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Cigarette smoking and the onset and persistence of depression
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ABSTRACT

Background: The present study investigated the relationship between daily cigarette smoking and risk of onset and persistence of major depressive disorder (MDD) over a 10-year period among adults in the United States and whether successful smoking cessation reduced risk for MDD.

Method: Data were drawn from the Midlife Development in the United States Survey (MIDUS; N=2,101) Waves I and II. Logistic regressions were used to investigate the relations between smoking and the onset and persistent of MDD, adjusting for demographic characteristics and substance use problems.

Results: Daily smoking in 1994 (OR=1.9 (1.2-3.2)) and persistent daily smoking (in 1994 and 2005) (OR=2.2 (1.3-3.7)) were both associated with a significantly increased likelihood of MDD in 2005. Additionally, abstinence compared to daily smoking for more than 10 years significantly reduced the risk of MDD in 2005 (OR=0.5 (0.3-0.87)) and persistent MDD (in 1994 & 2005; (OR=0.5 (0.3-0.87)).

Conclusions: Findings from this study provide new insights into the role of smoking in the onset and persistence of MDD. Namely, among those in mid-adulthood, smoking is associated with greater MDD risk and quitting may help to reduce such risk. These results suggest that there may be merit in targeting smoking to reduce the risk of MDD and the mental health benefits of quitting smoking in the form of reduced risk of MDD could usefully be added to common information listed as reasons to quit.

Keywords: Tobacco, Mood Disorders, Depression, Smoking, Adult, Epidemiology
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1. INTRODUCTION

There is substantial comorbidity between major depressive disorder (MDD) and smoking. For example, Lasser and colleagues (2000) reported approximately 60% of those with a lifetime history of MDD are current or past smokers. Conversely, smokers relative to non-smokers have significantly higher rates of MDD. Other work suggests that smokers who are nicotine dependent are significantly more likely to have a history of MDD.

There are a variety of streams of empirical work that suggest smoking-MDD relations are bi-directional. First, MDD may influence the developmental progression to smoking via self-medication or mood management mechanisms. For example, young adults with a history of MDD compared to those without such a history are significantly more likely to begin smoking. Yet, other studies have not found such MDD to smoking onset relations. Second, some work suggests smoking influences the onset and course of MDD; a pathway theorized to be influenced by neuro-physiologic processes altered by smoking. In fact, daily smoking is associated with increased risk for MDD in longitudinal studies. Finally, there is mixed evidence that a history of MDD is related to lower odds of cessation. Yet, moderate to severe levels of depressive symptoms prior to smoking cessation treatment are significantly associated with poorer cessation outcomes. In addition, therapeutic approaches that include depression treatment components compared to standard smoking cessation protocols appear to improve odds of quitting.

Despite progress in better understanding smoking-MDD developmental relations, there are at least three key limitations to past work. First, in terms of the developmental path from cigarette smoking to MDD, longer-term outcomes have been infrequently modeled. Indeed, most studies on the impact of smoking on the risk of future MDD have employed follow-up periods
that range only from 6 months to 5 years. Thus, there is a need for the replication and extension of past work using longer periods of time. Second, past studies have not yet explored the explanatory utility of persistence of smoking (i.e., 'stable' smoking measured between at least two time points) over time in relation to MDD. Such information is practically and theoretically important, as it will help shed novel insight into the role of persistent smoking behavior and relative risk for new and persistent cases of MDD. Finally, past work has infrequently examined how smoking cessation relates to the risk of recent incidence and persistence of MDD. Thus, the clinical significance of smoking as a risk factor for MDD prevention/intervention has not been fully explicated. Finally, a majority of past work has been completed in younger persons, and therefore, relatively little is known about these relations over the course of adulthood. This limitation is important because smoking is the leading cause of premature death among older adults.

Together, the current investigation examined the relation between smoking and MDD over a 10 year period. First, it was hypothesized that after controlling for gender, socioeconomic status, and substance use problems, daily smoking (compared to non-smoking) would be associated with increased likelihood of MDD. Second, it was hypothesized that successful smoking cessation (compared to smoking) would be associated with decreased likelihood of MDD.

2. METHODS

2.1. Participants

Data were drawn from the two waves of the Midlife Development in the United States Survey (MIDUS). The MacArthur Midlife Research Network collected Wave I data from
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1994 to 1995 and Wave II data from 2004 to 2006; a national survey of Americans in adulthood that investigated behavioral, psychological, and social factors related to physical and mental health. Wave I consisted of a nationally representative multistage probability sample (main sample) of community-dwelling English speakers in the continental United States (n = 3,032). Participants who completed the telephone interview were mailed a self-administered questionnaire. The response rate from the mailed questionnaire was 86.6%, yielding an overall response rate of 61% (.70 * .87 = .61). Approximately 70% of Wave I participants took part in the Wave II survey collected by the Institute on Aging at the University of Wisconsin–Madison and supported by the National Institute on Aging (2004 – 2006). Wave II participants completed a 30-min telephone interview and a self-administered questionnaire was mailed to them. Of the 3,032 participants from Wave I, 2,101 completed the Wave II telephone surveys (response rate of 69.5%). For this study, we analyzed only data from those who participated in the Wave I main sample who completed both the phone and mail-in surveys, participated in the Wave II survey, and had complete information for Wave II outcome variables.

2.2. Measures

2.2.1. Demographic characteristics.

At Wave 1, basic socio-demographic characteristics were obtained using a self-report questionnaire. These included age, race, gender, marital status and level of formal education obtained.

2.2.2. Smoking.
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At each Wave, participants who reported ever smoking at least one cigarette were asked whether they had ever smoked regularly (“regularly—meaning at least a few cigarettes every day”), the age they were when they last smoked regularly and whether they currently smoke regularly (“Do you smoke cigarettes regularly now?”). Those who reported no lifetime smoking were considered lifetime non-smoker. Those who reported lifetime daily smoking and were not current daily smokers at Wave 1 or 2 were designated considered former daily smokers with successful abstinence for more than 10 years. Those who reported current daily smoking at Wave 1 and 2 were considered persistent smokers.

2.2.3. Major depression.

Psychiatric diagnoses of MIDUS were based on the Composite International Diagnostic Interview Short Form scales (CIDI-SF; 38). CIDI-SF is a series of diagnostic-specific scales that were developed from item level analyses of the Composite International Diagnostic Interview questions during the National Comorbidity Survey. CIDI-SF scales were designed to reproduce the full Composite International Diagnoses as exactly as possible, with only a small subset of the original questions. Validity data suggests strong relationship between CIDI-SF-based and the full CIDI-based diagnoses. These measures were used in Wave 1 and 2 for the presence of the disorders during the past-12 month. Recent incidence of MDD by 2005 was defined as having past 12-month disorder at Wave 2 but not at Wave 1. Persistent MDD was defined as having past 12-month disorder at both Wave 1 and Wave 2.

2.3. Statistical Analysis

Differences in demographic characters between lifetime non-smokers, former daily smokers (abstinence for more than 10 years after history of daily smoking), and persistent
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smokers were identified using chi-square analyses. Logistic regression analyses were utilized to evaluate the relationships between a) daily smokers (1994) vs. lifetime non-smokers; b) persistent smokers vs. lifetime non-smokers; c) former daily smokers (successful quitters) vs. lifetime non-smokers; d) former daily smokers (successful quitters) vs. persistent smokers, and odds of (1) past 12-month MDD by 2005; (2) persistent/recurring MDD in 1994 and 2005. Analyses were adjusted for socio-demographic factors and alcohol and drug use problems.

3. RESULTS

3.1. Demographic Characteristics and Smoking

Compared with non-smokers, persistent smokers were less likely to be female, have lower age or fewer years of education, less likely to be married, and more likely to be separated, divorced, or never married (see Table 1). Moreover, compared to non-smokers, smokers who successfully quit were less likely to be female, had less education, and were more likely to be divorced and be older (see Table 1).

3.2. Daily Smoking and MDD

Smoking at 1994 compared to non-smoking was associated with an increased risk of incidence of MDD by 2005 and persistence of MDD from 1994 to 2005 (see Table 2). These associations remained significant after adjusting for the covariates.

3.3. Persistent Smoking and MDD

Persistent smoking compared to non-smoking was associated with increased risk of MDD (see Table 2); these effects were significant after adjusting for the covariates.
3.4 Former daily smoking (sustained abstinence for more than 10 years) and MDD

Compared to persistent smoking, sustained abstinence for more than 10 years was significantly related to less risk for MDD (see Table 3). Additionally, compared to lifetime non-smokers (see Table 3), sustained abstinence for more than 10 years was not significantly associated with MDD, even after adjusting for demographic factors, and alcohol/drug use problems. The only exception to this pattern of results was a slightly higher incidence of MDD at 2005 for those who had quit compared to non-smokers after adjusting for age and gender (see Table 3).

4. DISCUSSION

Smoking was significantly associated with increased risk for the onset and persistence of MDD even after controlling for socio-demographic characteristics and substance use problems. These observations are in line with previous findings and extend them to a 10 years period among a nationally representative sample of adults in the U.S. [5, 37] Moreover, smokers who quit and remained abstinent for more than 10 years compared to persistent smokers demonstrated lower odds of MDD. [21, 38-40] However, an alternative explanation could be that these successful quitters may have been as a result of the prior remission of MDD. Nonetheless, with replication in future work, this finding suggests quitting smoking may result in lower risk of MDD whether from an onset or maintenance perspective. This is a potentially clinically important observation that suggests there is merit to the utilization of smoking cessation as a method to prevent or reduce risk for MDD. [41-43]
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It is noteworthy that the risk of MDD for those that quit was not different from non-smokers. Regardless of possible explanations for this observation (i.e., whether quitting reduced the risk of MDD, or clinical improvement in MDD contributed to cessation), the extant literature has yielded inconsistent findings regarding the MDD-related prognoses of former smokers compared to non-smokers.\cite{22,27,44-53} These inconsistencies could be due to utilization of different methodologies\cite{49} and between-samples differences in variables like gender,\cite{27,49} comorbid anxiety,\cite{44} and genetic predisposition.\cite{54-57} However, even among the studies that report higher rates of MDD for former smokers compared to lifetime non-smokers, these rates are still lower than for current daily/persistent smokers.\cite{22,27,44}

The present study has a number of limitations. First, despite utilization of longitudinal methodology, it is not possible to discern the exact chronology of some theoretically and clinically-relevant events (e.g., quitting dates, dates of onset of past/recent MDD). A useful next step in this line of work therefore would be to isolate the temporal trajectories of such events. Second, due to our primary interest to investigate the effects of longer-term duration of abstinence on MDD, we did not include participants with equal or less than 10 years abstinence in this study. Future work may benefit by exploring smokers with differing levels of time abstinent from smoking and its relation to MDD and vice versa. Third, only MDD was studied based upon the a priori theoretical model. Thus, it is not possible to generalize the findings from these data to all mood disorders. Accordingly, further evaluation of the associations between different smoking trajectories and other mood (e.g., bipolar) and even anxiety disorders would be advisable. Fourth, we did not have the data on the MDD severity among participants. Therefore, it is unclear how severity of illness relates to smoking cessation. Fifth, MIDUS is a survey among persons aged 25–74. It is therefore not clear whether the findings are applicable to
Running head: Smoking status and Major depression

other age groups. Sixth, levels of nicotine dependence were not measured in this study. In light of evidence for the differential impact of levels of smoking heaviness\textsuperscript{[10, 58]} and nicotine dependence\textsuperscript{[3, 27, 59, 60]} in terms of MDD, future investigations could benefit from examining differential MDD-related predictive validity across levels of smoking heaviness (e.g., heavy smoking, light smoking).\textsuperscript{[58]} Finally, it is possible that the observed associations could result from unmeasured confounding effects of other MDD-relevant lifestyle factors such as diet, sleep, or exercise.\textsuperscript{[61]} Future examination of other health behaviors in models of smoking-MDD comorbidity would be useful.

Conclusion

The present findings highlight the clinically important role of smoking in terms of MDD over a 10-year period. These results suggest that there may be merit in targeting smoking to reduce the risk of MDD and the mental health benefits of quitting smoking in the form of reduced risk of MDD could usefully be added to common information listed as reasons to quit.
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**Highlights**
Persistent daily smoking is associated with an increased likelihood of MDD up to ten years later
Abstinence among former smokers, compared with persistent smoking, reduced the risk of MDD
Among adults in mid-adulthood, smoking is associated with greater MDD risk
Results suggest that quitting smoking reduces the risk of MDD

**Acknowledgments**
The MIDUS Study was funded by United States Department of Health and Human Services, the National Institutes of Health and the National Institute on Aging. We thank Bianca Jiang for her assistance with manuscript preparation.

**Declaration of interest**
All authors declare that they have no conflicts of interest.
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Table 1: Demographic characteristics* associated with remitted/former daily smoking (i.e. abstinence for more than 10 years) and persistent smoking among adults in the community.

<table>
<thead>
<tr>
<th></th>
<th>Lifetime non-smokers (N = 518)</th>
<th>Former daily smokers &quot;10+ years abstinence&quot; (N = 532)</th>
<th>Persistent smokers (N = 356)</th>
<th>p-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age-Mean (SD)</strong></td>
<td>43.8 (13.5)</td>
<td>49.9 (12.3)</td>
<td>41.3</td>
<td>&lt; .0001</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>177 (32.1%)</td>
<td>290 (54.5%)</td>
<td>176 (49.4%)</td>
<td>&lt; .0001</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>Female</td>
<td>-342 (65.9%)</td>
<td>-242 (45.5%)</td>
<td>-180</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td>-416 (87.4%)</td>
<td>-451 (91.1%)</td>
<td>-283</td>
<td>0.1</td>
<td>0.4</td>
</tr>
<tr>
<td>White</td>
<td>141 (32.1%)</td>
<td>172 (54.5%)</td>
<td>149 (49.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>-32 (6.7%)</td>
<td>-29 (5.9%)</td>
<td>-21 (6.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Native American</td>
<td>-3 (0.6%)</td>
<td>-1 (0.2%)</td>
<td>-1 (0.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian or Pacific Islander</td>
<td>-9 (1.9%)</td>
<td>-2 (0.4%)</td>
<td>-1 (0.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>141 (27.2%)</td>
<td>149 (41.9%)</td>
<td>-149 (41.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiracial</td>
<td>-4 (0.8%)</td>
<td>-5 (1.0%)</td>
<td>-1 (0.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td>-52 (10.0%)</td>
<td>-77 (14.5%)</td>
<td>-77 (21.6%)</td>
<td>&lt; .0001</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>Some Grade School</td>
<td>141 (27.2%)</td>
<td>149 (41.9%)</td>
<td>-149 (41.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High School Graduate</td>
<td>18.70%</td>
<td>28.00%</td>
<td>27.50%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Marital Status</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
<th>%1</th>
<th>%2</th>
<th>%3</th>
<th>p-value</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bachelor's Degree</td>
<td>-97</td>
<td>86</td>
<td>-20</td>
<td>18.70%</td>
<td>16.20%</td>
<td>5.60%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some graduate</td>
<td>-88</td>
<td>-86</td>
<td>-12</td>
<td>18.70%</td>
<td>16.20%</td>
<td>3.40%</td>
<td></td>
<td></td>
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<tr>
<td>school or beyond</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital Status</td>
<td>-361</td>
<td>-385</td>
<td>-227</td>
<td>69.80%</td>
<td>72.50%</td>
<td>63.60%</td>
<td>0.026</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>Married</td>
<td>-7</td>
<td>-8</td>
<td>-10</td>
<td>1.40%</td>
<td>1.50%</td>
<td>2.80%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Separated</td>
<td>-54</td>
<td>-69</td>
<td>-75</td>
<td>10.40%</td>
<td>13.00%</td>
<td>21.00%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Divorced</td>
<td>-46</td>
<td>-45</td>
<td>-17</td>
<td>8.90%</td>
<td>8.50%</td>
<td>4.80%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Widowed</td>
<td>-49</td>
<td>-24</td>
<td>-28</td>
<td>9.50%</td>
<td>4.50%</td>
<td>7.80%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never Married</td>
<td></td>
<td></td>
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</tbody>
</table>

*demographic characteristics reported at Wave 1
Table 2: Current daily smoking in 1994, and persistent daily smoking (in 1994 and 2005) and risk of depression onset and persistence in 2005, both compared to lifetime non-smoking.

<table>
<thead>
<tr>
<th></th>
<th>Lifetime non-smokers (N=518)</th>
<th>Current daily smokers 1994 (N=525)</th>
<th>OR (95% CI)</th>
<th>AOR(^a) (95% CI)</th>
<th>AOR(^b) (95% CI)</th>
<th>Persistent daily smokers(^1) (N=356)</th>
<th>OR (95% CI)</th>
<th>AOR(^a) (95% CI)</th>
<th>AOR(^b) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDD 2005 Only</td>
<td>6.1% (28)</td>
<td>11.2% (46)</td>
<td>1.9 (1.2, 3.2)</td>
<td>2.2 (1.4, 3.7)</td>
<td>1.8 (1.1, 3.1)</td>
<td>13.5% (38)</td>
<td>2.4 (1.4, 4.0)</td>
<td>2.8 (1.6, 4.7)</td>
<td>2.3 (1.3, 4.0)</td>
</tr>
<tr>
<td>MDD 1994 + 2005</td>
<td>5.1% (23)</td>
<td>10.4% (42)</td>
<td>2.2 (1.3, 3.7)</td>
<td>2.6 (1.5, 4.5)</td>
<td>2.5 (1.4, 4.3)</td>
<td>10.9% (30)</td>
<td>2.3 (1.3, 4.0)</td>
<td>2.7 (1.5, 4.9)</td>
<td>2.6 (1.4, 4.8)</td>
</tr>
</tbody>
</table>

Bold=p<0.05  
AOR\(^a\) = age and gender  
AOR\(^b\) = age, gender and alcohol/drug use problems at Wave 1 (1994)  
\(^1\)Smoking at both waves (1994 and 2005)
Table 3: Former daily smoking (i.e., abstinence for more than 10 years) and risk of depression onset and persistence in 2005, compared to Persistent daily smoking (1994 and 2005) and lifetime non-smoking.

<table>
<thead>
<tr>
<th></th>
<th>Former daily smokers &quot;10+ years abstinence&quot; (N=532)</th>
<th>Persistent daily smokers (N=356)</th>
<th>OR (95% CI)</th>
<th>AOR&lt;sup&gt;a&lt;/sup&gt; (95% CI)</th>
<th>AOR&lt;sup&gt;b&lt;/sup&gt; (95% CI)</th>
<th>Lifetime non-smokers (N=518)</th>
<th>OR (95% CI)</th>
<th>AOR&lt;sup&gt;a&lt;/sup&gt; (95% CI)</th>
<th>AOR&lt;sup&gt;b&lt;/sup&gt; (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MDD 2005 Only</strong></td>
<td>7.7% (36)</td>
<td>13.5% (38)</td>
<td>0.5 (0.3, 0.87)</td>
<td>0.6 (0.4, 1.06)</td>
<td>0.7 (0.4, 1.2)</td>
<td>6.1% (28)</td>
<td>1.3 (0.8, 2.1)</td>
<td>1.8 (1.03, 3.0)</td>
<td>1.7 (0.98, 2.9)</td>
</tr>
<tr>
<td><strong>MDD 1994 + 2005</strong></td>
<td>4.2% (19)</td>
<td>10.9% (30)</td>
<td>0.36 (0.2, 0.65)</td>
<td>0.5 (0.26, 0.93)</td>
<td>0.5 (0.26, 0.96)</td>
<td>5.1% (23)</td>
<td>0.8 (0.4, 1.5)</td>
<td>1.2 (0.6, 2.3)</td>
<td>1.1 (0.6, 2.2)</td>
</tr>
</tbody>
</table>

Bold =p<0.05
AOR<sup>a</sup> = age and gender
AOR<sup>b</sup> = age, gender and alcohol/drug use problems at Wave 1 (1994)
REFERENCES


