Smoking Topography, Brand Switching, and Nicotine Delivery: Results from an *In vivo* Study

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Abstract

Objective: **Exposure to toxins in tobacco smoke is influenced by how a cigarette is smoked. Cigarettes have been designed to allow for a range of puffing behavior and to provide different, nonlinear tar and nicotine yields in response to different puffing profiles. However, puffing behavior and its influence upon risk-exposure has yet to be assessed outside the laboratory, in smokers' natural environment.**

Method: **Fifty-nine adult smokers used a portable device to measure smoking topography over the course of three 1-week trials. Participants were asked to smoke their usual ''regular yield'' brand through the device for trial 1 and again, 6 weeks later, at trial 2. Half the subjects were then randomly assigned to switch to a ''low-yield'' brand for trial 3.**

Results: **The findings show a high degree of stability in puffing behavior within the same subject over time but considerable variability between smokers. Smokers who were switched to a ''low-yield'' cigarette increased their total smoke intake per cigarette by 40% (P = 0.007), with no significant change in their salivary cotinine levels. Cigarettes smoked per day and nicotine yield were only weakly associated with salivary cotinine levels; however, salivary cotinine was strongly associated with a composite measure that included cigarettes per day, brand elasticity, and puffing behavior (sr = 0.61, P < 0.001).**

Conclusions: **These findings provide strong evidence of behavioral compensation to low-yield cigarettes from *in vivo* measures of smoking behavior. The findings also show the importance of brand elasticity and smoking topography in predicting nicotine uptake and smoke exposure.** (Cancer Epidemiol Biomarkers Prev 2005;14(6):1370–5)

Introduction

The machine-measured levels of tar and nicotine in cigarettes have decreased substantially over the past 50 years. Between 1954 and 1993, the average machine-measured tar yield per cigarette decreased from 38 to 13 mg, while nicotine yields decreased from 2.7 to 0.9 mg, mainly due to the introduction of filters, filter ventilation, reconstituted and expanded tobacco, and more porous paper (1, 2). However, changes in cigarette design have also led to changes in how cigarettes are smoked. Whereas the machine-based testing standards for tar and nicotine have reflected declining yields, smokers have simply adjusted their puffing behavior, or ''smoking topography,'' to maintain their daily nicotine dosage (3-5). Indeed, laboratory research has shown that puffing behavior is sensitive to cigarette design features such as filter ventilation and nicotine yield (6, 7), so that smokers of ''low-yield'' cigarettes take larger, stronger, and more frequent puffs per cigarette than smokers of ''medium'' and ''high-yield'' cigarettes[3] (6, 8-10). However, the Federal Trade Commission (FTC) and International Standards Organization (ISO) protocols that determine tar, nicotine, and carbon monoxide yields fail to take compensatory behaviors into account and drastically underestimate human puffing behavior (5). Thus, FTC and ISO yields are poor predictors of uptake among smokers (11, 12). Ultimately, cigarettes that achieve low FTC and ISO yields through perforated filters and high paper porosity under ''standard'' machine-smoking conditions provide little or no reduction in health risk among smokers (13, 14).

Cigarettes have been designed not only to accommodate behavioral compensation for lower nicotine yields but to reward it (15). Many cigarette brands provide a larger boost in tar and nicotine than would be expected, once puff volumes increase beyond the 35-mL puffs taken by FTC and ISO smoking machines, to volumes more consistent with human smoking behavior. In other words, the ratio of smoke intake to tar and nicotine delivery is nonlinear: Larger, stronger puffs change the concentration of smoke constituents by reducing the filter retention and smoke dilution, particularly for highly ventilated cigarette brands (16, 17). This brand ''elasticity'' accomplishes two goals. First, it allows smokers to more effectively regulate the nicotine delivery of each cigarette through their puffing behavior. Second, it deceives both consumers and regulators as to the actual nicotine and tar delivery of a product. Not all cigarette brands offer the same elasticity, although more elastic brands seem to have the greatest market share (18).

Despite the importance of smoking topography to understanding product design and risk exposure, human patterns of smoking topography have been poorly characterized, largely because measures of puffing behavior have been limited to the laboratory setting. Laboratory studies have typically required participants to smoke one or two cigarettes through a mouthpiece attached to a desktop machine (9). There are inherent limitations to this design. Even in *ad libitum* trials, where participants are asked to smoke as they normally do, smoking topography has been shown to change based upon the number and timing of cigarettes smoked, as well as reactivity to the topography machine (19-21). Although biochemical values from conventional and ''machine'' smoking in a laboratory environment seem similar, this does not

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[3]Note that ''low yield'' typically refers to cigarettes with FTC machine-smoked yields below 0.8 mg of nicotine, although there is no standard definition or regulatory criteria.

indicate that laboratory smoking is the same as conventional smoking in a naturalistic setting. Considering that the total time spent puffing on a cigarette is, on average, <20 seconds, even small deviations from normal cigarette smoking behavior can have an effect upon estimates of smoke intake (9). Indeed, one of the first published studies of smoking behavior that helped to influence the protocols for the FTC method noted that subjects ''under examination'' are apt to be nervous and smoke somewhat more vigorously than normal (22). The few studies that have measured smoking topography outside of the laboratory also suggest that conventional puffing behavior may well differ from measures observed in the laboratory (23, 24). Unfortunately, studies outside of the laboratory have rarely been able to measure puff volumes, the critical measure necessary to calculate total smoke intake (19, 20, 23, 25, 26). In addition, with few exceptions (27), measurements of smoking topography have been limited to one or two cigarettes. Thus, those studies that have estimated the effects of brand switching on puffing behavior have had to rely on transient reactions to brand switching which may not relate well to longer-term changes in smoking topography. In summary, current estimates of smoking topography lack an important degree of external validity; indeed, knowledge of *in vivo* smoking topography is practically nonexistent outside tobacco industry documents (6, 28).

New portable smoking topography devices have recently been developed that allow for measures of puffing behavior in a smoker's natural environment. These devices can be operated by smokers themselves to record puffing behavior for cigarettes smoked during the course of their daily routine.

The current study sought to measure puffing behavior and the average smoke intake per cigarette using a portable device. The main objectives of the study were to (a) assess the between- and within-subject variability in smoking topography measures taken outside a laboratory setting; (b) to characterize changes in puffing behavior and cotinine levels when smokers switch from ''regular'' to low-yield cigarette brands; and (c) to examine the relationship among cigarette consumption, smoking topography, brand elasticity, and salivary cotinine levels.

Materials and Methods

Subjects. Participants were recruited through a random-digit dial telephone survey in the Waterloo Region of Ontario, Canada. Respondents who smoked a minimum of five cigarettes per day, had no intention to quit smoking in the next 3 months (the duration of the study period), and who smoked brands with ISO tar yields between 10 and 14 mg were invited to take part in the study. Participants were offered $60 CDN for completing each of three 1-week trials, for a maximum of $180 CDN.

Procedures. Participants responded to a phone survey that assessed smoking behavior, demographic profile, and key psychosocial variables such as intentions to quit. Respondents selected for the field study were recontacted to arrange for a home visit.

The field study consisted of three 1-week trials. For each trial, participants smoked at least five cigarettes a day through the smoking topography device for five consecutive days, beginning Monday until pick-up on Friday. For trial 1 (T1), participants smoked their usual brand of cigarettes. Approximately 6 weeks later, participants responded to a second phone survey, followed by a second 5-day trial (T2), using the device as before, with their usual cigarette brand. Trial 3 (T3) occurred during the week immediately following T2. For T3, half of the participants (n = 24) were randomly selected to smoke a ''lower-yield'' cigarette brand (Matinee Extra Mild, 4 mg tar/0.8 mg nicotine ISO yield), whereas half continued to smoke their usual brand (n = 27). These lower-yield cigarettes were matched for length and diameter with their usual brand cigarettes. All participants were provided with cigarettes for T3 (either their regular brand or the lower-yield brand), free of charge.

Before each trial, participants were provided with an overview of how to use the smoking topography device. Participants were instructed to use the device whenever they smoked a cigarette. Participants were also asked to model how they normally held their cigarette to identify vent blocking. Participants were then shown how to use the device with a similar grip, to allow for vent blocking, as with conventional smoking.

Participants completed daily diaries to record daily consumption and any difficulty with using the devices. Following each trial, participants responded to a 5-minute questionnaire and provided a saliva sample. The study protocol was cleared for ethics by the Research Ethics Board of the University of Waterloo and the Institutional Review Board of the Roswell Park Cancer Institute.

Measures

Smoking Topography. CReSSmicro (Plowshare Technologies, Inc., Baltimore, MD) is a battery-operated portable device that measures a full complement of smoking topography variables (puff volume, puff number, puff duration, average flow, interpuff interval, time, and date). The device is small (2.5 × 2.2 × 1.2 inch, 3.1 oz), allowing independent use in the participant's natural environment. CReSSmicro uses an orifice flow meter mouthpiece that produces a pressure drop related to the flow rate of smoke through the mouthpiece. This pressure drop is measured in real-time by the CReSSmicro device, by an onboard pressure transducer and is converted into the corresponding flow rate. All of the smoking topography variables are derived from the basic measurements of flow and time. Data was downloaded from the device immediately following each 1-week trial.

Cotinine Samples. Immediately following each smoking trial, participants were asked to provide a saliva sample, which was then frozen for storage. The saliva samples were analyzed for cotinine by Labstat International, Inc. (Kitchener, Ontario) using a rapid gas-liquid chromatographic method (29).

Brand Elasticity. Brand elasticity was calculated using the Brown and Williamson formula (30), which tests the increase in nicotine delivery relative to increases in puff volume, as follows:

$$\text{Elasticity} = (D_{56\text{mL}}/P_{56\text{mL}}) \times (P_{44\text{mL}}/D_{44\text{mL}}) \times (V_{44\text{mL}}/V_{56\text{mL}})$$

where D is the nicotine delivery, P = the number of puffs, and V = puff volume for cigarettes smoked at 44 and 56 mL puff volumes. Values of >1 indicate an ''elastic'' brand, with proportionally greater increases in delivery than puff volume. Elasticity values for the current study were drawn from tests conducted by Labstat International in 1997 (31). Twenty replicates of 115 Canadian brands were tested through a Filtrona smoking machine at 44 and 56 mL puff volumes under otherwise normal ISO smoking conditions (i.e., 2-second puffs, once per minute, with unobstructed vent holes). The number of puffs, nicotine, tar, and CO yields were determined under the 44 and 56 mL puffing regimes for each brand. Elasticity for each brand smoked by participants in the current study was calculated using the Brown and Williamson formula.

Daily Diary. Participants recorded the time of first cigarette and the total number of cigarettes smoked, including both cigarettes smoked using the CReSSmicro device and those

Table 1. Smoking topography for regular-yield cigarettes (*n* = 58)

	Puff number	Puff duration (s)	Interpuff interval (s)	Mean flow rate (mL/s)	Puff volume (mL)	Total smoke intake (mL)
Trial 1 (SD)	11.3 (3.4)	1.5 (0.2)	33.5 (17.6)	38.1 (5.6)	54.2 (10.3)	612.0 (195.7)
Trial 2 (SD)	11.1 (3.3)	1.4 (0.3)	35.6 (18.4)	37.9 (6.1)	52.3 (12.4)	580.5 (206.9)
Correlation (*P* level)	0.91 (<0.001)	0.82 (<0.001)	0.96 (<0.001)	0.85 (<0.001)	0.86 (<0.001)	0.87 (<0.001)

smoked without the device. The daily diary was also used to record any problems with the device or study protocol and any comments.

Post-Trial Questionnaire. Participants reported on their experience of using the device, including how ''natural'' it felt to smoke through the device and the extent to which they had to adjust their smoking behavior when using the machine. Any difficulties or anomalies in using the device were noted.

Data Reduction and Derived Variables. Before data analysis, all CReSSmicro smoking topography measures were checked for data accuracy. Three independent raters coded for invalid data due to device misuse, device inaccuracies, and unrealistic values. The three raters agreed on 90% of all data points; all other data points were dropped from the analyses to ensure conservative standards for data quality. Several derived variables were created. A measure of *smoke intake* per cigarette was calculated by multiplying the mean number of puffs per cigarette by the mean puff volume. In addition, three variables were created to predict salivary cotinine levels for each participant: (a) Health Canada's nicotine yield per cigarette[4] was multiplied by each participant's cigarettes per day, (b) nicotine yield was multiplied by each participant's smoke intake per cigarette and cigarettes per day, and (c) cigarettes per day was multiplied by a summary measure of each participant's smoke intake and elasticity for the brand smoked (Intake Elasticity), calculated as follows:

$$\text{Intake Elasticity} = [(\text{Pvol}_{\text{actual}}/\text{Pvol}_{44\text{mL}})\times (\text{Elasticity}_{44-56\text{mL}} \times \text{Nic}_{44\text{mL}}) \times \text{Pcount}_{\text{actual}}]$$

Where $\text{Pvol}_{\text{actual}}$ is mean puff volume for participants; $\text{Pvol}_{44\ \text{mL}}$ is the puff volume used in the modified puffing regime (i.e., 44); $\text{Elasticity}_{44\text{-}56\ \text{mL}}$ is the Elasticity value described in Materials and Methods; Nic*44mL* is the nicotine yield under the modified ISO puffing regime (i.e., ISO regime with 44 mL puffs); and $\text{Pcount}_{\text{actual}}$ is the mean number of puffs per cigarette for each participant.

Analysis

T tests were conducted to examine differences in smoking behavior between genders and experimental conditions. Pearson correlation coefficients were used to examine the stability of puffing behavior across trials. We examined the relative predictability of salivary cotinine under four models: (a) cigarettes per day alone; (b) cigarettes per day and nicotine yield; (c) cigarettes per day, nicotine yield, and measures of smoke intake; and (d) cigarettes per day, nicotine yield, smoke intake, and a measure of brand elasticity. Linear regression was used to predict salivary cotinine levels, adjusting for time of salivary collection and gender. Semipartial correlation coefficients (*sr*) are reported to indicate the independent contribution of each predictor to the multiple correlation (R^2; ref. 33). All analyses were conducted using SPSS Software (version 12.0).

Results

Sample. Of the 76 participants that began the study, 12 were excluded after trial 1 for failing to keep appointments or for violating study protocol, such as switching brands. Data from five additional participants were excluded during data cleaning, leaving a final sample of 59 participants. Of these, 52 participants had valid data for at least two waves, with an additional seven participants providing data for one trial only.

Of the 59 participants, 30 were male (51%). Participants reported a mean age of 37.1 (SD = 11.1), 81% had finished high school, and 38% had completed some form of post-secondary education. Participants smoked an average of 19.3 cigarettes per day (SD = 8.0) and 81% had previously tried to quit smoking. Although no participants intended to quit within 3 months (as per inclusion criteria), 73% planned to quit at some point beyond 3 months. There was no difference between experimental conditions and on any of these measures.

Use of the Smoking Topography Device. Participants smoked a total of 6,493 cigarettes through the CReSSmicro device. Participants each smoked an average of 67 cigarettes through the device during the first two trials (54% of all cigarettes smoked during this period) and 40 cigarettes through the device at T3 (52% of all cigarettes smoked), with no differences between the control and brand-switching groups. Only 2% of participants reported that the CReSSmicro device was ''hard'' to use and only 35% reported that using the machine did not feel ''natural.'' Approximately 42% reported that using the device did not change their smoking behavior ''at all,'' 50% reported it changed their smoking behavior ''a little,'' and 8% said it changed their behavior ''a lot.'' These measures were unrelated to smoking topography or experimental condition.

Table 2. Prediction of salivary cotinine for usual brand smoking at trial 1 (*n* = 53)

Measure	Semipartial correlation	Significance (*P*)	R^2
CPD	0.21	0.102	0.12
CPD × yield	0.25	0.055	0.14
CPD × yield × intake	0.54	<0.001	0.36
CPD × intake elasticity	0.61	<0.001	0.41

NOTE: Linear regression, adjusting for time of saliva collection and gender.
Abbreviation: CPD, cigarettes per day.

[4] Health Canada's testing regime = 55ml puffs, drawn every 30 seconds, with 100% obstruction of filter vent holes (ref. 32).

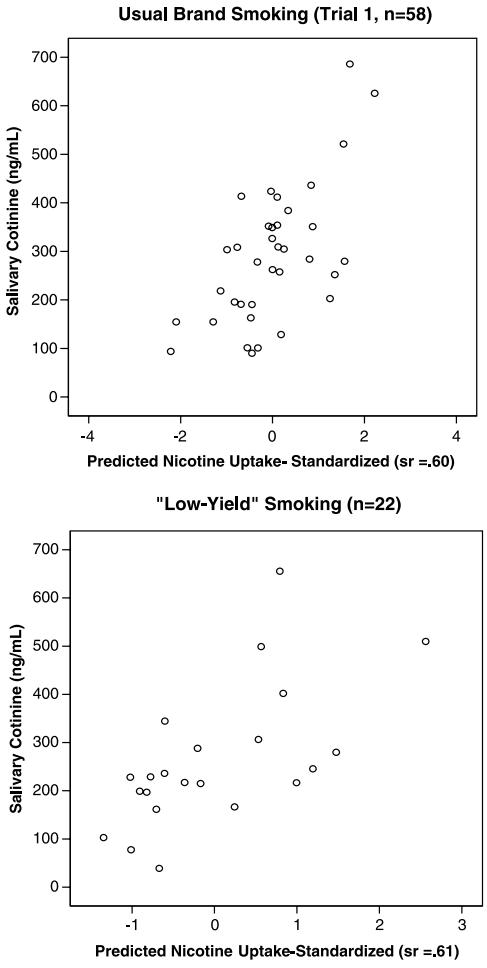

Figure 1. Salivary cotinine versus predicted levels (total cigarettes × intake elasticity).

Within and Between Variation in Measures of Smoking Topography. Table 1 provides measures of puff behavior for trials 1 and 2 (usual brand smoking). As Table 1 indicates, puffing behavior was stable within participants across the two trials separated by 6 weeks.

Substantial variability in smoke intake was observed between smokers. When measured in quartiles, smoke intake was 2.4 times greater for smokers in the highest (863.2 mL, SD = 111.0), versus the lowest quartile (359.4 mL, SD = 67.5; $t = 14.5$, $P < 0.001$). There were also considerable differences in the puff topography of men and women. Although females, on average, took one extra puff per cigarette, males took significantly larger puffs (57.8 mL, SD = 11.6) than females (47.3 mL, SD = 10.1; $t = 3.7$, $P < 0.001$). Total smoke intake was 71 mL or 12% greater among males (638.3 mL, SD = 214.1) than females (567.6, SD = 178.7; $t = 1.4$, $P = 0.18$).

Correlation between Measures of Smoke Topography. Participants who smoked more cigarettes per day waited longer between puffs ($r = 0.26$, $P = 0.04$), with a nonsignificant trend towards lower smoke intake per cigarette ($r = -0.22$, $P = 0.09$). Smoke intake per cigarette was unrelated to ISO yields for nicotine, tar, and carbon monoxide, even after controlling for cigarettes per day. Smoke intake per cigarette was primarily associated with two variables, puff number, and puff duration. A derived ''drag time'' variable (puff number × puff duration) was highly correlated with smoke intake across all three waves ($r = 0.92$, $P < 0.001$).

Smoking Topography as Predictor of Uptake. Cotinine levels were similar across the three waves (T1 = 297.4 ng/mL, SD = 143.5; T2 = 319.4 ng/mL, SD = 139.5; and T3 = 291.7 ng/mL, SD = 138.1). Table 2 compares predictors of salivary cotinine for usual brand smoking at T1.

As Table 2 indicates, cigarettes per day was not significantly associated with salivary cotinine levels, nor was the interaction between cigarettes per day and nicotine yield. The composite measure including smoke intake was significantly associated with salivary cotinine; however, the strongest predictor of salivary cotinine was the intake elasticity measure that represents the interaction between puffing behavior and product design. The superiority of the intake elasticity measure was consistent across trials for usual brand smoking, as well as for low-yield smoking at T3 (see Fig. 1).

Brand Switching. Approximately 73% of participants found it ''very different'' smoking another brand, whereas only one participant reported noticing no difference at all. As Fig. 2 illustrates, smoke intake per cigarette was 40% greater among those switched to a low-yield brand (779.2 mL, SD = 331.0) versus those who smoked their usual regular-yield brand (553.2 mL, SD = 240.5; $t = -2.8$, $P = 0.007$). The increase in smoke intake was mainly accomplished through higher puff volumes among low-yield smokers (58.3 mL, SD = 16.1), compared with regular-yield smokers (49.3 mL, SD = 11.5; $t = 2.32$, $P = 0.02$). There were no significant changes in smoking topography measures over the course of the 5-day trial among smokers in either condition; however, brand switchers increased their cigarette consumption from trial 2 relative to the usual brand condition (1.4 versus −1.2 cigarettes per day; $t = 2.4$, $P = 0.03$).

At T3, there was a nonsignificant trend towards lower cotinine levels among low-yield switchers (258 ng/mL, SD = 146.5) relative to usual brand smokers (325 ng/mL, SD = 123.5; $t = 1.8$, $P < 0.08$). Cotinine levels decreased 12% between T2 to T3 among brand switchers (299 versus 262 ng/mL; $t = 1.7$, $P = 0.07$), significantly less than would be predicted from the 38% decrease in ISO nicotine yields from smokers' usual brand smoked at T2 and the low-yield brand smoked at T3 (means = 0.95 and 0.36 mg, respectively; Fig. 3).

Discussion

This research represents the most comprehensive study to examine smoking topography, brand switching, and nicotine uptake outside a laboratory setting. The results show a high degree of stability in measures of smoking topography within the same subject over time but considerable variability in puffing behavior between smokers. The results for regular brand yields are generally consistent with previous lab-based research: 11 puffs per cigarette, for an average of 1.8 seconds,

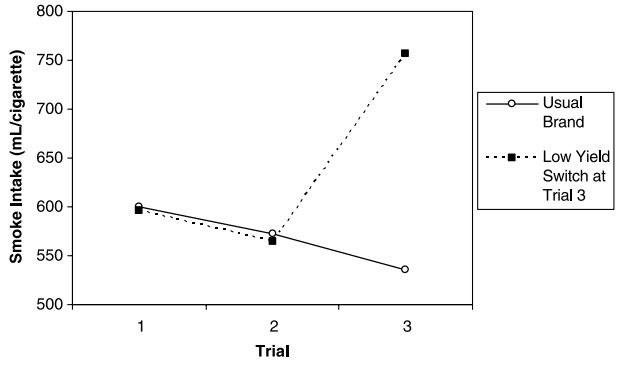

Figure 2. Effect of switching to low-yield cigarettes on smoke intake.

at intervals of 34 seconds for an average puff volume of 43 mL, and a per cigarette average of 591 mL (9). The current data are also consistent with the previous findings that total intake per cigarette is primarily determined by the time spent puffing the cigarette (10). However, puffing behavior for low-yield smoking in the current study was considerably more intense than previous laboratory estimates. This discrepancy suggests that even ''intensive smoking'' testing protocols, such as those mandated in Canada and Massachusetts, may continue to underestimate puffing behavior for a majority of smokers.

As evidenced by the large amount of variation in puffing behavior between smokers, not all of these differences are evidence of compensation in response to product design. Some smokers are simply lighter smokers and pursue lower levels of nicotine, whereas others smoking the same brand have higher nicotine thresholds and must smoke each cigarette more intensely. With regard to gender, the current findings support lab-based findings that women take more puffs but significantly smaller puffs then men, resulting in a substantially lower smoke intake per cigarette (34).

This study provides strong support for behavioral compensation in response to brand yield. Our *in vivo* measures of smoking topography confirm laboratory-based findings that smokers make substantial changes to puffing behavior when switching from regular-yield to low-yield cigarettes. In addition, these compensatory changes were stable, with no observable degradation over the course of 5 days.

To our knowledge, this is the first independent study to use brand elasticity and individual measures of smoking topography to predict nicotine uptake. The equation including elasticity, puffing behavior, and cigarette consumption represents a promising means of predicting individual uptake of smoke toxicants. Within this equation, elasticity functions as a summary measure of how different product features such as filter ventilation (perforations in the filter that dilute the smoke with air) and paper porosity interact with smoker behavior to produce different patterns of exposure. The findings are consistent with tobacco industry research in showing that the relationship between puff volume and yield is nonlinear and varies across brands (35). More generally, the findings reinforce the need for both researchers and regulators to test cigarettes under various puffing regimes that reflect the population parameters of human smokers.

The current study has limitations. First, the study participants were not necessarily representative of smokers in the population at large. We selected a sample that smoked regular-yield brands and who were not planning to quit in the near future. Nevertheless, the current study provides data from over 20 cigarette brands, including a range of nicotine and tar yields.

A second limitation is that we allowed smokers to choose only one low-yield brand when switching down from their usual brand. This was done to control for inherent differences across brands, but the results may not translate to what happens when smokers switch to a low-yield brand of their choice.

Third, the study only included smokers of Canadian brand cigarettes. Generalizations of the findings to smokers in other countries smoking different brands should be made with caution because it is known that Canadian cigarettes differ from other international brands on several important features, including tobacco blend, additives, and processing (36, 37). It is not clear how these differences are related to yield/delivery profiles.

Fourth, the elasticity coefficients used in the current study were calculated using data from 1996 brands. The design of these brands may have changed in the past 8 years; however, any changes would likely underestimate the associations reported in the current findings. Updated brand elasticity data may well increase the predictive power. Future research should replicate the current findings with a broader profile of smokers and cigarette brands to address these limitations.

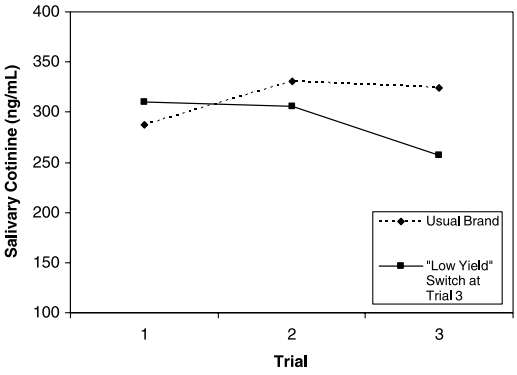

Figure 3. Effect of switching to low-yield cigarettes on salivary cotinine.

Finally, the current design does not control for any ''novelty effect'' among the brand-switching condition. However, the increases in puffing behavior and smoke intake are entirely consistent with previous research and we did not observe any attenuation or degradation of this effect over the course of 4 to 5 days of low-yield smoking, as would be expected with a novelty effect.

Understanding the relationship among product design, smoke toxicity, and individual exposure is fundamental to evaluating the health risk from tobacco products. Cigarettes have been designed to allow for a range of puffing behavior and to respond differently to different puffing profiles. Thus, smoking topography is a critical mediator within the product-risk relationship. Testing protocols for both traditional products and newer potential reduced harm products (38, 39) must incorporate accurate human smoking variables to validate industry health claims and to ensure accurate labeling and marketing of tobacco products.

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