Published in final edited form as:

Drug Alcohol Depend. 2009 January 1; 99(1-3): 240–247. doi:10.1016/j.drugalcdep.2008.08.007.

Tobacco and Cannabis Co-occurrence: Does Route of Administration Matter?

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Abstract

Background—Qualitative research suggests that a shared route of administration (i.e. via inhalation) for the common forms of both tobacco (i.e. cigarettes) and cannabis (i.e. joints) may contribute to their co-occurring use.

Methods—We used data on 43,093 U.S. adults who participated in the 2001–2002 National Epidemiological Study on Alcohol Related Conditions (NESARC) to examine whether cannabis use and abuse/dependence were associated with smoked (cigarettes, cigars, pipes) versus smokeless (snuff, chewed tobacco) forms of tobacco use, even after controlling for socio-demographic, psychiatric and substance-related covariates.

Results—Tobacco smoking was associated with a 3.3–4.5 times increased risk for cannabis use and abuse/dependence respectively. After covariate adjustment, importantly for nicotine dependence, smoked tobacco (but not smokeless tobacco) was still significantly associated with both cannabis use (multinomial odds-ratio (M.O.R.) 1.99) and cannabis dependence (M.O.R. 1.55). In contrast, use of smokeless tobacco was not significantly correlated with elevated rates of cannabis use (M.O.R. 0.96) or abuse/dependence (M.O.R. 1.04).

Conclusions—Route of administration may play an important role in the observed association between tobacco and cannabis use. This may represent a physiological adaptation of the aero-respiratory system and/or index social and cultural influences surrounding the use of smoked versus smokeless forms of tobacco.

Keywords

cannabis; tobacco; NESARC; smoked

1. INTRODUCTION

Worldwide, tobacco and cannabis are amongst the most widely used psychoactive substances (Hall et al., 2003; Mackay et al., 2006). For instance, an estimated 44.5 million adults in the U.S. report having smoked cigarettes (Centers for Disease Control (CDC), 2004). Current U.S. estimates also suggest that 41% of 12th grade students report lifetime cannabis use, with over 36% reporting use in the past year (Johnston et al., 2006). Associated with both tobacco and cannabis are symptoms of dependence (as well as abuse for cannabis) (American Psychiatric

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Association, 1994). A lifetime history of nicotine dependence is noted in about 24% of U.S. adults (Breslau et al., 2001), and is associated with sustained smoking (Breslau et al., 1996), which is the leading cause of preventable death in the U.S. (Centers for Disease Control (CDC), 2002). Cannabis abuse/dependence, although less frequent, is an emerging public health concern – in 2000, cannabis problems were noted as the primary drug problem in nearly 236,400 admissions to the U.S. public treatment systems (Substance Abuse and Mental Health Services Administration (SAMHSA), 2005).

Tobacco and cannabis use and misuse often co-occur (Coffey et al., 2003; Kandel, 2002; Patton et al., 2006). Nearly 52% of U.S. tobacco smokers aged 12-17 years report past month cannabis use (Substance Abuse and Mental Health Services Administration (SAMHSA), 2005). Compared with non-smokers, adolescents who smoke cigarettes are 9-15 times more likely to use cannabis (Johnston et al., 2005; Mathers et al., 2006). A variety of hypotheses have been proposed to explain the association between tobacco and cannabis use.

1.1 The gateway hypothesis

First, investigators have proposed that tobacco use may serve as a gateway substance to cannabis use (Kandel, 2002). For instance, nearly 72% of high school students report using cigarettes prior to their cannabis use, demonstrating sequence, an important characteristic of the gateway, whereby the putative 'gateway drug' is initiated earlier than other substances in the sequence (Kandel et al., 1993). These, and other, investigators have also demonstrated an increased likelihood of cannabis use in those who use tobacco (or association, another characteristic of gateway drugs) (Adler et al., 1981; Faeh et al., 2006; Kandel et al., 1985; Mathers et al., 2006; Patton et al., 2006; Suris et al., 2007).

1.2 The reverse gateway hypothesis

A second, related hypothesis that has been proposed more recently suggests that cannabis use may serve as a reverse gateway to onset and maintenance of tobacco use (Agrawal et al., 2007a; Agrawal et al., 2008; Clough et al., 2004; Ford et al., 2002; Humfleet et al., 2004; Patton et al., 2005; Timberlake et al., 2007). Patton and colleagues (2005) found that teenagers who had never used tobacco but had used cannabis on a weekly basis were 8.4 times more likely to initiate tobacco use when compared to their counterparts who never used cannabis. These authors further reported that even after accounting for level of tobacco use and other socio-demographic characteristics, daily cannabis users who were not tobacco dependent at age 20 were 3.6 times more likely to meet criteria for nicotine dependence at age 24 (Patton et al., 2005). In comparable analyses, Ford et al. (2002) in a study of interview data from the Baltimore Epidemiological Catchment Area Study, found that even after accounting for racial affiliation, educational attainment and marital status, those who had last used cannabis less than a month ago were at 1.9 greater odds of reporting continued tobacco smoking than those who never used cannabis.

1.3 The correlated genetic vulnerabilities hypothesis

A third hypothesis regarding the frequent co-occurring use of tobacco and cannabis revolves around mechanisms of correlated vulnerabilities to both substances. According to this hypothesis, common genetic and environmental factors contribute to the observed association between tobacco and cannabis. Both tobacco use (Madden et al., 1999) and cannabis use (Kendler et al., 1998; Agrawal & Lynskey, 2008) are heritable, and a recent study suggests that common genetic factors influence vulnerability to both substances (Neale et al., 2006).

1.4 The common environmental risks hypothesis

A fourth related hypothesis implies that, in addition to common genetic etiologies, co-use of cannabis and tobacco may occur due to common environmental and social influences. For instance, peer networks may not only play an important role in promoting cannabis and tobacco use, they may also encourage certain forms of use (i.e. smoking both forms) (Conrad et al., 1992; Ellickson et al., 2004; Gifford-Smith et al., 2005; Perkonig et al., 2008). Strong ethnic and cultural norms (Golub et al., 2005; Kelly, 2005) also govern use of certain forms of cannabis and tobacco.

1.5 Route of administration

What has been largely overlooked in the literature is the possible influence of a common route of administration i.e. via smoking/inhalation, as a contributor to the observed association between tobacco and cannabis use, and whether the role of route of administration is separate from that of a shared vulnerability to substance use/dependence and to the addictive potential of nicotine. In the U.S., the most common mode of both tobacco and cannabis use is via inhalation in cigarettes and joints respectively. In the National Survey of Drug Use and Health, cigarette smoking, followed by cigar smoking, is the most popular form of tobacco use in individuals aged 12 and older (Substance Abuse and Mental Health Services Administration (SAMHSA), 2005). In a sample of twins from Virginia, all participants endorsing cannabis use reported smoked marijuana as their primary mode of cannabis use (Agrawal et al., 2004).

If route of administration contributes to the association between tobacco and cannabis use, we hypothesize that cannabis use and abuse/dependence will be more strongly associated with smoked versus smokeless tobacco use, even after accounting for the confounding effects of nicotine dependence and other covariates. Prospective data are ideally suited for the test of this hypothesis, where the evolution of cannabis trajectories can be contrasted across individuals using different forms of smoked or smokeless tobacco. However, this line of research has been challenging - smokeless forms of tobacco are unavailable and uncommon in several countries (Mackay et al., 2006), and thus several databases have neglected to include measures of smokeless tobacco use. In the U.S., however, both smoked and smokeless forms of tobacco are commonly used (Substance Abuse and Mental Health Services Administration (SAMHSA), 2005). However, given the lower prevalence of smokeless tobacco, even in the U.S., large sample sizes are required to discriminate smoked and smokeless forms of tobacco. Cross-sectional studies can afford larger sample sizes, and while causal inferences cannot be drawn from such a sampling framework, we may still test whether individuals reporting use of smoked tobacco are more likely to also report cannabis use and abuse/dependence when compared to those reporting use of smokeless tobacco. We, therefore, utilized data from a very large and nationally representative sample of 43,093 participants from the National Epidemiological Survey on Alcohol and Related Conditions (NESARC), which assessed smoked (cigarettes, cigars and pipes) and smokeless (snuff and chewed tobacco) tobacco use, cannabis use and abuse/dependence as well as a wide array of socio-demographic, psychiatric and substance-related characteristics of U.S. adults. This sample was adequately sized to address our hypothesis of the important role of route of administration in the association between tobacco and cannabis use.

2. METHODS

2.1 Sample

The National Epidemiological Survey on Alcohol and Related Conditions (NESARC) was designed and conducted by the National Institute on Alcohol Abuse and Alcoholism (Grant et al., 2003b). Under the direction of NIAAA, data were collected by the U.S. Census Bureau. Currently, data on 43,093 individuals, including adult, non-institutionalized U.S. citizens and

non-citizens (including Alaska and Hawaii) constitute the first wave (2001-2002) of this longitudinal survey. The sample includes data from 18,518 (43%) men and 24,575 women with a mean age of 46.4 years (SD=18.2). The sample is racially diverse (19% ethnically Hispanic and multiracial identifications of 76% White, 20% Black/African American, 0.8% Native Hawaiian/Pacific Islander, 3.1% Asian, 3.0% American Indian/Alaskan Native) with over-sampling for non-Hispanic Black households and for young adults aged 18-24 years (page 6, ref#12, for details). All U.S. census regions (Northeast: 19%, Midwest: 21%, South: 38%, West: 22%) were utilized. Complete details regarding the sampling strategy, study design and estimation of weights for generalizability are presented on the website for the NESARC data (available at http://niaaa.census.gov/pdfs/source_and_accuracy_statement.pdf) . After complete description of the study to the subjects, informed consent was obtained. Statements regarding the strict confidentiality of respondent privacy are available at <http://niaaa.census.gov/confidentiality.html>

2.2 Measures

The NESARC used the NIAAA AUDADIS-IV (Grant et al., 2003a) for data collection.

Tobacco—Tobacco use was differentiated by route of administration into smoked (100+ cigarettes or 50+ cigars or smoked a pipe 50+ times) and smokeless (used snuff 20+ times or used chewing tobacco 20+ times). About 42% of the sample reported smoking 100+ cigarettes, 6% had smoked 50+ cigars, 5% had smoked a pipe 50+ times while 4% each reported using snuff or chewing tobacco 20+ times in their lifetime. In total, 23,901 individuals had used neither smoked nor smokeless forms of tobacco, 16,644 (39% of the sample) had exclusively used smoked forms, 583 (1.4% of the sample) had exclusively used smokeless forms of tobacco while 1,965 (4.6% of the sample) reported using both smoked and smokeless forms of tobacco.

Cannabis—A lifetime measure of cannabis use (reported by 19% of the sample) and a lifetime history of DSM-IV cannabis abuse/dependence (reported by 7.7% of the sample) were used in these analyses.

Potential Covariates—Onset of cannabis use and subsequent abuse/dependence is associated with a variety of influences that may also impact tobacco use, and thus confound the potential relationship between cannabis and tobacco. To control for potential socio-demographic, psychiatric and substance-related confounds, we also included as covariates, measures which may potentially differ across those exclusively using smoked versus smokeless forms of tobacco, or using neither or both.

Socio-demographic: Sex, Age (18-49 years at time of interview), self-reported Caucasian ethnicity, completion of a college education (Fergusson et al., 2003; Lynskey et al., 2000), living below the poverty line at the time of interview, not being born in the United States (immigrant) and residing in the Southern or Midwestern United States at the time of the interview.

Psychiatric: These covariates were selected based on the literature that suggests their effects on smoking and cannabis involvement. DSM-IV diagnoses (based on the AUDADIS-IV (Grant et al., 2003a)) of a lifetime history of conduct disorder (e.g. Fergusson et al., 1993; King et al., 2004; Macleod et al., 2004), major depressive disorder (e.g. Degenhardt et al., 2003), generalized anxiety disorder (e.g. Agrawal et al., 2007b), panic disorder and social anxiety disorder (e.g. Buckner et al., 2006), created by NIAAA.

Substance-related: DSM-IV diagnoses of a lifetime history of alcohol abuse/dependence and nicotine dependence. Lifetime history of other illicit drug use (cocaine, stimulants, sedatives,

hallucinogens, opiates, psychedelics, tranquilizers and inhalants) was also included as was a report of whether either biological parent had ever had an alcohol or drug-related problem was also included.

The response rate for NESARC was 81.2%. The reliability of these measures is good, based on a re-interview of a subset of 2,657 randomly selected respondents. As reported by Grant and colleagues (2003), short term reliability (2-3 months after main interview) for the lifetime psychiatric and substance use diagnostic measures ranged from 0.74 (alcohol abuse and dependence) to 0.42 (panic and generalized anxiety disorder (Grant et al., 2003a).

2.3 Statistical analyses

Associations between smoked and smokeless forms of tobacco use and both cannabis use and abuse/dependence were tested and compared for statistically significant differences in a logistic regression framework. All analyses were appropriately weighted, clustered on primary sampling units (PSU), and adjusted for strata (Grant et al., 2003b). All analyses were conducted using the *svy* options in STATA which allows for specification of design effects (weights, PSU and stratum). The *idonepsu* option was used to account for strata with single PSUs (Sarver, 2001).

Multinomial logistic regression in STATA (Stata Corp, 2003) was used to determine the pattern of covariates associated with using smoked forms of tobacco only, or smokeless forms alone or using both forms. Those who had used neither form served as the reference group (0=neither, 1=smoked only, 2=smokeless only, 3=both) for the calculation of multinomial odds ratios (MOR or, relative risk ratios). Post-hoc Wald chi-square tests were used to test whether the multinomial odds ratios varied across the three groups (smoked only vs. smokeless only vs. both).

Multinomial logistic regression models were fitted to data in STATA (Stata Corp, 2003) to also determine the association between using smoked only, smokeless only and using both forms of tobacco and cannabis use and abuse/dependence. Models were fit without (unadjusted odds-ratios) and with the inclusion of the socio-demographic, psychiatric and substance-related covariates (adjusted odds-ratios). Post-hoc Wald chi-square tests were used to examine whether the association between cannabis use (or abuse/dependence) and each form of tobacco use (smoked only/smokeless only/both) were statistically different from each other.

3. RESULTS

3.1. Route of tobacco use and cannabis-related behaviors

Cannabis use and abuse/dependence were more common in those who reported any tobacco use when compared to those who had never used tobacco (Table 1) and was most common in those who had used both smoked and smokeless forms of tobacco. However, when examining exclusive routes of administration, both cannabis use and abuse/dependence were more common in those who reported using smoked forms of tobacco than those reporting only use of smokeless tobacco.

3.2 Characteristics of smoked and smokeless tobacco users

There were also a number of socio-demographic, psychiatric and substance –related measures that differed between individuals using smoked tobacco products exclusively and those who reported use of smokeless tobacco alone (Table 2). Men were more likely than women to use smokeless forms of tobacco as were those who were from older (50+ years of age) cohorts. The smokeless forms of tobacco were significantly more popular in those from the South/Midwest (MOR=1.96) and more common in those who were U.S. born (MOR=12.5). No

notable differences were observed between these two groups for ethnicity or living below the poverty line. College education was not associated with using smokeless tobacco only.

Psychiatric diagnoses varied significantly across the smoked only and smokeless only groups (Table 2). Major depression, generalized anxiety disorder and panic disorder were markedly more common in those reporting smoked forms of tobacco use, even higher than in those using both forms of tobacco, with the prevalence in the smokeless group being equal or less than the prevalence in those who used neither form. For instance, those with a history of DSM-IV major depression were 1.64 times more likely to be exclusive users of smoked tobacco – this multinomial odds ratio could be equated to the MOR in those using both smoked and smokeless forms (MOR=1.47) and was not statistically significant in those using smokeless tobacco alone (MOR=0.80).

Conversely, alcohol abuse/dependence was more common in those reporting smokeless tobacco use (MOR=5.40, see Table 2). A modest overrepresentation of a family history of substance-related problems and other illicit drug use was noted in the smoked versus smokeless groups. While we do not show the multinomial odds ratios for nicotine dependence in Table 2 (primarily, because the reference group is never using any form of tobacco regularly, the MORs for nicotine dependence are rather large), post-hoc tests revealed that those using both forms of tobacco were most likely to be nicotine dependent, followed by those using smokeless forms only with the least risk in those using smoked forms alone.

3.3 Smoked tobacco and cannabis-related behaviors

To test the hypothesis that smoked forms of tobacco use would be more strongly associated with cannabis use and abuse/dependence, than smokeless forms, even after covariate adjustment, we conducted multinomial logistic regression analyses comparing those who exclusively used smoked forms, those who exclusively used smokeless forms and those who used both forms of tobacco. The odds of cannabis use and abuse/dependence were highest in those reporting use of both smoked and smokeless forms (Table 3). Those using smoked forms of tobacco (cigarettes, cigars or pipes) were 3.3 and 4.5 times more likely to also report a lifetime history of cannabis use and abuse/dependence respectively, with the risk being considerably lower in those endorsing use of smokeless forms only. Remarkably, even after controlling for socio-demographic, psychiatric and substance-related covariates, including nicotine dependence (which was strongly associated with cannabis use and abuse/dependence), a smoked route of tobacco administration was significantly associated with cannabis use (MOR 1.99) and abuse/dependence (MOR 1.55). In contrast, smokeless forms of tobacco use were not significantly associated with cannabis use and abuse/dependence (MOR 0.96 and 1.04) after covariate adjustment. The odds-ratios in those who used smoked forms alone could be equated to the odds in those who used both smoked and smokeless forms, suggesting that after covariate adjustment, only smoked tobacco use was associated with cannabis use and abuse/dependence.

4.0 DISCUSSION

Using a nationally representative sample, we demonstrated that route of tobacco administration plays an important role in the observed association between tobacco and cannabis use and abuse/dependence. Those who used smoked forms of tobacco were significantly more likely to be cannabis users and to develop cannabis abuse/dependence, even after controlling for covariates, including nicotine dependence. Despite the cross-sectional nature of the sample, our analyses suggest that the form of tobacco commonly used is a potent correlate of cannabis involvement.

4.1 The potential role of inhaled smoke in the tobacco-cannabis relationship

There is overwhelming evidence for the association between tobacco and cannabis-related behaviors (Amos et al., 2004; Chen et al., 1995; Clough et al., 2004; Coffey et al., 2003; Humfleet et al., 2004; Kandel et al., 1993; Kandel et al., 1997; Patton et al., 2005; Patton et al., 2006; Suris et al., 2007; Viveros et al., 2006). Tobacco use often precedes cannabis use and tobacco users are significantly more likely to become cannabis users. There have been several hypotheses proposed to explain this association, including shared genetic vulnerability, receptor cross-sensitization (Cahill et al., 2007; Cohen et al., 2005; Gelfand et al., 2006; Le et al., 2004), co-use (e.g. blunts), exposure opportunity/availability (Wagner et al., 2002; Wagner et al., 2005) and peer influences (Lynskey et al., 1998) as well as route of administration. The latter is especially intriguing as the most common mode of tobacco and cannabis use is via inhalation. We would hypothesize that individuals who have experimented with inhaled tobacco smoke will be more willing to experiment with another psychoactive substance with a similar route of administration. We may also posit that smoked tobacco users are somewhat better adapted to the sensation of inhaled smoke in their lungs, and consequently may enjoy the sensations of their first joints more than those naïve to the sensation of inhaled smoke. Results from studies examining co-effects of cannabis and tobacco use, however, have been equivocal. Simmons et al., (1995) found similar depth of inhalation and breath-holding in cannabis only, tobacco only and cannabis + tobacco users. Nemeth-Coslett reported no change in tobacco inhalation patterns in cannabis users (Nemeth-Coslett et al., 1986). Aung et al (Aung et al., 2004) also found no differences in topographical (e.g. puff volume) or physiological (e.g. carbon monoxide change) in heavy tobacco smokers with varied levels of cannabis use. Therefore, further detailed epidemiological and topographical research is required to address these hypotheses.

4.2 The role of shared predisposition to addiction

Our findings are especially intriguing because we show an association between route of administration of tobacco use and cannabis use and abuse/dependence, even after controlling for covariates, including DSM-IV nicotine dependence, which has been shown to be influenced by genetic and environmental factors shared with cannabis use and abuse/dependence (Neale et al., 2006). By controlling for nicotine dependence, as well as other socio-demographic and psychiatric or substance-related outcomes which may be markers for genetic or environmental susceptibility to both cannabis and tobacco use and dependence, we show that the mechanisms underlying the association between cannabis and tobacco use extend beyond aspects of shared genetic and environmental vulnerability, and that one such influence may be the common route of administration for both psychoactive substances. While it is plausible that this still represents a shared genetic predisposition towards experimentation with ‘inhaled substances’, it is more likely that this represents physiological adaptation, and that the aero-respiratory systems of regular tobacco smokers are more adept at dealing with cannabis smoke than those of smokeless tobacco users.

4.3 Smoked versus smoked + smokeless tobacco

Prior to adjustment for covariates, the association between cannabis use, abuse/dependence and using both smoked and smokeless tobacco (‘Both’ category) was considerably higher than the association with the smoked only category. One possible explanation for this is the significantly higher levels of externalizing psychopathology (conduct disorder, alcohol abuse/dependence, substance use and family history of alcohol/drug problems) in the group using both smoked and smokeless forms of tobacco. However, when these covariates are adjusted for, no statistical difference between the two groups remained. This findings has potential public health ramifications – most users of smokeless tobacco also used smoked forms (Rigotti et al., 2000), however our study suggests that this combined use may be a marker for increased

vulnerability to a host of externalizing problems, including other forms of substance use and misuse.

4.4. The social milieu of smoked vs. smokeless tobacco

It is noteworthy that, with these data, we cannot conclude that aero-respiratory adaptation is the only contributor to the observed co-occurrence of smoked tobacco use and cannabis involvement. Choice of smoked versus smokeless tobacco may be governed by personal (e.g. expectancies) and social (e.g. cultural norms, availability) factors that also impact the decision to subsequently use cannabis – such variables are unmeasured in NESARC. Peer groups play an important role in an adolescent's decision to use smoked versus smokeless forms of tobacco, and subsequently likely influence their choices regarding other drugs, like cannabis (Ary et al., 1987; Hill et al., 1992). Another sub-culture, where smokeless tobacco is fairly popular is young athletes, especially those with higher levels of participation (Melnick et al., 2001; Rigotti et al., 2000) – in such a prosocial environment, cannabis use is often discouraged. Hence, in conjunction with physiological mechanisms, it is possible that important social norms underlie the association between smoked tobacco and cannabis use.

4.5 Study Limitations

Some limitations of our study are worth discussion: First, while the NESARC does inquire about marijuana (commonly smoked) and hashish (may be ingested), data describing route of administration were not available. However, 97.5% of all cannabis users, in a subsequent section of the interview, reported on a quantitative measure of joint smoking (with 2.5% not able to recollect the number of joints smoked) suggesting that smoked marijuana was the predominant form of cannabis use in this sample. Most U.S. samples also report that ingestion of hashish in the absence of a lifetime history of smoked marijuana is exceedingly rare (Agrawal et al., 2004; McCrady et al., 1999). Second, we did not exclude cigar/pipe smoking, which traditionally, does not involve inhalation of tobacco smoke. Third, measures of blunt smoking (rolling tobacco and marijuana together) were not assessed in the NESARC. Fourth, and importantly, these data are cross-sectional and conclusions that are causal in nature cannot be drawn.

4.6 Conclusion

The association between tobacco and cannabis use is reciprocal, whereby regular tobacco use increases chances of experimentation with and regular use of cannabis, while early and frequent cannabis use may contribute to nicotine dependence and persistent smoking. We demonstrate that the mechanisms underlying this association may possibly extend beyond aspects of shared vulnerability. Prior qualitative research has suggested that adolescents often use cannabis-related paraphernalia to smoke tobacco and vice versa (Amos et al., 2004; Highet, 2003; Highet, 2004). To our knowledge, this is the first study to demonstrate that tobacco smokers are more likely to report cannabis use and abuse/dependence, than users of smokeless tobacco, and that this common route of administration may be a factor worth consideration in future studies from both physiological and social viewpoints.

Acknowledgements

Drs. Agrawal and Lynskey receive support from DA23668 (AA) and DA18660 (MTL). Dr. Lynskey is also supported by DA18267.

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Table 1

Prevalence of cannabis use and abuse/dependence in those using neither smoked nor smokeless tobacco, smoked tobacco only, smokeless tobacco only and those using both smoked and smokeless tobacco.

	Neither	Smoked form only	Smokeless form only	Both
Cannabis Use	10.7%	28.3%	21.5%	41.5%
Cannabis Abuse/Dependence	3.1%	12.4%	8.8%	23.2%
N	23,901	16,644	583	1965

Table 2

Multinomial odds ratios [95% Confidence intervals] showing the association between route of administration of tobacco use and socio-demographic, psychiatric and substance use covariates in the NESARC.

	Smoked only	Smokeless only	Both
<i>Socio-demographic:</i>			
Sex (Female)	0.66 [0.62-0.69]	0.07 [0.05-0.10]	0.03 [0.03-0.04]
Age (18-49)	1.78 [1.69-1.88]	0.43 [0.33-0.56]	1.16 [1.04-1.31]
Caucasian	1.70* [1.57-1.83]	2.20* [1.63-2.95]	3.53 [2.90-4.31]
Poverty	0.85* [0.80-0.93]	0.65* [0.47-0.89]	0.72* [0.60-0.88]
College education	0.58 [0.54-0.62]	0.91 [0.72-1.13]	0.46 [0.39-0.53]
Census division (Midwest/South)	1.09 [0.98-1.21]	1.96 [1.44-2.66]	1.45 [1.12-1.88]
Immigrant	0.45 [0.41-0.49]	0.08* [0.04-0.18]	0.10* [0.07-0.15]
<i>Psychiatric:</i>			
Conduct Disorder	2.88* [2.54-3.28]	2.51* [1.62-3.89]	5.93 [4.92-7.14]
Major depressive disorder	1.64* [1.53-1.76]	0.76 [0.56-1.04]	1.47* [1.27-1.69]
Generalized Anxiety Disorder	1.63* [1.44-1.84]	0.50 [0.27-1.02]	1.46* [1.11-1.91]
Panic Disorder	2.13* [1.91-2.41]	0.83 [0.42-1.63]	1.72* [1.31-2.27]
Social Anxiety Disorder	1.36* [1.22-1.51]	1.00 [0.61-1.67]	1.47* [1.15-1.87]
<i>Substance Use:</i>			
Alcohol abuse/Dependence	3.34 [3.12-3.57]	5.40 [4.38-6.65]	10.78 [9.34-12.44]
Other illicit drug use	3.44 [3.13-3.79]	2.05 [1.52-2.78]	6.88 [5.87-8.06]
Family history of substance problems	1.82 [1.71-1.95]	1.30 [1.02-1.66]	2.17 [1.91-2.46]

Footnote to Table 2: The reference group is those who never used smoked or smokeless forms of tobacco. Estimates are statistically significant if the 95% confidence limits do not include 1.0. The estimates labeled "*" are statistically equal to each other, based on post-hoc Wald chi square tests for 1 degree of freedom.

N.B. Multinomial odds ratios are equivalent to relative risk ratios (RRR);

Table 3

Unadjusted and adjusted multinomial odds ratios [with 95% Confidence Intervals] for the association between smoked only, smokeless only and both smoked and smokeless forms of tobacco use and cannabis use and abuse/dependence

	Smoked only	Smokeless only	Both
<i>Unadjusted odds-ratios</i>			
Cannabis Use	3.27 [3.02-3.55]	2.21 [1.73-2.82]	6.27 [5.44-7.21]
Cannabis Abuse/dependence	4.54* [4.03-5.13]	3.41* [2.43-4.76]	10.16 [8.57-12.06]
<i>Adjusted odds-ratios</i>			
Cannabis Use	1.99* [1.80-2.20]	0.96 [0.73-1.27]	2.12* [1.76-2.55]
<i>Significant Covariates</i>	1-5, 7, 9, 11-16	1-3,6-7, 13-14	1-3, 5-7, 12-16
Cannabis Abuse/dependence	1.55* [1.31-1.83]	1.04 [0.69-1.58]	1.68* [1.35-2.10]
<i>Significant Covariates</i>	1-5,7,9, 11-16	1-3,6-7	1-3,5-7,12-16

Footnote to Table 3: Those using neither smoked nor smokeless forms are the reference group. Estimates are statistically significant if the 95% confidence limits do not include 1.0. The estimates labeled '*' are statistically equal to each other, based on post-hoc Wald chi square tests for 1 degree of freedom.

N.B. Multinomial odds ratios are equivalent to relative risk ratios (RRR);

Covariates: 1=sex, 2=age, 3=Caucasian, 4=poverty, 5=college education, 6=South/Midwest, 7=immigrant, 8=conduct disorder, 9=major depression, 10=generalized anxiety disorder, 11=panic disorder, 12=social anxiety disorder 13=nicotine dependence, 14=alcohol dependence, 15=other illicit drugs, 16= family history.