

Original investigation

# Use of High-Nicotine/Tar-Yield (Full-Flavor) Cigarettes and Risk for Nicotine Dependence in Nationally Representative Samples of US Smokers

Ryan Redner PhD<sup>1,2</sup>, Thomas J. White PhD<sup>1,3</sup>, Janice Y. Bunn PhD<sup>4</sup>,  
Stephen T. Higgins PhD<sup>1,3,5</sup>

<sup>1</sup>Vermont Center on Behavior and Health, University of Vermont, Burlington, VT; <sup>2</sup>Behavior Analysis and Therapy Program, Rehabilitation Institute, Southern Illinois University, Carbondale, Carbondale, IL; <sup>3</sup>Department of Psychiatry, University of Vermont, Burlington, VT; <sup>4</sup>Department of Medical Biostatistics, University of Vermont, Burlington, VT; <sup>5</sup>Department of Psychology, University of Vermont, Burlington, VT

Corresponding Author: Stephen T. Higgins, PhD, Vermont Center on Behavior and Health, University of Vermont, UHC Campus, Rm 3100B Old Hall, 1 S. Prospect Street, Burlington, VT 05401, USA. Telephone: 802-656-9614; Fax: 802-656-9628; E-mail: [stephen.higgins@uvm.edu](mailto:stephen.higgins@uvm.edu)

## Abstract

**Introduction:** The present study examines whether use of machine-estimated high-nicotine/tar-yield (full-flavor) cigarettes predicts greater risk of nicotine dependence after controlling for the influence of potential confounding factors in US nationally representative samples.

**Methods:** Data were obtained from multiple years of the National Survey on Drug Use and Health (NSDUH). Nicotine dependence was measured by (1) the Nicotine Dependence Syndrome Scale and (2) latency to first cigarette after waking. Associations between use of high-nicotine/tar-yield cigarettes and risk for nicotine dependence were examined using multiple logistic regression.

**Results:** The odds of nicotine dependence were reliably greater among users of high- compared to lower-nicotine/tar-yield cigarettes even after adjusting for sociodemographic and other smoking characteristics ( $P_s < .0001$ ). This relationship was (1) generally graded across differing nicotine/tar-yield cigarettes, (2) discernible across two definitions of nicotine dependence and multiple NSDUH survey years, and (3) observed among adult and adolescent smokers.

**Conclusion:** Use of high-nicotine/tar-yield cigarettes is associated with increased odds of nicotine dependence, a relationship that has important tobacco regulatory implications. Whether the widespread marketing and availability of high-nicotine/tar-yield cigarettes is increasing risk of nicotine dependence among US smokers warrants further research.

**Implications:** This study adds additional empirical evidence to the relation of machine measured high-yield cigarettes and likelihood of nicotine dependence, and draws some implications in regards to regulation.

## Introduction

Understanding the relationship between nicotine levels in cigarettes and risk for dependence is more important than ever now that

passage of the Family Smoking Prevention and Tobacco Control Act (2009) gives the US Food and Drug Administration (FDA) regulatory authority over nicotine content levels in tobacco products.<sup>1</sup> While

the legislation prohibits the FDA from eliminating nicotine completely, it allows the agency to establish maximal levels. That authority creates the opportunity to eventually require that levels fall below the threshold necessary to produce nicotine dependence, although greater understanding of the relationships between nicotine content, yield, and dependence risk will be necessary to achieve that goal.<sup>2</sup> In the present study we examine whether use of commercially available, machine-estimated high-nicotine/tar-yield (ie, full-flavor) cigarettes is associated with increased risk of nicotine dependence compared to lower-nicotine/tar-yield cigarettes in nationally representative samples of US smokers.

Reviews on smoking of commercially available cigarette brands with reduced machine-estimated nicotine yields document partial compensation of approximately 70%, with greater compensation at intermediate yields compared to lower yields.<sup>3</sup> Several rigorous experimental brand-switching studies document that switching from relatively high-yield usual brand cigarettes (~1.0 mg/cigarette) to yields of 0.2 mg/cigarette and below reliably results in reductions in plasma nicotine and cotinine levels that are stable over time and related in an orderly manner to, although still exceeding, machine-estimated yield.<sup>4-6</sup> Results from experimental brand switching between higher- and intermediate-yield cigarettes are less consistent. Some reports note significant reductions in plasma nicotine/cotinine levels including graded reductions as a function of estimated yield,<sup>6,7</sup> while others report no change from levels seen with usual brand smoking.<sup>4</sup> Of direct relevance to the present study, Benowitz et al.<sup>4</sup> conducted a longitudinal study in which participants were experimentally switched to progressively lower-yield commercial cigarettes starting with usual brand and reducing in 1-week decrements to 0.9 mg, 0.6 mg, 0.4 mg, 0.2 mg, and 0.1 mg yields after which participants were allowed to return to smoking their usual brand and followed for an additional 4 weeks. Nicotine dependence levels were assessed at baseline, end of taper at week 6, and end of study at week 10, which was 4 weeks after participants were permitted to return to their usual brand. Dependence levels at week 10 were significantly lower than at baseline and week 6. Turning to experimental studies examining research cigarettes with varying nicotine content levels, significant reductions in nicotine dependence among smokers experimentally assigned to using very low nicotine content cigarettes have been documented across multiple studies, including among smokers motivated to quit<sup>8,9</sup> and those with no current plans to do so.<sup>10-12</sup>

Considered together, the results from these experimental studies across commercial and research cigarettes would suggest greater biological exposure to nicotine and increased risk of nicotine dependence among those who regularly smoke machine-estimated commercial high- versus low-yield cigarettes, with less clear predictions about those using intermediate-yield brands. Yet, to our knowledge, there have been no prior studies on this question reported in nationally representative samples of US smokers. The purpose of the present study was to examine that possibility. The National Survey on Drug Use and Health (NSDUH) was utilized to examine this question because it is a nationally representative survey, assesses cigarette smoking status in adults and adolescents, reports type of cigarettes typically smoked, and assesses nicotine dependence using two different validated measures. We examined whether odds of nicotine dependence vary in an orderly manner as a function of varying machine-estimated nicotine/tar yields (ie, dose dependence), which would be expected if nicotine/tar yield is a direct contributor to this relationship. We also explored whether any association between use of higher-nicotine/tar-yield cigarettes and risk of

nicotine dependence in adult smokers was also evident in adolescent smokers, an especially vulnerable age for developing a life-long pattern of cigarette smoking. We also chose to analyze results among adults and adolescents separately as there are considerable differences between the two age groups in legal constraints on purchasing cigarettes, which could potentially influence their ability to purchase and use their preferred brands.

## Methods

### Data Source

The NSDUH is a nationally representative survey of the US non-institutionalized population aged at least 12 years that is designed to measure prevalence and correlates of drug use, including use of cigarettes.<sup>13</sup> Data were collected from the three most recent datasets that were available for public use at the time the study was completed (2011, 2012, and 2013).<sup>14-16</sup> The primary analysis among adults was conducted using the most recent available survey year at the time this study was initiated (2013). In order to test the reliability of results from the 2013 NSDUH among adults, analyses were repeated using the 2012 NSDUH. Analyses were also conducted with adolescent smokers using data combined across three survey years (2011–2013) to accommodate the lower prevalence of smoking in that population.

NSDUH recruitment across each of the survey years was completed using a multistage area probability sample design in which a predetermined number of participants were randomly recruited by home address within each state (2011 *N* = 58 397, 2012 *N* = 55 268, 2013 *N* = 55 160). Respondents were selected from the civilian noninstitutionalized population, including group homes, shelters, and college dormitories. Individuals on active military duty, in drug treatment programs, in jail, or homeless without residence were not surveyed per survey design. The sample was weighted and adjusted to reflect the US population from the 2010 Census. Respondents completed computer- and audio-assisted structured interviews and were compensated \$30 for completing the interview. The weighted interview response rate was 74.4%, 73.0%, and 71.7% in the 2011, 2012, and 2013 NSDUH, respectively. A detailed description of survey procedures has been provided by SAMHSA.<sup>13</sup>

### Cigarette Type

Smokers in the NSDUH indicate characteristics about their cigarette smoking, including the type of cigarette they usually smoke. Current smokers were asked “During the past 30 days, what type of cigarettes did you smoke most often?”. Respondents selected one of four options: Full-flavor, medium, light, or ultra-light. The number of current smokers (including adolescents and adults) who selected a cigarette type was 12 285 of 12 549 (97.9%), and 11 659 of 11 950 (97.6%) in the 2012 and 2013 NSDUH, respectively. In the 2011 NSDUH, where only adolescent data were used, 1485 of 1594 (93.1%) of adolescent smokers selected a cigarette type.

### Measures of Nicotine Dependence

NSDUH respondents who report current smoking are assessed for nicotine dependence using two measures. (1) They complete the Nicotine Dependence Syndrome Scale (NDSS),<sup>17</sup> which is a 17-question validated multidimensional assessment of nicotine dependence that includes questions of smoking-related mood changes, craving, feelings of control, and smoking patterns. Each question on the

NDSS is scored from 1 to 5, with higher scores indicating greater severity. A respondent is scored as dependent if the average of all questions is at least 2.75. (2) They also answer the first item on the Fagerstrom Test for Nicotine Dependence<sup>18</sup>: “How soon after waking do you smoke your first cigarette?” Respondents who report smoking within 30 minutes after waking are considered nicotine dependent. Through the remainder of this report this item is referred to as “Time-to-1<sup>st</sup>-cigarette.”

### Statistical Methods

Descriptive statistics and simple and multiple logistic regression analyses were conducted to estimate the relationship between the nicotine/tar yield of cigarettes usually smoked and nicotine dependence controlling for the potentially confounding influence of sociodemographic characteristics and other smoking characteristics. Nicotine yield was categorized as full-flavor, medium, light, and ultra-light. While full-flavor cigarettes are the reference category for all analyses, results are reported as the reciprocal of the original odds ratio (OR), thus allowing comparison of the odds of smoking full-flavor cigarettes to the odds of smoking each of the other categories of cigarettes. Nicotine dependence was measured using the NDSS and Time-to-1<sup>st</sup>-cigarette. Age at first cigarette and number of cigarettes smoked per day were measured in a continuous fashion. Age was coded into 17 categories (ie, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22–23, 24–25, 26–29, 30–34, 35–49, 50–64, ≥65) as defined in the public release codebook,<sup>13</sup> and considered as an ordinal variable in all models. Marital status was coded as married versus unmarried, with the latter category including never married, divorced and widowed. Race was dichotomized as non-Hispanic white versus other. Educational attainment was used as the marker of socioeconomic status, as is common in studies of socioeconomic health and other disparities,<sup>19,20</sup> and coded into four categories: less than high school, high school, some college, and college graduate, with college graduate as the reference category. Respondents were considered unemployed if they were not employed and actively looking for work; those working full- or part-time, volunteering, disabled, keeping a house, retired, in school or not having a job for some other reason were considered as other. Analyses for adults were limited to those reporting their age as 18 years or older, while adolescent analyses were restricted to those 12–17 years old. Age groups (adults and adolescents) in the present study were separated by the ability to legally purchase cigarettes (< and ≥18 years of age). Analyses with adolescents were not adjusted for educational attainment, marital status, or unemployment. Variables that were significantly ( $P < .05$ ) associated with nicotine dependence in simple logistic regression

analyses were included in subsequent multiple logistic regression models. Variables that were not statistically significant in the multiple logistic regression models were dropped from the final model (except for core demographic variables, which were always retained, including age, sex, race, and education).

The statistical software STATA, version 13.1 was used for all analyses, and all analyses took the complex sampling design of the survey into consideration. The weight, stratum, and probability sampling unit variables were provided by NSDUH. Standard errors were computed using the Jackknife repeated replication method. ORs and 95% confidence intervals (CIs) are reported, with statistical significance set to  $P < .05$ .

## Results

### Smoking Characteristics of Study Samples

Prevalence of current cigarette smoking among adults in the 2013 survey was 22.8%, with 43.8% reporting use of full-flavor, 9.4% medium, 38.6% light, and 8.1% ultra-light cigarettes. In the 2012 survey, prevalence of current smoking was 23.8%, with 44.3% reporting use of full-flavor, 8.1% medium, 38.1% light, and 9.5% ultra-light cigarettes. Prevalence of nicotine dependence was 37.6% and 47.9% across the NDSS and Time-to-1<sup>st</sup>-cigarette (<30 minutes) dependence measures, respectively, in the 2013 survey and 39.9% and 48.0% in the 2012 survey.

Smoking prevalence in the combined 2011–2013 survey years examined with adolescent smokers was 6.7%, with 48.3% of smokers reporting use of full-flavor, 15.2% medium, 31.4% light, and 5.1% ultra-light cigarettes. Prevalence of nicotine dependence was 19.9% and 27.5% across the NDSS and Time-to-1<sup>st</sup>-cigarette (<30 minutes) measures, respectively.

Among adults prevalence of nicotine dependence varied by cigarette type, with the highest levels of nicotine dependence being seen among users of full-flavor cigarettes in both the 2013 and 2012 NSDUH (Table 1, left two panels). Prevalence of nicotine dependence also varied by cigarette type among adolescents across both measures of nicotine dependence. Consistent with the pattern observed in adults, the highest level of dependence was seen among users of full-flavor cigarettes (Table 1, right panel).

### Adjusted Models of Use of Full-Flavor Cigarettes and Odds of Nicotine Dependence in the General Adult Smoker Population

Odds of nicotine dependence was elevated among those using full-flavor versus other cigarette types in the 2013 survey even after

**Table 1.** Prevalence of Nicotine Dependence (NDSS and Time-to-1<sup>st</sup>-Cigarette) by Cigarette Type Among Adults and Adolescents (2011–2013 National Survey of Drug Use and Health [NSDUH])

Cigarette type	Adults, 2013 NSDUH ( <i>n</i> = 10 361)		Adults, 2012 NSDUH ( <i>n</i> = 11 092)		Adolescents, 2011–2013 NSDUH ( <i>n</i> = 3682)	
	NDSS (%)	Time-to-1 <sup>st</sup> -cigarette (<30 min) (%)	NDSS (%)	Time-to-1 <sup>st</sup> -cigarette (<30 min) (%)	NDSS (%)	Time-to-1 <sup>st</sup> -cigarette (<30 min) (%)
Full-flavor	46.4	58.8	47.7	59.0	32.2	41.8
Medium	31.1	40.8	40.1	45.9	18.5	18.4
Light	31.1	38.9	32.2	38.3	8.7	18.0
Ultra-light	32.8	43.7	37.5	40.4	4.7	10.8

NDSS = Nicotine Dependence Syndrome Scale.

controlling for the potential confounding influence of sociodemographic characteristics and other smoking characteristics (Table 2). The odds of dependence across cigarette types examined in the adjusted model varied in a relatively graded manner corresponding to increasing estimated nicotine/tar yield (Table 2). While the point estimates were graded, there was overlap in CIs across the different nicotine/tar-yield cigarette types.

Similar results were noted in the 2012 survey year (Table 3), although the graded nature of the relationship with the NDSS was somewhat less in 2012 than in the 2013. The only significant increase in odds of nicotine dependence noted in 2012 using the NDSS measure was in comparing full-flavor to light cigarettes (AOR = 1.70, CI = 1.43–2.01). When classifying dependence in the 2012 survey using the Time-to-1<sup>st</sup>-cigarette measure, however, the relationship remained graded as in the 2013 survey ( $P < .0001$ ). Again, there was overlap in CIs around the point estimates across the different cigarette types.

Other reliable predictors of nicotine dependence in the final multivariate regression models included age of first cigarette, cigarettes per day, sex, and education across the NDSS and Time-to-1<sup>st</sup>-cigarette measures in the 2013 and 2012 survey years (Tables 2 and 3, respectively).

### Adjusted Models of Use of Full-Flavor Cigarettes and Odds of Nicotine Dependence in Adolescent Smokers

Use of full-flavor cigarettes was associated with increased odds of nicotine dependence even after controlling for potential confounds among adolescents (Table 4) consistent with the associations observed among adults (Tables 2 and 3). This same association was noted using both measures of nicotine dependence although in a less graded manner with the Time-to-1<sup>st</sup>-cigarette than the NDSS dependence measure.

Other significant predictors of nicotine dependence in the final multivariate regression model among adolescents included age of

first cigarette and cigarettes per day across the NDSS and Time-to-1<sup>st</sup>-cigarette measures (Table 4). None of the sociodemographic characteristics examined in adolescents were consistently related to nicotine dependence.

### Discussion

The results from the present study support our hypothesis of increased odds of nicotine dependence among users of high-yield or full-flavor commercial cigarettes compared to cigarettes with lower machine-estimated nicotine/tar yields. Indeed, the odds of nicotine dependence appear to increase in a graded or dose-dependent manner corresponding to increasing machine-estimated nicotine/tar yields consistent with patterns of biological exposure reported in experimental studies of brand-switching between high- to low-yield commercial cigarettes.<sup>6,7</sup> Importantly, this association remains significant even after controlling for the potentially confounding influences of other smoking and sociodemographic characteristics including the number of cigarettes smoked per day. This relationship was observed across two different measures of nicotine dependence and across two survey years among adults demonstrating its reliability. The relationship was also evident across two definitions of dependence among adolescent smokers suggesting that the relationship is discernible despite legal restrictions against purchasing cigarettes among adolescents and thus certainly of relevance to this especially vulnerable sub-population of smokers. The relatively large difference in prevalence of dependence between users of full-flavor and ultra-light cigarettes noted among adolescents is particularly striking.

While the graded relationship in the point estimates around the odds of nicotine dependence corresponding to cigarette type is consistent with a direct contribution of nicotine/tar yield to the increased odds of dependence, the present cross-sectional survey study cannot support causal inferences. That limitation notwithstanding, it is important to underscore the consistency between these survey results and those from the experimental literature discussed

**Table 2.** Likelihood of Nicotine Dependence by Cigarette Type in Adults ( $\geq 18$  years) in the 2013 National Survey on Drug Use and Health (NSDUH;  $n = 10\,832$ )

	NDSS			Time-to-1 <sup>st</sup> -cigarette		
	AOR	95% CI	P	AOR	95% CI	P
Cigarette type			<.0001			<.0001
FF vs. medium	<b>1.41</b>	1.06, 1.88		<b>1.45</b>	1.09, 1.93	
FF vs. light	<b>1.54</b>	1.29, 1.84		<b>1.93</b>	1.60, 2.33	
FF vs. ultralight	<b>2.01</b>	1.36, 2.95		<b>2.18</b>	1.62, 2.93	
Age of first cigarette	<b>0.94</b>	0.92, 0.97	<.0001	<b>0.97</b>	0.95, 0.99	.001
Cigarettes per day	<b>1.13</b>	1.11, 1.14	<.0001	<b>1.14</b>	1.12, 1.15	<.0001
Age	1.01	0.97, 1.05	.55	<b>1.14</b>	1.10, 1.18	<.0001
Male	<b>0.68</b>	0.58, 0.80	<.0001	<b>0.81</b>	0.69, 0.95	.01
Married				<b>0.83</b>	0.71, 0.98	.03
Non-Hispanic white	1.11	0.92, 1.34	.28	1.04	0.85, 1.27	.70
Education			<.0001			<.0001
Some college	<b>1.57</b>	1.21, 2.03		1.29	0.98, 1.70	
High school grad	<b>1.91</b>	1.50, 2.43		<b>1.86</b>	1.41, 2.45	
Less than HS	<b>1.92</b>	1.42, 2.61		<b>2.06</b>	1.52, 2.80	
Unemployment	<b>1.49</b>	1.18, 1.88	.001	<b>1.31</b>	1.03, 1.66	.03

AOR = adjusted odds ratio; CI = confidence interval; FF = Full-flavor cigarettes; HS = high school; NDSS = Nicotine Dependence Syndrome Scale. **Bold** = significant. Final model multiple logistic regressions with cigarette type, smoking characteristics and sociodemographics predicting nicotine dependence based on the Nicotine Dependence Syndrome Scale and Time-to-1<sup>st</sup>-cigarette. Odds ratios represent an increased (>1) or decreased (<1) likelihood of dependence.

**Table 3.** Likelihood of Nicotine Dependence by Cigarette Type in Adults ( $\geq 18$  years) in the 2012 National Survey on Drug Use and Health (NSDUH;  $n = 11\ 054$ )

	NDSS			Time-to-1 <sup>st</sup> -cigarette		
	AOR	95% CI	P	AOR	95% CI	P
Cigarette type			<.0001			<.0001
FF vs. medium	1.07	0.82, 1.39		<b>1.42</b>	1.12, 1.80	
FF vs. light	<b>1.70</b>	1.43, 2.01		<b>2.08</b>	1.76, 2.47	
FF vs. ultralight	1.39	0.90, 2.17		<b>2.33</b>	1.57, 3.45	
Age of first cigarette	<b>0.96</b>	0.94, 0.98	<.0001	<b>0.97</b>	0.95, 0.99	.01
Cigarettes per day	<b>1.14</b>	1.13, 1.16	<.0001	<b>1.13</b>	1.12, 1.15	<.0001
Age	1.01	0.98, 1.05	.45	<b>1.13</b>	1.09, 1.17	<.0001
Male	<b>0.73</b>	0.62, 0.87	.001	<b>0.69</b>	0.60, 0.79	<.0001
Non-Hispanic white	<b>1.26</b>	1.02, 1.55	.03	0.95	0.77, 1.17	.61
Education			<.0001			<.0001
Some college	<b>1.47</b>	1.12, 1.92		<b>1.46</b>	1.10, 1.93	
High school grad	<b>1.72</b>	1.29, 2.30		<b>2.26</b>	1.74, 2.93	
Less than HS	<b>2.43</b>	1.73, 3.40		<b>2.98</b>	2.27, 3.91	
Unemployment				<b>1.41</b>	1.13, 1.77	.003

AOR = adjusted odds ratio; CI = confidence interval; FF = full-flavor cigarettes; HS = high school; NDSS = Nicotine Dependence Syndrome Scale. **Bold** = significant. Final model multiple logistic regressions with cigarette type, smoking characteristics and sociodemographics predicting nicotine dependence based on the Nicotine Dependence Syndrome Scale and Time-to-1<sup>st</sup>-cigarette. Odds ratios represent an increased (>1) or decreased (<1) likelihood of dependence.

**Table 4.** Likelihood of Nicotine Dependence by Cigarette Type in Adolescents (12–17 years) in the 2011–2013 National Survey on Drug Use and Health (NSDUH;  $n = 3682$ )

	NDSS			Time-to-1 <sup>st</sup> -cigarette		
	AOR	95% CI	P	AOR	95% CI	P
Cigarette type			<.0001			<.0001
FF vs. medium	<b>1.45</b>	1.05, 2.00		<b>2.51</b>	1.82, 3.45	
FF vs. light	<b>2.81</b>	1.91, 4.15		<b>1.92</b>	1.48, 2.48	
FF vs. ultralight	<b>4.00</b>	1.76, 9.11		<b>2.93</b>	1.50, 5.74	
Age of first cigarette	<b>0.87</b>	0.83, 0.92	<.0001	<b>0.93</b>	0.89, 0.97	.002
Cigarettes per day	<b>1.24</b>	1.18, 1.31	<.0001	<b>1.22</b>	1.18, 1.27	<.0001
Age	1.12	0.99, 1.27	.08	1.06	0.95, 1.19	.27
Male	<b>0.71</b>	0.57, 0.89	.004	1.05	0.85, 1.30	.65
Non-Hispanic white	1.19	0.87, 1.62	.26	0.99	0.74, 1.33	.95

AOR = adjusted odds ratio; CI = confidence interval; FF = full-flavor cigarettes; NDSS = Nicotine Dependence Syndrome Scale. **Bold** = significant. Final model multiple logistic regressions with cigarette type, smoking characteristics and sociodemographics predicting nicotine dependence based on the Nicotine Dependence Syndrome Scale and Time-to-1<sup>st</sup>-cigarette. Odds ratios represent an increased (>1) or decreased (<1) likelihood of dependence.

in the Introduction to this report demonstrating that switching from higher-yield commercial or high nicotine content research cigarettes to very low yield or content cigarettes decreases biological exposure levels and nicotine dependence.<sup>4,6,7,10-12</sup> Thus it seems likely that at least some portion of the variance in the odds of nicotine dependence observed between users of full-flavor versus ultra-light commercial cigarettes in the present study is due to the differences in nicotine/tar yield of those cigarettes. Considering that the odds of dependence associated with use of the medium and light brands in the present study fall between those two extremes to form what appears to be a graded dose-effect function further bolsters the possibility of a direct contribution of the differing nicotine/tar yields of these cigarettes to the observed differences in risk for nicotine dependence. There is no way to dissociate the contributions of reduced exposure to nicotine versus tar in the present results, but there is at least one experimental study that demonstrated reductions in nicotine dependence among smokers switched to very low nicotine content cigarettes independent of whether cigarette tar levels were relatively high or low.<sup>12</sup>

In terms of a potential mechanism for why high-nicotine/tar-yield brands would have greater dependence risk, the most parsimonious explanation would be differences in the relative reinforcing value of the cigarettes related to their differing nicotine yields. While smokers compensate when using lower-nicotine-yield cigarettes, the level of compensation is often partial especially when yield differences are large and thus represents a lower-reinforcement magnitude per cigarette relative to the higher-yield cigarettes.<sup>3</sup> A related factor is that compensation requires more effort to obtain the same level of nicotine. That is, smokers must modify their typical smoking pattern either by smoking more cigarettes, or changing smoking topography by increasing puff number, increasing puff volume, inhaling differently, blocking the filter vents, or some combination of these when smoking lower- compared to higher-yield cigarettes.<sup>21</sup> These increases in response effort to acquire the same level of nicotine may be functionally equivalent to increasing the unit price of the nicotine, which is well known to impact the reinforcing effects of nicotine and other drugs.<sup>22,23</sup>

There are at least two alternative accounts for the present results that cannot be ruled out based on the data available in the present study. Rather than high nicotine yields increasing the odds of dependence, smokers who develop nicotine dependence may switch brands to higher nicotine/tar yields in order to more effectively avoid withdrawal or switch to lower yields to reduce the severity of their dependence. Brand switching is certainly common among regular cigarette smokers and longitudinal studies of smoking in naturalistic settings have shown that brand switching to higher- and lower-yield commercial cigarettes is associated with changes in biological exposure levels.<sup>24,25</sup> Still another possibility is that a third variable (eg, individual differences in health consciousness or delay discounting) is responsible for both the increased risk for preferring high-yield cigarettes and for developing nicotine dependence. We know that individual differences in characteristics such as delay discounting are associated with differences in risk for cigarette smoking as well as consumption of other drug reinforcers.<sup>26</sup> One can envision where such differences might also increase vulnerability to the different advertising and other messaging associated with the different yield commercial cigarettes although we do not know of any such evidence. What also must be considered, of course, is that some combination of these different directions of causality is responsible for the present results.

There is little question that nicotine dependence is a well established and serious adverse effect of cigarette smoking that as the present results demonstrate is present in almost half of current adult and one-third or more adolescent cigarette smokers depending on the measure used. Nicotine dependence is associated with numerous adverse outcomes, including greater difficulties initiating and sustaining abstinence.<sup>19,20,27</sup> As such, the findings of the present study when considered in combination with the experimental studies on this topic have potentially important regulatory implications regarding nicotine levels in cigarettes. The present study provides evidence that use of the highest-yield, or full-flavor, cigarettes is associated with several-fold greater odds of dependence compared to relatively lower-yield cigarettes. The dose-dependent nature of this association suggests, although certainly does not prove, a causal relationship. Should evidence along these lines continue to accumulate a regulation that reduces nicotine in cigarettes below levels currently available in commercial full-flavor cigarettes should be considered. Such a regulation has the potential to reduce the prevalence of nicotine dependence in adult and adolescent US smokers, especially when levels are at those in commercially available ultra-light cigarettes. Important to underscore, however, is that turning to currently available low-nicotine-yield cigarettes as alternatives to full-flavor cigarettes in order to lower dependence risk is not a viable option. While doing so would likely reduce the odds of nicotine dependence, there is also abundant evidence indicating that it will be associated with sufficient compensatory smoking to neutralize any benefits in terms of protection against smoking-related morbidity and mortality.<sup>28</sup> A key contributor to this problem appears to be that commercially available lower-yield cigarettes typically have the same nicotine content as their higher-yield counterparts, with the reductions in yield being achieved through filter efficiency, air dilution through ventilation, decreased tobacco density, or by decreasing the available length of the tobacco column.<sup>21</sup> Even though compensation is often only partial, it nevertheless appears to be sufficient to sustain compensatory smoking and attendant adverse health consequences. What appears to be a more promising alternative is a policy that reduces nicotine yield in cigarettes by reducing the nicotine content of the

cigarette to very low levels.<sup>29</sup> Results from experimental studies using research cigarettes suggests that lowering the nicotine content of the cigarette to levels of 1.0mg/g or below can reduce nicotine dependence with minimal increases in compensatory smoking and attendant increases in biological exposure to smoking-related toxins.<sup>8-11,29</sup> That would appear to be the direction that tobacco regulators may want to consider.

The limitations of the cross-sectional survey used in the present study notwithstanding, the results provide new epidemiological evidence for the FDA to consider in combination with the experimental research discussed above in deliberations around whether to set an upper limit on nicotine content levels in commercial cigarettes marketed in the United States. They also provide a strong empirical rationale for additional research to enhance scientific understanding of the influence of nicotine yield in cigarettes on risk for nicotine dependence.

## Funding

This research was supported by National Institute on Drug Abuse (NIDA) and US Food and Drug Administration Tobacco Centers of Regulatory Science Award P50DA036114, NIDA Institutional Training Award T32DA07242, and National Institute of General Medical Sciences (NIGMS) Centers of Biomedical Research Excellence Center Award P20GM103644. The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Food and Drug Administration.

## Declaration of Interests

None declared.

## References

1. Ashley DL, Backinger CL, van Bommel DM, Neveleff DJ. Tobacco regulatory science: research to inform regulatory action at the Food and Drug Administration's Center for tobacco products. *Nicotine Tob Res.* 2014;16(8):1045-1049. doi:10.1093/ntr/ntu038.
2. Benowitz NL, Henningfield JE. Establishing a nicotine threshold for addiction – the implications for tobacco regulation. *New Engl J Med.* 1994;331(2):123-125. doi:10.1056/NEJM199407143310212.
3. Scherer G, Lee PN. Smoking behavior and compensation: a review of the literature and meta-analysis. *Regul Toxicol Pharmacol.* 2014;70(3):615-628. doi:10.1016/j.yrtph.2014.09.008.
4. Benowitz NL, Dains KM, Hall SM, et al. Progressive commercial cigarette yield reduction: biochemical exposure and behavioral assessment. *Cancer Epidem Biomar.* 2009;18(3):876-883. doi:10.1158/1055-9965.EPI-08-0731.
5. Gori GB, Lynch CJ. Analytical cigarette yields as predictors of smoke bioavailability. *Regul Toxicol Pharm.* 1985;5(3):314-326. doi:10.1016/0273-2300(85)90045-5.
6. Zacny JP, Stitzer ML. Cigarette brand-switching: effects on smoke exposure and smoking behavior. *J Pharmacol Exp Ther.* 1988;246(2):619-627.
7. Russell MAH, Sutton SR, Iyer R, Feyerabend C, Vesey CJ. Long-term switching to low-tar low-nicotine cigarettes. *Brit J Addict.* 1982;77(2):145-158. doi:10.1111/j.1360-0443.1982.tb01416.x.
8. Hatsukami DK, Kotlyar M, Hertsgaard LA, et al. Reduced nicotine content cigarettes: effects on toxicant exposure, dependence and cessation. *Addiction.* 2010;105(2):343-355. doi:10.1111/j.1360-0443.2009.02780.x.
9. Hatsukami DK, Hertsgaard LA, Vogel RI, et al. Reduced nicotine content cigarettes and nicotine patch. *Cancer Epidem Biomar.* 2013;22(6):1015-1024. doi:10.1158/1055-9965.EPI-12-1439.
10. Benowitz NL, Hall SM, Stewart S, Wilson M, Dempsey D, Jacob P. Nicotine and carcinogen exposure with smoking of progressively reduced

- nicotine content cigarette. *Cancer Epidem Biomar.* 2007;16(11):2479–2485. doi:10.1158/1055-9965.EPI-07-0393.
11. Benowitz NL, Dains KM, Hall SM, et al. Smoking behavior and exposure to tobacco toxicants during 6 months of smoking progressively reduced nicotine content cigarettes. *Cancer Epidem Biomar.* 2012;21(5):761–769. doi:10.1158/1055-9965.EPI-11-0644.
  12. Donny EC, Smith TT, Benowitz NL, Hatsukami DK. Emerging science related to the reduction of nicotine in cigarettes. Paper presented at Society for Research on Nicotine and Tobacco; February 25–28, 2015; Philadelphia, PA.
  13. Center for Behavioral Health Statistics and Quality. *2013 National Survey on Drug Use and Health Public Use File Codebook.* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2014. [www.icpsr.umich.edu/cgi-bin/file?comp=none&study=35509&ds=1&file\\_id=1166336&path=SAMHDA](http://www.icpsr.umich.edu/cgi-bin/file?comp=none&study=35509&ds=1&file_id=1166336&path=SAMHDA). Accessed June 16, 2015.
  14. Substance Abuse and Mental Health Services Administration (SAMHSA). *Results From the 2011 National Survey on Drug Use and Health: Summary of the National Findings, NSDUH Series H-44 (HHS Publication No. (SMA) 12-4713).* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2012.
  15. Substance Abuse and Mental Health Services Administration (SAMHSA). *Results from the 2012 National Survey on Drug Use and Health: Summary of the National Findings, NSDUH Series H-46 (HHS Publication No. (SMA) 13-4795).* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2013.
  16. Substance Abuse and Mental Health Services Administration (SAMHSA). *Results From the 2013 National Survey on Drug Use and Health: Summary of the National Findings, NSDUH Series H-46 (HHS Publication No. (SMA) 14-4863).* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2014.
  17. Shiffman S, Waters AJ, Hickcox M. The nicotine dependence syndrome scale: a multidimensional measure of nicotine dependence. *Nicotine Tob Res.* 2004;6(2):327–348. doi:10.1080/1462220042000202481.
  18. Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom KO. The Fagerström test for nicotine dependence: a revision of the Fagerstrom Tolerance Questionnaire. *Brit J Addict.* 1991;86(9):1119–1127. doi:10.1111/j.1360-0443.1991.tb01879.x.
  19. Breslau N, Johnson EO, Hiripi E, Kessler R. Nicotine dependence in the United States: prevalence, trends, and smoking persistence. *Arch Gen Psychiat.* 2001;58(9):810–816. doi:10.1001/archpsyc.58.9.810.
  20. Baker TB, Piper ME, McCarthy DE, et al. Time to first cigarette in the morning as an index of ability to quit smoking: implications for nicotine dependence. *Nicotine Tob Res.* 2007;9(suppl 4):S555–S570. doi:10.1080/14622200701673480.
  21. Kozlowski LT, O'Connor RJ, Sweeney CT. Cigarette design. In: Burns DM, Benowitz NL, eds. *Smoking and Tobacco Control Monograph 13.* Bethesda, MD: US Department of Health and Human Services, Public Health Services, National Institutes of Health; 2001:13–38. <http://cancercontrol.cancer.gov/brp/tcrb/monographs/13/>. Accessed June 16, 2015.
  22. Smith TT, Sved AF, Hatsukami DK, Donny EC. Nicotine reduction as an increase in the unit price of cigarettes: a behavioral economics approach. *Prev Med.* 2014;68:23–28. doi:10.1016/j.ypmed.2014.07.005.
  23. DeGrandpre R, Bickel WK, Hughes JR, Higgins ST. Behavioral economics of drug self-administration. *Psychopharmacology.* 1992;108(1-2):1–10. doi:10.1007/BF02245277.
  24. Lynch CJ, Benowitz NL. Spontaneous cigarette brand switching: consequences for nicotine and carbon monoxide exposure. *Am J Public Health.* 1987;78(9):1191–1194.
  25. Melikian AA, Djordjevic MV, Chen S, Richie J, Stellman SD. Effect of delivered dosage of cigarette smoke toxins on the levels of urinary biomarkers of exposure. *Cancer Epidem Biomar.* 2007;16(7):1408–1415. doi:10.1158/1055-9965.EPI-06-1097.
  26. Bickel WK, Odum AL, Madden GJ. Impulsivity and cigarette smoking: delay discounting in current, never, and ex-smokers. *Psychopharmacology.* 1999;146(4):447–454. doi:10.1007/PL00005490.
  27. Fagerström K, Russ C, Yu CR, Yunis C, Foulds J. The Fagerström Test for Nicotine Dependence as a predictor of smoking abstinence: a pooled analysis of varenicline clinical trial data. *Nicotine Tob Res.* 2012;14(12):1467–1473. doi:10.1093/ntr/nts018.
  28. U.S. Department of Health and Human Services. *Smoking and Tobacco Control Monograph 13: Risks Associated With Smoking Cigarettes With Low Machine-Measured Yields of Tar and Nicotine.* Bethesda, MD: US Department of Health and Human Services, Public Health Services, National Institutes of Health; 2001. <http://cancercontrol.cancer.gov/brp/tcrb/monographs/13/>. Accessed June 16, 2015.
  29. Donny EC, Hatsukami DK, Benowitz NL, Sved AF, Tidey JW, Cassidy RN. Reduced nicotine product standards for combustible tobacco: building an empirical basis for effective regulation. *Prev Med.* 2014;68:17–22. doi:10.1016/j.ypmed.2014.06.020.