnicity, age, urban or rural residence, and geographic area were also observed.

Effects of Wave 1 characteristics on Wave 2 SRO

From here on, reported statistics are for the sample of persons reporting low mood at Wave 2. The overall incidence rate of SRO (occurring between the Wave 1 and Wave 2 interviews) was 28.2% (s.e.=0.33%). Table 2 shows weighted percentages and odds ratios for Wave 2 SRO by smoking history, prior SRO, and the control variables as reported in Wave 1. Unadjusted odds ratios (OR) and 95% CI for future SRO are shown as reference points. The adjusted odds ratios (AOR) and 95% CI show significantly higher risk of Wave 2 SRO for both Wave 1 current smokers (AOR=1.41, 95% CI= 1.28, 1.55) and former smokers (AOR=1.32, 95% CI=1.21, 1.43) relative to never smokers. The difference in point estimates of risk between current versus former smokers was not significant ($\chi 2$=1.95, p = 0.16).

The multivariate model showed that SRO in Wave 1 is the strongest predictor of a Wave 2 SRO (AOR=3.49, 95% CI= 3.18, 3.84). Significant, independent risk of future SRO was also observed for individuals who were female, Hispanic, younger, cohabiting, divorced or separated, of lower income, unemployed, and resided outside the Northeast region. Of the DSM-IV Axis I disorders, only anxiety (AOR= 1.08, 95% CI=1.01, 1.17) and ADHD (AOR=1.56, 95% CI=1.36, 1.79) showed significantly elevated risk of Wave 2 SRO; mood disorder was correlated with reduced Wave 2 SRO risk (AOR=0.77; 95% CI=0.70, 0.84). Three of the DSM-IV Axis II disorders, i.e., borderline personality, schizotypal, and avoidant personality, showed significantly increased risk for Wave 2 SRO.

Smoking status change from Wave 1 to Wave 2

The great majority of the sample (90.5%) did not change their smoking status as never, former, or current smoker, between Waves 1 and 2 (Table 3). Among the remaining 9.5%, over half (5.3%) had shifted from being current smokers to former smokers; more than a fourth (2.6%) were never smokers in Wave 1 who became current smokers in Wave 2; and a smaller proportion (<2%) who were former smokers in Wave 1 relapsed to smoking in Wave 2.

a) *Effects on Wave 2 SRO*. Table 3 shows adjusted odds ratios indicating significant risk for SRO among all categories of ever-smokers relative to the persistent never smokers. The highest risk was seen for relapsers (former smoker to current smoker) (AOR=3.42, 95% CI=2.85, 4.11); new smokers (never smoker to current smoker) showed the next highest risk (AOR=1.82, 95% CI=1.51, 2.19); and long-term former smokers (during both Wave 1 and 2) showed the least elevated, yet still significant, risk (AOR=1.22, 95% CI=1.12, 1.34). The seventh category consisting of never smokers in Wave 1 who reported former smoker status in Wave 2 was too small for a valid analysis.

b) *Comparative risks by abstinence duration, relapse, and new smoking*. Pair-wise chi-squared tests for equality of coefficients permitted a comparison of risk estimates for Wave 2 SRO (shown in Table 3) between categories of smoking status change. Given the three-year interval between Waves 1 and 2 and the coding requirement that former smoking status is assigned only upon reporting of at least 12 months of abstinence, long-term former smokers (Category 2, Table 3) would have been abstinent for at least four years. Persons who shifted from current smoking in Wave 1 to former smoking in Wave 2 (Category 3, Table 3) would have been abstinent for at least 12 months and a maximum of four years.

The analysis showed that the AOR for Wave 2 SRO among recent former smokers (Category 3) did not differ from persistent current smokers (Category 4) (χ^2 (1) =1.26, p=0.26). However, long-term former smokers (Category 2) showed a significantly lower AOR for Wave 2 SRO than persistent current smokers (χ^2 (1) =16.9, p<0.0001). These data suggest that a reduction in risk for future SRO with past smoking becomes apparent after a considerable period of abstinence. Of additional interest were the risk estimates associated with re-starting (i.e. relapse) and with beginning to smoke in Wave 2. Compared to persistent current smokers, the AOR for Wave 2 SRO was significantly higher for both relapsers (χ^2(1) =56.00, p<0.0001), and smoking beginners in Wave 2 (χ^2 (1) =4.11, p=0.04). Further, the AOR for Wave 2 SRO was significantly higher among relapsers than beginning smokers (χ^2 (1)=19.0, p<0.0001).

Does prior SRO predict smoking?

A multiple regression model on current smoking in Wave 2 was fit using the identical list of control variables for predicting Wave 2 SRO. This second model did not show a direct effect of prior SRO on Wave 2 current smoking. Persons with Wave 1 SROs were *less* likely to report current smoking status at Wave 2 than were persons who did not experience SRO in Wave 1 (AOR=0.81, 95% CI=0.72, 0.90).

To understand the temporal relationship between smoking and SRO, the effects of the interaction of Wave 1 smoking status (current vs. never smoker and former vs. never smoker) with history of prior SRO were examined. Table 4 shows adjusted odds ratios from separate multiple regression models on SRO and on current smoking in Wave 2 for combined effects of smoking status and prior SRO reported in Wave 1. Never smokers without a prior SRO at Wave 1 comprised the reference group in each model. These analyses did not fundamentally change the

finding that smoking predicts increased risk of SRO and that the reverse relationship does not hold, but indicates nuanced impact of both SRO and smoking history.

The model on Wave 2 SRO (Table 4 section a) shows that, other characteristics (e.g., demographics and psychopathology) being equal: a) all combinations of smoking status and SRO history had statistically significant risks for Wave 2 SRO relative to never smokers without prior SRO; and b) for each smoking category, the risks were considerably greater when the combined group involved a prior SRO. The data also show that former smoking and current smoking, in the absence of prior SRO, are valid predictors of an *initial* SRO. However, once a person has had a SRO, smoking status history does not change the risk prediction - the risk of *recurrence* is fully predicted by that prior SRO and the other characteristics. The second model, on Wave 2 current smoking (Table 4 section b), shows an expectedly substantial likelihood of being a current smoker in Wave 2 for current smokers in Wave 1, regardless of SRO history. Of interest, prior SRO predicted a contrasting *reduction* in the likelihood of smoking uptake in Wave 2 for former smokers and never smokers.

DISCUSSION

The main findings from the present sample of persons reporting low mood are: 1) current and past smoking predicted increased risk for SRO independently of demographics, psychiatric factors, and prior SRO; 2) long-term smoking abstinence was associated with lower risk than persistent smoking; 3) new smoking due to relapse after a period of abstinence or to initiation of smoking by erstwhile never smokers was associated with an increased risk of SRO relative to persistent smoking; 4) prior SRO did not increase the risk of future smoking.

For three Axis I disorders, i.e., mood, alcohol use, and substance use, the adjusted odds ratios indicated either insignificant effects or a decreased risk of future SRO. These results differ from the increased risks found in the unadjusted analyses, indicating confounding effects of correlated predictors of SRO, for example, prior SRO and comorbid psychiatric disorders (3-5). In further analysis that excluded prior SRO in the multivariate model, a positive, predictive effect of mood disorder on future SRO (AOR=2.05, 95% CI=1.92,2.17) was observed, contrary to the reduced effect of mood disorder in the full model that adjusted for prior SRO (results available upon request). This finding exemplifies an instance when collinearity with a stronger predictor (e.g., Wave 1 SRO) overwhelmed the explanatory power of other predictors with weaker relationships. It is thus remarkable that significant effects of smoking on risk of SRO remained despite the evidence of effect suppression due to confounding. Ranked in decreasing order, the significant predictors of SRO risk in the present sample were: prior SRO, borderline personality disorder, ADHD, schizotypal disorder, current smoking, former smoking, avoidant personality disorder, and selected demographic characteristics.

Other than the present one, there have been seven longitudinal epidemiological studies of smoking and SRO (14-20). The positive effect of current smoking on future SRO reported here was also observed in three studies (14-16). Problems of recall due to the long, ten year, interval between data time points could explain the negative finding of the study by Kessler et al (17); while the younger age of the samples in two studies (19-20) could have masked a future effect. Of clinical and public health importance is the finding, first reported here, that longer abstinence from smoking decreased the risk for SRO. The latter observation, not considered in two negative studies regarding past smoking (14, 16), could account for the inconsistent findings. Notably, the divergence according to longevity of abstinence is consistent with evidence for lung cancer

and other smoking-related disorders that risk reduction from stopping smoking occurs only after multiple years of abstinence (30, 31). The worrisome observation that relapsers and new smokers are at even higher risk of future SRO than persistent smokers suggests particular targets for increased therapeutic attention. Finally, the data negated a reverse temporal relationship of SRO on smoking, as also seen in a study of adolescents (15). Instead, a reduction in risk for future smoking was observed among former and never smokers with prior SRO in Wave 1 compared to their counterparts without prior SRO. Perhaps among those former and never smokers, already inclined towards the pro-health behaviour of not currently smoking, was a subset spurred by the prior SRO to undertake further health-promoting and therapeutic actions, which immunized them against future smoking. Their counterparts who did not experience a prior SRO were less likely to be as self-protective or to seek counselling and similar treatments, and were less immunized against resorting to new smoking. The serendipitous observation from the present sample that prior SRO and treatment seeking were well-correlated (r=0.43, p=0.0001) is consistent with that conjecture.

Strengths and limitations of the study are noted. An important strength is the concomitance of rigorous methods and materials not found in prior work on the smoking-suicide question – face-to-face interviews, a longitudinal design, a large sample, a validated instrument, and a comprehensive range of putative predictors that permitted statistical control of key background factors and comorbidities. A further strength is the use of a simple yet meaningful measure of smoking status (i.e., never, former or current smoking), that is easy for a questioner to administer and for the respondent to recall and understand. Even so, study limitations call for cautious interpretation of the findings. The present sample comprised the subgroup (22%) of Wave 2 participants (N=34,653) who self-reported low mood during the three-year interval

between the interviews. This selectivity yields findings relevant to mental health settings that are likely to serve persons experiencing mood problems; however, they may not generalize to the rest of the NESARC sample or to the national population. Second, the sample did not include persons who had completed suicide attempts. Using the U.S. rate of 11.1 per 100,000 population per year (32), the Wave 1 sample of 43,093 could be expected to include about 14 persons with completed suicides before Wave 2 (95% CI= 6.8, 21.6), introducing a non-trivial, although likely small, selection bias. Third, the present study did not assess the effects of medical conditions which are possibly causally related, albeit in different directions, to smoking and to SRO. Fourth, self-reported smoking information was not biologically validated. Fifth, the NESARC did not obtain information from adolescents, a subgroup with a known high risk for SRO (2). Finally, in exploratory, unadjusted, analyses, predictive effects of current smoking were observed across the individual SRO whereas past smoking predicted want to die and suicidal ideation, but not suicide attempt. Validation and articulation of these preliminary observations need to be accomplished in future work.

The rigorous methodology employed in the NESARC gives eminent credence to the central findings of this analysis - an independent effect of smoking on SRO and the absence of a positive influence of prior SRO on future smoking. These results are consistent with the hypothesis that smoking exerts a contributing, and not simply a correlational, effect on risk of SRO. By contrast, these results are inconsistent with the hypothesis that SRO causes smoking or that a third factor causes both smoking and SRO. The neurobiological, genetic, psychiatric and psychological underpinnings of these associations warrant further investigation. The knowledge gained could advance prevention and treatment options for reducing the prevalence of tobacco use and suicide.

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Lirio Covey and Ivan Berlin conceptualized this study and, with Mei-Chen Hu, designed the analysis. Jahn Hakes had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Lirio Covey was the lead writer of the manuscript. All authors participated in the interpretation of findings and writing of the manuscript. All authors had full access to the statistical reports, tables, and the manuscript; and take responsibility for the integrity of the data and the accuracy of the data analysis. The U.S. Census Bureau, NIAAA, and other employers of the authors had no role in the study design, implementation of the study, analysis and interpretation of data, in the writing of the report, and the decision to submit the article for publication.

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In order to safeguard sensitive personal information, NESARC data are not available for public use. The restricted use data sets are maintained by the U.S. Census Bureau on behalf of NIAAA, and any requests to use NESARC data for replication or other purposes may be directed to the NIAAA coordinator for NESARC, Aaron White (whitea4@mail.nih.gov).

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Table 1: Wave 1 characteristics of the low mood sample and the rest of the NESARC Wave 2 sample. Weighted percentages[a] (%) and standard error (s.e)

Variable	Total Wave 2 sample %	s.e.	Low mood sample[b] %	s.e.	Rest of sample[c] %	s.e.
Sample size	34,653		7,352		27,301	
Smoking status						
Current smoker	27.02	0.17	31.65	0.38	25.85	0.19
Former smoker	19.58	0.16	17.84	0.28	20.02	0.17
Never smoker	53.40	0.19	50.51	0.42	54.13	0.20
Wave 1 Suicide related outcomes (SRO)	11.42	0.10	25.55	0.27	7.84	0.10
Want to die	10.17	0.10	23.35	0.26	6.82	0.10
Suicidal ideation	8.42	0.09	19.27	0.27	5.66	0.09
Suicide attempt	2.35	0.04	6.09	0.17	1.40	0.04
Demographics						
Gender						
Female	52.08	0.16	64.13	0.40	49.02	0.17
Male	47.92	0.16	35.87	0.40	50.98	0.17
Race/Ethnicity						
White	70.93	0.24	71.39	0.40	70.81	0.25
Black	10.75	0.20	10.61	0.22	10.79	0.21
Hispanic	11.56	0.10	11.20	0.15	11.65	0.12
Asian/Pac. Islander	4.36	0.06	3.50	0.10	4.58	0.06
Amer. Indian/Alaska Native	2.40	0.11	3.29	0.20	2.17	0.11
Age: 18-19	4.02	0.07	4.47	0.15	3.91	0.08
20-29	17.78	0.14	19.28	0.30	17.40	0.15
30-44	30.90	0.17	32.28	0.29	30.54	0.18
45-64	31.08	0.15	31.64	0.24	30.94	0.17
65and over	16.22	0.10	12.32	0.25	17.21	0.12
Household Income:						
Less than $20,000	20.35	0.17	25.07	0.32	19.15	0.19
$20,000 to $34,999	19.62	0.13	20.84	0.27	19.31	0.15
$35,000 to $59,999	26.27	0.16	24.85	0.31	26.63	0.17
$60,000 and over	33.76	0.16	29.24	0.33	34.91	0.17
Marital status:						
Married	59.81	0.17	54.75	0.35	61.10	0.17
Cohabiting	3.25	0.06	3.60	0.11	3.16	0.07
Widowed	6.04	0.07	5.37	0.12	6.21	0.08
Divorced	8.45	0.06	10.73	0.19	7.87	0.07
Separated	1.98	0.04	2.98	0.12	1.73	0.04
Never Married	20.46	0.17	22.57	0.33	19.93	0.17

Education:						
Less than HS	14.65	0.13	16.25	0.26	14.24	0.14
High School diploma	29.03	0.18	29.35	0.35	28.95	0.20
College	56.32	0.22	54.40	0.38	56.81	0.23
Unemployed	7.16	0.09	12.31	0.25	5.85	0.09
Not unemployed	92.84	0.09	87.69	0.25	94.15	0.09
Urban	28.89	0.26	30.59	0.41	28.46	0.25
Rural/Not in Central City	71.11	0.26	69.41	0.41	71.54	0.25
Northeast	19.67	0.08	18.57	0.15	19.95	0.10
Midwest	23.15	0.16	23.52	0.32	23.05	0.21
South	35.21	0.15	34.89	0.39	35.29	0.19
West	21.97	0.11	23.02	0.23	21.71	0.15
Lifetime Psychiatric Disorders						
Axis I Disorders						
Alcohol Use	30.43	0.20	33.57	0.39	29.63	0.20
Substance Use	10.42	0.11	15.06	0.26	9.25	0.11
Nicotine Dependence	17.47	0.13	24.33	0.37	15.73	0.13
Anxiety disorder	17.88	0.17	31.00	0.34	14.55	0.17
Mood disorder	21.09	0.13	41.82	0.33	15.82	0.13
Attention Deficit/Hyperactivity	2.51	0.06	5.82	0.19	1.67	0.05
Axis II Disorders						
Borderline	5.89	0.08	18.44	0.28	2.70	0.07
Schizotypal	3.93	0.06	11.20	0.24	2.09	0.05
Narcissistic	6.18	0.08	11.88	0.23	4.74	0.08
Avoidant	2.32	0.05	6.14	0.17	1.36	0.05
Antisocial	3.63	0.07	5.86	0.21	3.07	0.07
Dependent	0.43	0.02	1.36	0.09	0.19	0.01
Obsessive-Compulsive	8.07	0.10	13.50	0.31	6.69	0.09
Paranoid	4.33	0.07	9.66	0.21	2.98	0.06
Schizoid	3.06	0.06	6.44	0.21	2.21	0.05
Histrionic	1.80	0.04	3.68	0.15	1.32	0.04

[a]The sampling weight variable in Wave 2 was used.
[b]Respondents in NESARC Wave 2 who reported low mood lasting two weeks or more during the three-year interval covered in the Wave 2 NESARC and were asked the three suicidal behavior questions.
[c]Respondents in NESARC Wave 2 who did not report low mood and were not asked the three suicidal questions.

Table 2: Weighted percentage of suicide related outcomes (SRO)[a] reported in Wave 2 by Wave 1 characteristics, and unadjusted and adjusted odds ratios for risk of Wave 2 SRO among persons reporting low mood at the NESARC Wave 2 interview. (N=7352)[b]

Variable	n/N	Weighted percentage of Wave 2 SRO	Standard error	OR[c]	95% CI	AOR[d]	95% CI
Smoking history							
Current smoker in Wave 1	809/2217	35.73	0.64	1.77	1.64, 1.90	1.41	1.28, 1.55
Former Smoker in Wave 1	339/1280	26.68	0.67	1.16	1.07, 1.25	1.32	1.21, 1.43
Never Smoker in Wave 1	981/3855	23.94	0.43	1.00		1.00	
SRO in Wave 1	1009/1940	50.01	0.76	3.84	3.60, 4.10	3.49	3.18, 3.84
Demographics							
Female	1488/5090	28.51	0.36	1.05	0.98, 1.12	1.13	1.04, 1.22
Male	641/2262	27.54	0.59	1.00		1.00	
White	1253/4295	28.38	0.36	1.00		1.00	
Black	333/1352	26.53	0.70	0.91	0.84, 0.99	0.84	0.76, 0.92
Hispanic	438/1342	30.33	0.52	1.10	1.04, 1.17	1.26	1.16, 1.36
Asian/Pacific Islander	47/ 169	22.68	0.84	0.74	0.67, 0.82	0.93	0.82, 1.06
American Indian	58/ 194	27.18	2.81	0.94	0.71, 1.25	0.69	0.51, 0.92
Age 18-19	94/ 264	36.65	1.73	1.00		1.00	
Age 20-29	410/1287	31.40	0.67	0.83	0.69, 0.98	0.77	0.63, 0.94
Age 30-44	750/2438	29.32	0.62	0.75	0.64, 0.88	0.73	0.60, 0.90
Age 45-64	679/2395	26.82	0.63	0.66	0.56, 0.78	0.69	0.56, 0.84
Age 65 and over	196/ 968	20.90	0.93	0.47	0.39, 0.57	0.68	0.54, 0.86
Married	836/3309	24.87	0.49	1.00		1.00	
Cohabiting	86/ 230	35.58	1.67	1.67	1.42, 1.96	1.27	1.07, 1.51
Widowed	128/ 562	24.26	1.09	0.97	0.85, 1.10	0.92	0.78, 1.07
Divorced	390/1104	36.01	0.84	1.70	1.57, 1.84	1.20	1.10, 1.32
Separated	130/ 338	37.93	1.78	1.85	1.58, 2.15	1.29	1.06, 1.56
Never married	559/2129	30.87	0.69	1.35	1.24, 1.46	0.97	0.87, 1.09
Less than High School	440/1358	31.58	0.92	1.17	1.04, 1.32	1.09	0.95, 1.25
High School Diploma	606/2111	28.27	0.74	1.00		1.00	
Some College or more	1083/3883	27.08	0.35	0.94	0.87, 1.02	1.08	1.00, 1.17
Lifetime Psychiatric Disorder							
Axis I Disorders							
Alcohol Use	811/2350	32.74	0.60	1.40	1.31, 1.49	0.95	0.87, 1.04
Substance Use	427/1033	38.42	0.94	1.75	1.61, 1.89	0.98	0.88, 1.09

Anxiety	843/2278	37.57	0.60	1.72	1.62, 1.83	1.08	1.01, 1.17
Mood	1217/3151	36.62	0.48	2.04	1.92, 2.17	0.77	0.70, 0.84
Attention Deficit Hyperactivity Disorder	208/ 394	51.14	1.42	2.87	2.56, 3.22	1.56	1.36, 1.79
Axis II Disorders							
Borderline	821/1433	55.75	0.79	4.49	4.22, 4.77	2.91	2.69, 3.16
Schizotypal	485/ 886	53.41	1.26	3.44	3.09, 3.84	1.50	1.31, 1.72
Narcissistic	443/ 993	42.49	1.01	2.08	1.89, 2.29	1.03	0.92, 1.14
Avoidant	245/ 446	51.87	1.37	2.97	2.66, 3.32	1.29	1.05, 1.58
Antisocial	188/ 395	41.55	1.39	1.89	1.68, 2.13	0.85	0.72, 1.01
Dependent	58/ 90	56.90	2.90	3.44	2.74, 4.30	1.04	0.76, 1.41
Ob-Com	377/ 961	36.07	1.05	1.53	1.39, 1.69	0.90	0.80, 1.00
Paranoid	364/ 756	45.74	1.16	2.37	2.14, 2.62	0.95	0.82, 1.10
Schizoid	210/ 473	43.81	1.26	2.10	1.89, 2.33	1.01	0.88, 1.16
Histrionic	129/ 266	44.42	1.83	2.10	1.82, 2.43	0.76	0.63, 0.93

[a]SRO (Suicide related outcome: feel like want to die, suicide ideation, suicide attempt; 0=None, 1=any SRO).

[b]Missing observations for specific variables: Race – 43, Hispanic origin – 2, age – 13, marital status-4, educational attainment – 70, household income-2544, unemployed – 28, Wave 2 individual suicide related outcomes – 12-18 "unknown" changed to "no". Treatment of unknown values in determination of psychiatric diagnosis variables is known only to original NESARC project staff at NIAAA.

[c]Odds Ratios (OR) and 95% confidence intervals (CI) based on simple regression models estimating Wave 2 SRO as a function of an individual predictor variable.

[d]Adjusted Odds Ratios (AOR) and 95% CI based on a multiple logistic regression estimating Wave 2 SRO as a function of age, sex, race/ethnicity, marital status, income, education, unemployed status, Census region, urban residence, smoking status, Axis I and Axis II disorders (as described in text), and lifetime SRO prior to Wave 1.

Table 3: Effects on Wave 2 suicide related outcomes (SRO) according to smoking status change as reported in NESARC Wave 1 and Wave 2 interviews.

			Wave 2 SRO[a]	
Smoking status in Wave 1 to Wave 2	n/N	Weighted percentage[b] (standard error)	AOR[c]	95% CI
1. Consistent never smoker (in Wave 1 and Wave 2)	897/3653	47.8 (0.40)	1.00	
2.Long-term former smoker (in Wave 1 and Wave 2)	293/1185	16.4 (0.26)	1.22	1.12, 1.34
3. Recent former smoker (current smoker in Wave 1, former smoker in Wave 2)	126/393	5.3 (0.14)	1.37	1.16, 1.63
4. Persistent current smoker (in Wave 1 and Wave 2)	683/1824	26.3 (0.35)	1.50	1.35, 1.66
5. New current smoker (never smoker in Wave 1, current smoker in Wave 2)	82/194	2.6 (0.10)	1.82	1.51, 2.19
6. Relapser (former smoker in Wave 1, current smoker in Wave 2)	46/95	1.5 (0.08)	3.42	2.85, 4.11
	N=7352[d]			

[a]Any of three items: want to die, suicidal ideation, suicide attempt

[b]The sampling weight variable in Wave 2 was used.

[c]AORs are adjusted odds ratio with 95% confidence intervals (CI) based on multiple logistic regression of Wave 2 SRO as a function of age, sex, race/ethnicity, marital status, income, education, unemployed status, Census region, urban residence, smoking status, Axis I and Axis II disorders (as described in text), and lifetime SRO reported in Wave 1.

[d]The seventh group (n=8), which consisted of persons who were never smokers in Wave 1, began to smoke and then stopped smoking in Wave 2, was too small for a valid assessment of risk.

Table 4: Combined effects of smoking status and prior SRO[a] reported in Wave 1 on a) Wave 2 SRO and b) Wave 2 current smoking

Wave 1 Smoking status and Wave 1 SRO	n/N	Weighted percentages (standard error)	AOR[b]	95% CI
a) Effect on Wave 2 SRO				
Never smoker - No prior SRO (referent)	550 /2978	17.5 (0.4)	1.00	N.A.[c]
Never smoker - Prior SRO	431 / 877	46.8 (1.0)	4.12	3.65, 4.64
Former smoker - No prior SRO	187 / 968	20.6 (0.8)	1.42	1.28, 1.57
Former smoker - Prior SRO	152 / 312	48.2 (1.6)	4.58	3.60, 5.82
Current smoker - No prior SRO	383 /1466	26.6 (0.7)	1.56	1.41, 1.74
Current smoker - Prior SRO	426 / 751	54.1 (1.2)	4.77	3.70, 5.87
b) Effect on Wave 2 Current smoking				
Never smoker – No prior SRO (referent)	166 /2978	5.3 (0.2)	1.00	N.A.[c]
Never smoker –Prior SRO	28 / 877	4.3 (0.4)	0.70	0.60, 0.82
Former smoker – No prior SRO	71 / 968	8.6 (0.5)	2.20	1.77, 2.31
Former smoker – Prior SRO	24 / 312	6.9 (0.6)	1.15	0.83, 1.61
Current smoker – No prior SRO	1204 /1466	82.7 (0.5)	82.9	73.7, 93.2
Current smoker – Prior SRO	620 / 751	84.2 (0.8)	77.0	57.6,104.8

[a]Any of three items: want to die, suicidal ideation, suicide attempt

[b]AORs are adjusted odds ratios with 95% confidence intervals (CI) based on multiple logistic regression models controlling for demographics and psychiatric history at Wave 1 (shown in Table 1).

[c]Not applicable

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.