ORIGINAL INVESTIGATION

Probing the Smoking–Suicide Association: Do Smoking Policy Interventions Affect Suicide Risk?

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ABSTRACT

Introduction: Smokers exhibit elevated risk for suicide, but it is unknown whether smoking interventions reduce suicide risk. We examined whether state-level policy interventions—increases in cigarette excise taxes and strengthening of smoke-free air laws—corresponded to a reduction in suicide risk during the 1990s and the early 2000s. We also examined whether the magnitude of such reductions correlated with individuals' predicted probability of smoking, which would be expected if the associations stemmed from changes in smoking behavior.

Methods: We paired individual-level data on suicide deaths from the U.S. Multiple Cause of Death files, years 1990–2004, with living population data from the same period. These were linked with state data on cigarette excise taxes and smoke-free air policies. Utilizing a quasiexperimental analytical approach, we estimated the association between changes in policy and suicide risk. To examine whether associations correlated with individuals' probability of smoking, we used external survey data to derive a predicted probability of smoking function from demographic variables, which was then used to stratify the population by predicted smoking prevalence.

Results: Cigarette excise taxes, smoke-free air policies, and an index combining the two policies all exhibited protective associations with suicide. The associations were strongest in segments of the population where predicted smoking prevalence was the highest and weaker in segments of the population where predicted smoking prevalence was the lowest, suggesting that the protective associations were related to changes in smoking behavior.

Conclusion: These results provide support for the proposition that population interventions for smoking could reduce risk for suicide.

INTRODUCTION

Prospective cohort studies across multiple populations have consistently shown that smokers exhibit two- to fourfold higher risk for suicide than nonsmokers (see Li *et al.* [2012] for a review and meta-analysis). This may be because of factors that influence risk for both smoking and suicide, such as psychiatric disorders, including alcohol and drug use disorders (Angst & Clayton, 1986, 1998; Clayton, Ernst, & Angst, 1994; Doll & Peto, 1976; Hemmingsson & Kriebel, 2003). Markedly elevated rates of smoking are found among people with anxiety disorders, alcohol and drug dependence, and schizophrenia and other diagnoses, in both clinical and general population studies (De Leon et al., 1995; Hughes, Hatsukami, Mitchell, & Dahlgren, 1986; Kalman, Morissette, & George, 2005; Lasser *et al.*, 2000). However, it is also possible that smoking is not merely a marker for psychiatric disorders, but rather directly increases the risk for such disorders, which in turn increases the risk for suicide (Hughes, 2008; Leistikow, 2003; Leistikow & Shipley, 1999). Major lines of evidence to support this proposition include biological plausibility studies (e.g., Clark, Lindgren, Brooks, Watson, & Little, 2001; Collins & Izenwasser, 2004; Mineur & Picciotto, 2010; Picciotto, Brunzell, & Caldarone, 2002; Poorthuis, Goriounova, Couey, & Mansvelder, 2009) and longitudinal studies examining the sequence of changes in smoking status and changes in psychiatric disorder in human populations and references (e.g., Breslau & Klein, 1999; Breslau, Peterson, Schultz, Chilcoat, & Andreski, 1998; Cavazos-Rehg et al, 2014; Fleming, Leventhal, Glynn, & Ershler, 1989; Isensee, Wittchen, Stein, Höfler, & Lieb, 2003; Johnson *et al.*, 2000).

While many studies have provided evidence that smoking has adverse psychiatric consequences, few designs are able to address causality in humans. *In vitro* studies and animal models

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are limited by their lack of direct generalizability to humans, whereas observational studies leave open the possibility of confounding by factors such as common genetic liability and adverse environments. As such, it is an open question whether smoking is a direct risk factor for poor mental health outcomes and, by extension, suicide. If so, this would have significant implications for public health and clinical practice because it would establish smoking as a common and modifiable risk factor for suicide. In this case, more effective tobacco control policies and other smoking interventions could be promising means for suicide risk mitigation.

The objective of this article is to investigate the proposition that smoking is a direct risk factor for suicide. There is no practical experimental way to examine this hypothesis in a human population. Hypothetically, one could conduct mortality follow-ups of randomized controlled trials to examine whether post-trial suicide rates were lower among treatment groups than among control groups. If so, this would provide evidence that smoking cessation decreases suicide risk. However, this approach would require prohibitively large samples. In this study, we describe a parallel approach that takes advantage of historical state-level tobacco control policies as natural experiments. We leveraged state-level changes in two of the most effective tobacco control policies: smoke-free air legislation and cigarette excise taxes (Chaloupka & Warner, 2000; Levy, Chaloupka, & Gitchell, 2004). Our reasoning was that if smoking makes a substantial contribution to suicide risk, states that implemented more stringent tobacco control policies would have experienced more favorable changes in suicide risk than states that did not. Moreover, policy-related differences in suicide risk would be most pronounced among those most likely to smoke as there would be no reason to expect tobacco control policy to be related to suicide risk among nonsmokers (Gruber & Mullainathan, 2005). The advantage of studying policy rather than studying smoking directly is that tobacco control policy is largely outside of individual-level control and therefore can be considered to be a true environmental factor. The policy changes that have taken place in recent decades provide a tool for probing causation in the well-documented associations between smoking and suicide.

METHODS

Analytical Strategy

Our goal was to test the proposition that smoking is a direct risk factor for suicide. If so, then we expect interventions that influence smoking prevalence to have secondary effects on risk for suicide. We employed state-level cigarette excise taxes and smoke-free air policies as antismoking interventions and utilized individual-level data from mortality files and from U.S. population databases to examine suicide risk. State and time are the major determinants of which tobacco control policies an individual experiences, thus we postulate that policy exposure is essentially random at the individual level after adjusting for these. By including state and year as unordered categorical covariates, associations between policy and suicide are expected to be observed only if the magnitudes of within-state changes in policy correlate with within-state changes in the prevalence of suicide. This is because all time-invariant state characteristics are absorbed by the state effects, while the year effects account for national trends in suicide rates. This results in a quasiexperimental "differences-in-differences" approach that relates changes in suicide rates to changes in state policy (Bertrand, Duflo, & Mullainathan, 2004; Angrist & Pischke, 2008; Norberg, Bierut, & Grucza, 2009). The inclusion of state and time effects accounts for unobserved time-invariant factors but leaves open the possibility of confounding by time-varying state-level variables. Therefore, we also estimated models that included a number of observed, time-varying state characteristics and examined the consistency of estimates across models.

We proposed that tobacco control policies are associated with suicide as a result of their influence on smoking, specifically, through prevention of initiation, inducement of cessation, or reduction in number of cigarettes smoked among smokers. If this is the case, we would expect policy to be associated with the greatest reductions in relative risk for suicide among individuals with the highest probability of smoking (Gruber & Mullainathan, 2005). That is, those who are most likely to smoke independently of policy are the most likely to experience any protective effects of policy interventions. Because we are relying on vital statistics data, we do not have data on individuals' smoking histories. Instead, we used external datasets to derive and validate a smoking probability function using demographic variables. Smoking probability was then estimated in the main dataset to determine whether any association between tobacco control policies and suicide were strongest among likely smokers.

Dependent Variable and Data Sources

We examined suicide risk in all 50 states for the period 1990 through 2004 in relation to tobacco control policy changes. We chose this observation window for several reasons. First, we wanted to examine a period during which both smoke-free air policy and cigarette excise taxes were changing. An increasing number of states began passing smoke-free air legislation and continued to increase cigarette excise taxes during the 1990s (Giovino *et al.*, 2009). Second, policy changes during this era are well characterized, and it is generally accepted that these changes contributed to declines in the prevalence and intensity of smoking (Cavazos-Rehg *et al.*, 2012; DeCicca, Kenkel, & Mathios, 2008; Ross & Chaloupka, 2004; Tauras & Chaloupka, 1999). The year 2004 was selected as the end of the observation window because it is the last year that state identifiers are available in public use mortality data from the National Vital Statistics System (confidentiality restrictions went into place beginning with 2005 mortality data).

Data on individual suicide deaths were obtained from the Multiple Cause of Death files for 1990–2004, collected by the National Center for Health Statistics. Files containing individual-level data were obtained through the National Bureau of Economic Research (http://www.nber.org/data/multicause.html). From the complete set of death records, we selected observations for which either suicide was the underlying cause, or among the contributing causes of death using codes from the International Classification of Disease, versions 9 and 10 (codes E950-E959 and X60-X84, Y87, respectively). Living population data were constructed from 1% samples of the 1990 and 2000 U.S. Census and from the 2001–2004 American Community Surveys. These datasets were obtained from the Integrated Public Use Microdata Series maintained by the Minnesota Population Center (Ruggles *et al.*, 2010).

Living population estimates for unobserved years (1991–1999) were imputed using a linear interpolation algorithm: for 1991 through 1999, each yearly population was estimated as [(9 – # years after 1990) × (1990 population) + (# years after 1990) × (2000 population)]/9. This interpolation was conducted separately for each state and demographic combination (state, year of birth, sex, race/ethnicity). Because smoking is relatively rare among older individuals, we restricted main analyses to individuals aged between 18 and 65 years. However, analyses stratified by age and smoking probability included individuals older than 65 to maximize variance with respect to smoking prevalence.

Primary Independent Variables: State Tobacco Policies

State Excise Tax per Pack of Cigarettes

Annual state excise tax data were obtained from "The Tax Burden on Tobacco" historical compilation (Orzechowski & Walker, 2012). Values were adjusted for inflation to reflect 2012 dollars using the consumer price index obtained from the Bureau of Labor Statistics (www.bls.gov/cpi/); all reported results reflect these adjusted values.

State Smoke-Free Air Policies

Smoke-free air policy data were retrieved from the State Cancer Legislative Database (National Cancer Institute, n.d.). Three key policies were scored, covering private worksites, restaurants, and bars (International Agency for Research on Cancer, 2009). Total scores were assigned ranging from 0 to 6 that represent the sum of a 3-point scale for each policy (0 for no policy, 1 for restrictions with less than a complete ban, and 2 for a complete ban).

The policies were linked with subjects by state of residence and year. We used 6-year averages of each of the tobacco policies as independent variables, that is, scores from the year of observation and the previous 5 years were averaged. This approach assumes that both contemporaneous and prior policy exposures could influence risk. An empirical justification for this decision and results of models using alternative time-averages are provided in the Supplementary Material. Because cigarette excise taxes and smoke-free air policies tend to be correlated, we created an index combining the two policies based on the effect sizes of each in relation to smoking; these are also presented in the Supplementary Material. Results of analyses of U.S. smoking data from the time period of interest suggested that the effect of a $1 increase in cigarette excise tax on the prevalence of smoking was equivalent to a 5-point increase on the clean indoor air scale. Thus, an index was created where index = 6-year average tax + (6-year average clean indoor air score/5).

Covariates

Individual-level covariates extracted from mortality records included state of residence, year, sex, age, year of birth, and race/ethnicity. Year was coded as an unordered categorical variable. Race/ethnicity was coded as non-Hispanic White, non-Hispanic Black, Hispanic, and other. Age categories were established by dividing the 18- to 65-year-old population into quartiles (18–29 years, 30–40 years, 41–51 years, 52–65 years). We also selected several time-varying state-level factors to include as covariates. We chose variables that could potentially influence both tobacco control policy and suicide rates or that may correlate with such factors. These included (a) a measure of citizen political ideology (Berry, Ringquist, Fording, & Hanson, 1998); (b) state mental health agency expenditures per capita (National Association of State Mental Health Directors Research Institute, n.d.); (c) proportion of population in rural areas (U.S. Census Bureau, 2000); (d) state excise tax on beer (Ponicki, 2004); (e) percentage of household incomes under poverty level, (f) percentage of individuals without health insurance; (g) infant mortality rates; and (h) the state annual unemployment rate (United Health Foundation, n.d.). For state mental health spending and rural population, data were not available for all years; missing years were imputed via linear interpolation.

Statistical Analysis

All models utilized logistic regression analysis in which suicide was predicted from the 6-year averages of the tobacco policies. The most basic models controlled for age, sex, race, and categorical indicators for state and year. First, cigarette excise tax and clean indoor air score were assessed in the models separately (Models A and B). Then the index combining the two policies was assessed (Model C). In more refined models, we incorporated the state-level covariates. Parameter estimates and standard errors were calculated using the SAS statistical package "surveylogistic" procedure. To account for intracorrelation of residuals within states and across time in the estimation of standard errors, we employed a two-way clustering procedure described by Petersen (2009). The District of Columbia was excluded from all analyses as not all state-level covariates were available.

We took two approaches to examining whether policy–suicide associations were stronger among those with a higher likelihood of smoking. First, because prevalence of smoking is a strong function of age (Centers for Disease Control and Prevention [CDC], 2002), we examined the policy–suicide association separately in each age quartile of the 18- to 65-year old population and also in those aged 65 and older. Because the oldest age group has a very low probability of smoking, we expected that any association reflecting changes in relative risk for suicide would be weaker for that group than for younger age groups. Second, we created a multivariable function to predict the probability of smoking using data from two nationally representative surveys taken during the observation period. This function employed demographic variables that are reliably assessed on both death certificates and in census data, allowing us to group individuals in our mortality dataset by smoking risk. We then divided the sample into quartiles based on the predicted probability of smoking and examined policy–suicide associations for each quartile, with the expectation that the magnitude of the association would correlate with predicted probability of smoking. Full details on the derivation and validation of the predicted probability of smoking function are provided in the Supplemental Material.

RESULTS

Prior to regression modeling, we conducted a graphical analysis in which suicide rates were compared across groups of states categorized by magnitude of policy change during

the observation window. The 10 states that implemented the strongest changes in tobacco control policies, as measured by the policy index described above (6-year average tax + (6-year average clean indoor air score/5), were contrasted with the 10 states that implemented the weakest changes in tobacco control policies. The rate in each group was divided by the national rate to control for other secular trends, yielding a measure of relative risk over time in each group. The group with the strongest policy changes includes states that implemented excise tax increases up to $1.07 (New York) and increases in the smoke-free policy score of up to 5 points out of a possible 6 points (California). The group with the weakest policy changes included 9 states whose excise taxes decreased once inflation was considered and 9 states whose smoke-free score did not increase. Relative risk over time for each group is plotted in Figure 1. The Figure shows a widening gap between states that implemented strong tobacco control policies and those that did not, with relative risk increasing in the latter and decreasing in the former.

Results of analyses predicting suicide rates from tobacco control policies while controlling for demographic covariates, state, and year are summarized in Table 1, leftmost columns. Significant protective effects of higher cigarette tax per pack, smoke-free air score, and an index combining the two policies were observed. An increase of $1 in state excise tax per pack of cigarettes was associated with a 12.4% reduction in risk of suicide. An increase of 1 point on the 6-point smoke-free air score was associated with an approximately 3% reduction in risk of suicide. Combining the two policies into one index, which equates a $1 excise tax increase to a 5-point increase in smoke-free air score, each unit increase in the index was associated with an approximately 12% reduction in risk of suicide. Inclusion of the state-level covariates had little effect on the associations, as shown in the right-hand columns of Table 1. Note that Table 1 lists only the main parameters (odds ratio for policy–suicide associations); a detailed tabulation of covariate parameters for the final model is provided in Table 2.

Age-stratified results for analyses of the association between the tobacco control policy and suicide are shown in Table 3. For ease of comparison across subgroups, Table 3 presents the results of the analyses using the tobacco policy index only. These analyses also included subjects older than 65, in contrast to the previous analyses that were limited to ages ≤ 65, as outlined in the Methods section. Associations between policy variables and suicide outcomes were strongest in the three youngest age groups (ages 18 through 51), who exhibited the highest predicted prevalence of smoking, based on analyses of health survey data (~25%). The association between the policy index and suicide for individuals aged 52–65 was significantly weaker than for the younger age groups, but still nominally significant ($p = .049$), whereas the association for subjects over the age of 65, for whom smoking predicted prevalence was under 10%, was not significantly different from 1. Results of analyses for which the data were stratified by predicted probability of smoking, computed from multiple demographic variables, are also presented in Table 3. These results also showed

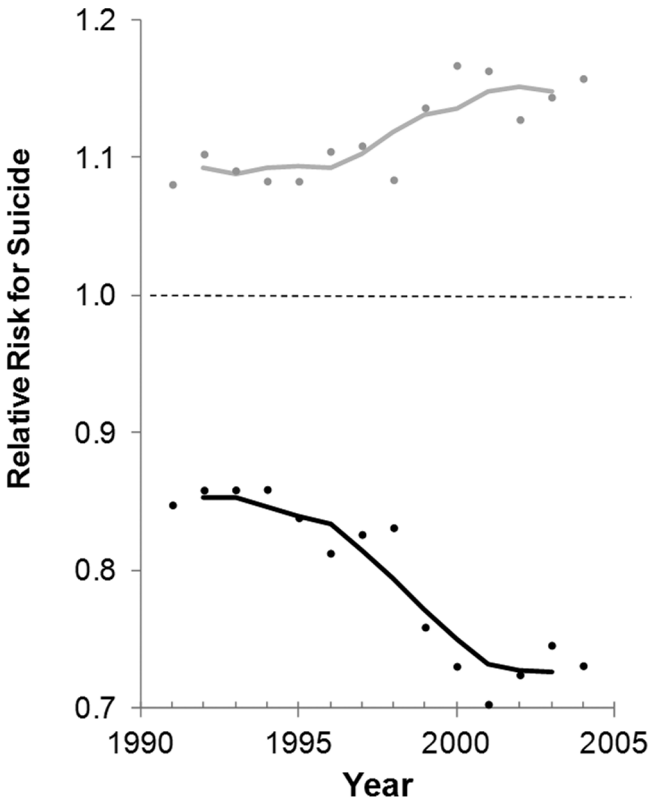

Figure 1. Ratio of suicide rate to national average in 10 states that implemented the strongest tobacco control policies between 1990 and 2004 (black), and 10 states that implemented the least strong policies during this period (gray). Strength of policy is gauged by change in the policy index described in Methods section, which combines excise taxes and smoke-free air scores. Trend lines are 5-year moving-window averages of the plotted ratio. Please note that because suicide rates are based on population counts (as opposed to statistical sampling), confidence intervals are not applicable.

Table 1. Associations Between State Tobacco Policies and Suicide Among Adults Aged 18–65 Years, Adjusted for State and Year-Fixed Effects and Other Covariates, 1990–2004

	Adjusted for demographics (sex, race, and age group)		Adjusted for demographics and state characteristics[a]	
Tobacco policy	*OR* (95% CI)	*p* value	*OR* (95% CI)	*p* value
Model A				
Tax per pack of cigarettes, per dollar (6-year average)	0.876 (0.764, 0.958)	.007	0.885 (0.866, 0.925)	<.001
Model B				
Smoke-free air score (6-point scale, 6-year average)	0.965 (0.955, 0.974)	<.001	0.972 (0.961, 0.982)	<.001
Model C				
Combined index of tax per pack and smoke-free air score (6-year averages)[b]	0.881 (0.847, 0.917)	<.001	0.895 (0.866, 0.925)	<.001

Note. All models include state and year as unordered categorical fixed effects in addition to covariates described in the column header. *OR* = odds ratio; CI = confidence interval.
[a]State characteristics include rural population percentage, citizen political ideology, poverty rate, infant mortality rate, percentage of uninsured individuals, beer tax rate, mental health expenditures per capita, and unemployment rate.
[b]Results of models using policy averaged over other lengths of time are shown in Supplemental Table S4.

Table 2. Associations Between State Tobacco Policies Index and Suicide Among Adults Aged 18–65 Years

	OR (95% CI)	*p* value
Index of tax per pack and smoke-free air score (6-year averages)	0.895 (0.866, 0.925)	<.001
Sex, female vs. male	0.252 (0.238, 0.261)	<.001
Race		
Caucasian	Ref.	
African American	0.581 (0.526, 0.643)	<.001
Hispanic	0.452 (0.395, 0.518)	<.001
Other	0.458 (0.390, 0.538)	<.001
Age		
18–29 years	Ref.	
30–40 years	1.039 (1.008, 1.070)	.013
41–51 years	1.072 (1.009, 1.138)	.024
52–65 years	0.975 (0.921, 1.031)	.374
Rural population (%)	1.002 (0.987, 1.016)	.804
Citizen political ideology	0.999 (0.997, 1.001)	.368
Poverty rate (%)	1.003 (0.998, 1.008)	.230
Infant mortality rate (%)	1.014 (0.991, 1.039)	.238
Uninsured (%)	0.996 (0.990, 1.002)	.215
Beer tax per barrel, per dollar	1.003 (0.997, 1.008)	.316
State mental health agency per capita expenditures (per $100)	0.998 (0.934, 1.067)	.957
Unemployment rate (%)	1.017 (1.006, 1.028)	.003

Note. These are the complete covariates from Model C as described in Table 1 and the text. This model included state and year as unordered categorical fixed effects in addition to covariates listed. *OR* = odds ratio; CI = confidence interval.

a correspondence between predicted smoking prevalence and the magnitude of the policy–suicide association in the expected direction, with a significant difference in the magnitude of the association between the highest predicted smoking prevalence quartile and the lowest.

DISCUSSION

We hypothesized that past changes in tobacco policies that resulted in reduced prevalence of smoking would also be associated with reduced suicide rates. We found that increases in both smoke-free indoor air policies and cigarette excise taxes were associated with reduced suicide rates during the period 1990 through 2004. This was true when the policies were analyzed separately and when they were combined into a single index, scaled to reflect each policy's association with smoking prevalence. Because our analyses controlled for state and time effects, these results indicate that within-state changes in tobacco control policy were associated with within-state changes in suicide risk. Changes in relative risk for suicide associated with policy were strongest among groups with high-predicted smoking prevalence and lowest among groups with low-predicted smoking prevalence. This is consistent with the interpretation that the effect is a result of policy influence on smoking behavior, rather than stemming from confounding with other environmental variables. Moreover, the associations were robust to adjustment for relevant time-varying state variables such as per capita mental health spending and economic factors.

The results of our study imply that the beneficial impact of stricter tobacco control policies may extend beyond reductions

Table 3. Associations Between State Tobacco Policy Index (Model C in Table 1) and Suicide Among Adults by Age Group and Demographic Smoking Probability Quartile

	Estimated smoking prevalence[a]	*OR* (95% CI)	*p* value
By age group (year)			
18–29	24.9%	0.882 (0.843, 0.928)	<.001
30–40	25.1%	0.849 (0.809, 0.903)	<.001
41–51	25.1%	0.884 (0.841, 0.931)	<.001
52–65	20.4%	0.950 (0.901, 1.000)	.056
>65	9.7%	0.972 (0.929, 1.015)	.223
By smoking probability quartile[b]			
Fourth quartile	29.7%	0.850 (0.794, 0.909)	.003
Third quartile	26.2%	0.917 (0.877, 0.966)	.022
Second quartile	20.7%	0.924 (0.871, 0.990)	.001
First quartile	10.8%	0.935 (0.899, 0.979)	<.001

Note. All models include state and year as unordered categorical fixed effects in addition to individual and state-level covariates described in Table 1. *OR* = odds ratio; CI = confidence interval.
[a]Smoking prevalence estimates from similar demographic group in the TUS-CPS survey.
[b]See supplementary material for further information on derivation of smoking probability quartiles and on TUS-CPS.

in chronic disease prevalence and into the realm of mental health. Based on our results, we estimate that a $1 increase in cigarette excise taxes across the United States could result in a 10.5% relative reduction in risk for suicide. Given an adult suicide rate of 16.1 per 100,000 in 2010 (CDC, 2012), this would correspond to nearly 4,000 fewer suicides per year. Reductions in suicide rates might also be brought about by stricter smoke-free air policies nationally, a combination of these policies, or novel policy interventions that would reduce smoking prevalence. Our results are consistent with mounting evidence that tobacco control policies may reduce the prevalence of psychiatric disorders and substance abuse—two key risk factors for suicide. Two recent studies utilizing a nationally representative panel of U.S. smokers showed that increases in cigarette excise taxes and stricter smoke-free air policies were associated with decreased alcohol consumption and alcohol use disorder remission, respectively (Young-Wolff, Hyland, *et al.*, 2013; Young-Wolff, Kasza, Hyland, & McKee, 2013). Mojtabai and Crum (2013) use the same dataset to show that regular smoking is associated with new onset mood and anxiety disorders; they also used cigarette excise taxes and social attitudes toward smoking as instrumental variables to argue that the association is causal, implying that stronger tobacco control policies could reduce the prevalence of these disorders. Finally, Gruber and Mullainathan (2005) conducted separate analyses of U.S. and Canadian data to show that cigarette excise taxes were associated with a reduction in the number of people reporting subjective unhappiness and that these effects were limited to people with high probability of smoking. Self-reported happiness and other subjective measures are inversely associated with suicide risk, so those results are concordant with the results of our study (Koivumaa-Honkanen, Honkanen, Koskenvuo, & Kaprio, 2003; Xu & Roberts, 2010).

In concert with previous literature on the smoking–suicide and smoking–mental health links, our findings raise critical questions about the long-term neurobehavioral consequences of nicotine exposure. Studies of cigarette smoking cannot tease apart the effects of other components of smoke from those of nicotine (Swan & Lessov-Schlaggar, 2007). Nonetheless, studies of nicotine exposure in animals and *in vitro* suggest that the psychiatric health effects of nicotine are far from benign, and our results are consistent with this literature (Clark *et al.*, 2001; Collins & Izenwasser, 2004; Gutknecht *et al.*, 2012; Lê, Wang, Harding, Juzytsch, & Shaham, 2003; Mineur & Picciotto, 2010; Picciotto *et al.*, 2002) The rapid rise of new nicotine users relying on alternative tobacco and nicotine products such as electronic cigarettes raises concern about the mental health risks associated with such products (CDC, 2013; Chatterji *et al.*, 1997).

A limitation of our work is that the vital statistics data that were analyzed lacked information about smoking. Mitigating this limitation, however, we were able to demonstrate significant moderation of the policy–suicide association by probability of smoking, as indicated either by age alone or by a smoking probability function assembled from multiple demographic variables. The strongest policy–suicide associations were observed among those with high probability of smoking, while weak or insignificant effects were observed among groups with low smoking probability. These trends are consistent with policy associations with suicide occurring as a result of policy effects on smoking.

Several additional limitations should be kept in mind when interpreting these results. First, although unobserved state-invariant and time-invariant covariates are implicitly controlled by analytical design, and additional observed covariates were explicitly specified, no observational design can unambiguously establish causation. Potential confounders include any factors that changed in the same states and at the same times as excise taxes and smoke-free air policies. Furthermore, the regression parameters we estimate for the 1990–2004 period may not precisely extend to the current period as associations between policy and smoking may have changed over time due to more stringent tobacco control policies and further declines in smoking. A final limitation is that our models focused on state-level smoke-free air policies and excise taxes, but local-level policy may also influence smoking behaviors. The presence of these policies would result in misclassification error; the bias that might result from such error would most likely be toward the null hypothesis. Limitations notwithstanding, these results suggest that stronger tobacco control policies could

reduce suicide rates, and they constitute a novel line of evidence that smoking may increase risk for suicide. While further studies may be required to establish a compelling weight of evidence, this study provides strong epidemiological support in favor of the proposition that smoking is a causal risk factor for suicide.

SUPPLEMENTARY MATERIAL

Supplementary material can be found online at http://www.ntr.oxfordjournals.org

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DECLARATION OF INTERESTS

LJB is listed as an inventor on issued U.S. Patent 8,080,371, Markers for Addiction, covering the use of certain genetic markers in determining the diagnosis, prognosis, and treatment of addiction.

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REFERENCES

Angrist, J. D., & Pischke, J.-S. (2008). *Mostly harmless econometrics: An empiricist's companion*. Princeton, NL: Princeton University Press.

Angst, J., & Clayton, P. (1986). Premorbid personality of depressive, bipolar, and schizophrenic patients with special reference to suicidal issues. *Comprehensive Psychiatry*, *27*, 511–532. doi:10.1016/0010-440X(86)90055-6

Angst, J., & Clayton, P. J. (1998). Personality, smoking and suicide: A prospective study. *Journal of Affective Disorders*, *51*, 55–62. doi:10.1016/S0165-0327(98)00156-6

Berry, W. D., Ringquist, E. J., Fording, R. C., & Hanson, R. L. (1998). Measuring citizen and government ideology in the American states, 1960–93. *American Journal of Political Science*, *42*, 327–348. doi:10.2307/2991759

Bertrand, M., Duflo, E., & Mullainathan, S. (2004). How much should we trust differences-in-differences estimates? *Quarterly Journal of Economics*, *119*, 249–275. doi:10.1162/003355304772839588

Breslau, N., & Klein, D. F. (1999). Smoking and panic attacks: An epidemiologic investigation. *Archives of General Psychiatry*, *56*, 1141–1147. doi:10.1001/archpsyc.56.12.1141

Breslau, N., Peterson, E. L., Schultz, L. R., Chilcoat, H. D., & Andreski, P. (1998). Major depression and stages of smoking. A longitudinal investigation. *Archives of General Psychiatry*, *55*, 161–166. doi:10.1001/archpsyc.55.2.161

Cavazos-Rehg, P. A., Breslau, N., Hatsukami, D., Kruass, M. J., Spitznagel, E. L., Grucza, R. A., . . . Bierut, L. J. (2014). Smoking cessation is associated with lower rates of mood/anxiety and alcohol use disorder. *Psychological Medicine*. Advance online publication. doi:10.1017/S0033291713003206

Cavazos-Rehg, P. A., Krauss, M. J., Spitznagel, E. L., Chaloupka, F. J., Luke, D. A., Waterman, B., . . . Bierut, L. J. (2012). Differential effects of cigarette price changes on adult smoking behaviours. *Tobacco Control*, *23*, 113–118. doi:10.1136/tobaccocontrol-2012–050517

Centers for Disease Control and Prevention. (2002). Cigarette smoking among adults—United States, 2000. *Morbidity and Mortality Weekly Report*, *51*, 642–645.

Centers for Disease Control and Prevention. (2013). Notes from the field: Electronic cigarette use among middle and high school students—United States, 2011–2012. *Morbidity and Mortality Weekly Report*, *62*, 729–730.

Centers for Disease Control and Prevention (CDC), National Center for Health Statistics. (2012). Multiple cause of death 2010 on CDC WONDER [Online Database released 2012]. Retrieved March 19, 2014, from http://wonder.cdc.gov/mcd-icd10.html

Chaloupka, F. J., & Warner, K. E. (2000). Chapter 29. The economics of smoking. In A. J. Culyer & J. P. Newhouse (Eds.), *Handbook of health economics* (Vol. *1*, Part B, pp. 1539–1627). doi:10.1016/S1574-0064(00)80042-6. Elsevier. Retrieved from http://www.sciencedirect.com/science/article/pii/S1574006400800426

Chatterji, S., Saunders, J. B., Vrasti, R., Grant, B. F., Hasin, D., & Mager, D. (1997). Reliability of the alcohol and drug modules of the Alcohol Use Disorder and Associated Disabilities Interview Schedule--Alcohol/Drug-Revised (AUDADIS-ADR): An international comparison. *Drug and Alcohol Dependence*, *47*, 171–185. doi:10.1016/S0376-8716(97)00088-4

Clark, A., Lindgren, S., Brooks, S. P., Watson, W. P., & Little, H. J. (2001). Chronic infusion of nicotine can increase operant self-administration of alcohol. *Neuropharmacology*, *41*, 108–117. doi:10.1016/S0028-3908(01)00037-5

Clayton, P. J., Ernst, C., & Angst, J. (1994). Premorbid personality traits of men who develop unipolar or bipolar disorders. *European Archives of Psychiatry and Clinical Neuroscience*, *243*, 340–346. doi:10.1007/BF02195728

Collins, S. L., & Izenwasser, S. (2004). Chronic nicotine differentially alters cocaine-induced locomotor activity in adolescent vs. adult male and female rats. *Neuropharmacology*, *46*, 349–362. doi:10.1016/j.neuropharm.2003.09.024

De Leon, J., Dadvand, M., Canuso, C., White, A. O., Stanilla, J. K., & Simpson, G. M. (1995). Schizophrenia and smoking: An epidemiological survey in a state hospital. *American Journal of Psychiatry*, *152*, 453–455.

DeCicca, P., Kenkel, D., & Mathios, A. (2008). Cigarette taxes and the transition from youth to adult smoking: Smoking initiation, cessation, and participation. *Journal of Health Economics*, *27*, 904–917. doi:10.1016/j.jhealeco.2008.02.008

Doll, R., & Peto, R. (1976). Mortality in relation to smoking: 20 years' observations on male British doctors. *British Medical Journal*, *2*, 1525–1536. doi:10.1136/bmj.2.6051.1525

Fleming, R., Leventhal, H., Glynn, K., & Ershler, J. (1989). The role of cigarettes in the initiation and progression of early substance use. *Addictive Behaviors*, *14*, 261–272. doi:10.1016/0306-4603(89)90057-9

Giovino, G., Chaloupka, F., Hartman, A., Joyce, K. G., Chriqui, J., Orleans, C., . . . Gibson, J. (2009). *Cigarette smoking prevalence and policies in the 50 states: An era of change–the Robert Wood Johnson Foundation ImpacTeen Tobacco Chart Book* (pp. 9–36). Buffalo, NY: University at Buffalo, State University of New York.

Gruber, J. H., & Mullainathan, S. (2005). Do cigarette taxes make smokers happier. *Advances in Economic Analysis & Policy*, *5*. doi:10.2202/1538-0637.1412

Gutknecht, L., Araragi, N., Merker, S., Waider, J., Sommerlandt, F. M. J., Mlinar, B., . . . Hamon, M. (2012). Impacts of brain serotonin deficiency following Tph2 inactivation on development and raphe neuron serotonergic specification. *PloS one*, *7*, e43157. doi:10.1371/journal.pone.0043157

Hemmingsson, T., & Kriebel, D. (2003). Smoking at age 18–20 and suicide during 26 years of follow-up-how can the association be explained? *International Journal of Epidemiology*, *32*, 1000–1004.

Hughes, J R, Hatsukami, D. K., Mitchell, J. E., & Dahlgren, L. A. (1986). Prevalence of smoking among psychiatric outpatients. *American Journal of Psychiatry*, *143*, 993–997.

Hughes, J. R. (2008). Smoking and suicide: A brief overview. *Drug and Alcohol Dependence*, *98*, 169–178. doi:10.1016/j.drugalcdep.2008.06.003

International Agency for Research on Cancer. (2009). Evaluating the effectiveness of smoke-free policies. In *IACR handbooks of cancer prevention, tobacco control* (Vol. *13*). Lyon, France: World Health Organization.

Isensee, B., Wittchen, H.-U., Stein, M. B., Höfler, M., & Lieb, R. (2003). Smoking increases the risk of panic: Findings from a prospective community study. *Archives of General Psychiatry*, *60*, 692–700. doi:10.1001/archpsyc.60.7.692

Johnson, J. G., Cohen, P., Pine, D. S., Klein, D. F., Kasen, S., & Brook, J. S. (2000). Association between cigarette smoking and anxiety disorders during adolescence and early adulthood. *Journal of the American Medical Association*, *284*, 2348–2351. doi:10.1001/jama.284.18.2348

Kalman, D., Morissette, S. B., & George, T. P. (2005). Co-morbidity of smoking in patients with psychiatric and substance use disorders. *American journal on addictions*, *14*, 106–123. doi:10.1080/10550490590924728

Koivumaa-Honkanen, H., Honkanen, R., Koskenvuo, M., & Kaprio, J. (2003). Self-reported happiness in life and suicide in ensuing 20 years. *Social Psychiatry and Psychiatric Epidemiology*, *38*, 244–248. doi:10.1007/s00127-003-0625-4

Lasser, K., Boyd, J. W., Woolhandler, S., Himmelstein, D. U., McCormick, D., & Bor, D. H. (2000). Smoking and mental illness: A population-based prevalence study. *Journal of the American Medical Association*, *284*, 2606–2610. doi:10.1001/jama.284.20.2606

Lê, A. D., Wang, A., Harding, S., Juzytsch, W., & Shaham, Y. (2003). Nicotine increases alcohol self-administration and reinstates alcohol seeking in rats. *Psychopharmacology*, *168*, 216–221. doi:10.1007/s00213-002-1330-9

Leistikow, B. (2003). Commentary: Questionable premises, overadjustment, and a smoking/suicide association in younger adult men. *International Journal of Epidemiology*, *32*, 1005–1006. doi:10.1093/ije/dyg326

Leistikow, B. N., & Shipley, M. J. (1999). Might stopping smoking reduce injury death risks? A meta-analysis of randomized, controlled trials. *Preventive Medicine*, *28*, 255–259. doi:10.1006/pmed.1998.0412

Levy, D. T., Chaloupka, F., & Gitchell, J. (2004). The effects of tobacco control policies on smoking rates: A tobacco control scorecard. *Journal of Public Health Management and Practice*, *10*, 338–353.

Li, D., Yang, X., Ge, Z., Hao, Y., Wang, Q., Liu, F., . . . Huang, J. (2012). Cigarette smoking and risk of completed suicide: A meta-analysis of prospective cohort studies. *Journal of Psychiatric Research*, *46*, 1257–1266. doi:10.1016/j.jpsychires.2012.03.013

Mineur, Y. S., & Picciotto, M. R. (2010). Nicotine receptors and depression: Revisiting and revising the cholinergic hypothesis. *Trends in Pharmacological Sciences*, *31*, 580–586. doi:10.1016/j.tips.2010.09.004

Mojtabai, R., & Crum, R. M. (2013). Cigarette smoking and onset of mood and anxiety disorders. *American Journal of Public Health*, *103*, 1656–1665. doi:10.2105/AJPH.2012.300911

National Association of State Mental Health Directors Research Institute. (n.d.). State Mental Health Agency Profiles System (Profiles) and Reneue Expendtures Study: Prior years revenues & expenditures reports. Retrieved from http://www.nri-inc.org/projects/Profiles/RevExpPrior/2002Table32.pdf

National Cancer Institute (NCI). (n.d.). State Cancer Legislative Database, Database Search. Retrieved September 27, 2013, from http://www.scld-nci.net/db_search/index.cfm

Norberg, K. E., Bierut, L. J., & Grucza, R. A. (2009). Long-term effects of minimum drinking age laws on past-year alcohol and drug use disorders. *Alcoholism: Clinical and Experimental Research*, 33, 2180–2190. doi:10.1111/j.1530-0277.2009.01056.x

Orzechowski, W., & Walker, R. (2012). *The tax burden on tobacco: Historical compilation 2012* (Vol. 47). Arlington, VA: Orzechowski & Walker Consulting.

Petersen, M. A. (2009). Estimating standard errors in finance panel data sets: Comparing approaches. *Review of Financial Studies*, *22*, 435–480. doi:10.1093/rfs/hhn053

Picciotto, M. R., Brunzell, D. H., & Caldarone, B. J. (2002). Effect of nicotine and nicotinic receptors on anxiety and depression. *Neuroreport*, *13*, 1097–1106. doi:10.1097/00001756-200207020-00006

Ponicki, W. (2004). *Statewide availability data system II: 1933–2003. National Institute on Alcohol Abuse and Alcoholism Research Center Grant P60-AA006282-23*. Berkeley, CA: Pacific Institute for Research and Evaluation Prevention Research Center.

Poorthuis, R. B., Goriounova, N. A., Couey, J. J., & Mansvelder, H. D. (2009). Nicotinic actions on neuronal networks for cognition: General principles and long-term consequences. *Biochemical Pharmacology*, *78*, 668–676. doi:10.1016/j.bcp.2009.04.031

Ross, H., & Chaloupka, F. J. (2004). The effect of public policies and prices on youth smoking. *Southern Economic Journal*, 796–815. doi:10.2307/4135273

Ruggles, S., Alexander, J. T., Genadek, K., Goeken, R., Schroeder, M. B., & Sobek., M. (2010). Integrated Public Use Microdata Series: Version 5.0 [Machine-readable database]. Minneapolis., MN: University of Minnesota.

Swan, G. E., & Lessov-Schlaggar, C. N. (2007). The effects of tobacco smoke and nicotine on cognition and the brain. *Neuropsychology Review*, *17*, 259–273. doi:10.1007/s11065-007-9035-9

Tauras, J. A., & Chaloupka, F. J. (1999). *Price, clean indoor air, and cigarette smoking: Evidence from the longitudinal data for young adults*. Cambridge, MA: National Bureau of Economic Research.

U.S. Census Bureau. (2000). *2000 Census of Population and Housing*. Washington, DC: U.S. Census Bureau

United Health Foundation. (n.d.). America's health rankings (custom report). Retrieved from http://www.americashealthrankings.org/

Xu, J., & Roberts, R. E. (2010). The power of positive emotions: It's a matter of life or death--subjective well-being and longevity over 28 years in a general population. *Health Psychology*, *29*, 9–19. doi:10.1037/a0016767

Young-Wolff, K. C., Hyland, A. J., Desai, R., Sindelar, J., Pilver, C. E., & McKee, S. A. (2013). Smoke-free policies in drinking venues predict transitions in alcohol use disorders in a longitudinal U.S. sample. *Drug and Alcohol Dependence*, *128*, 214–221. doi:10.1016/j.drugalcdep.2012.08.028

Young-Wolff, K. C., Kasza, K. A., Hyland, A. J., & McKee, S. A. (2013). Increased cigarette tax is associated with reductions in alcohol consumption in a longitudinal U.S. sample. *Alcoholism, Clinical and Experimental Research*. doi:10.1111/acer.12226