

Smoke Yields of Tobacco-Specific Nitrosamines in Relation to FTC Tar Level and Cigarette Manufacturer: Analysis of the Massachusetts Benchmark Study

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SYNOPSIS

Objectives. This research assessed the relationship between the deliveries of carcinogenic tobacco-specific nitrosamines (TSNAs) and the Federal Trade Commission (FTC) "tar" ratings of US commercial cigarettes.

Methods. Analysis of covariance (ANCOVA) was used to assess the explanatory power of FTC tar, the particular manufacturer, and other cigarette characteristics to predict the yields of four TSNAs (N'-nitrosonornicotine [NNN], 4-(N-methyl-N-nitrosamino)-1-(3-pyridyl)-1-butanone [NNK], N'-nitrosoanatabine [NAT], and N'-nitrosoanabasine [NAB]) in 26 US commercial brands tested in the 1999 Massachusetts Benchmark Study.

Results. When FTC tar alone was used to predict TSNA yield, the squared correlation coefficient (R^2) was only 38% for NNN, 76% for NNK, 46% for NAT, and 49% for NAB. Inclusion of manufacturer-specific variables significantly ($p < 0.001$) increased the estimated R^2 for three of the four species of nitrosamine to: 78% for NNN, 88% for NNK, and 81% for NAT. Inclusion of other cigarette characteristics (filter type, paper permeability, tobacco weight, tip dilution) did not reduce the significance of the manufacturer-specific effects. Federal Trade Commission nicotine and carbon monoxide (CO) yields were no better at predicting TSNA levels.

Conclusions. FTC ratings for tar, nicotine, and carbon monoxide do not tell the entire story about the comparative yields of toxic agents in marketed cigarette brands. The significant manufacturer-specific effects suggest that proprietary blending and processing of tobacco matter as well. Public, brand-by-brand disclosure of the yields of TSNA and possibly other smoke constituents appears to be warranted.

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The opinions expressed are the author's sole responsibility and do not necessarily represent the views of the Massachusetts Institute of Technology, the Massachusetts General Hospital, the Massachusetts Department of Public Health, or any other organization.

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The Federal Trade Commission (FTC) has published standardized “tar” and nicotine ratings since 1967 and carbon monoxide (CO) ratings since 1980 on all cigarettes marketed in the United States.¹ Public health specialists and policy makers, however, have repeatedly raised two concerns about the adequacy of the FTC ratings. First, the parameters of the FTC’s smoking-machine measurements—such as puff volume, the number of puffs per cigarette, and the depth of insertion of the cigarette tipping into the machine’s mouthpiece—may not reflect actual human smoking of currently marketed “low tar” cigarettes.² Second, the FTC’s published ratings of tar, nicotine, and CO may not correlate with the yields of other harmful constituents of cigarette smoke.³ These concerns have led some governments, including the Canadian province of British Columbia,⁴⁻⁵ Canada’s national health authority,⁶ and the state of Massachusetts,⁷ to propose or to mandate more complete disclosure of the yields of many other smoke chemicals under more realistic test conditions.

This article focuses on the second concern; that is, the adequacy of the FTC tar rating as an indicator of the yields of other toxic chemicals in cigarette smoke. Tobacco-specific nitrosamines are especially important smoke constituents to test the adequacy of the FTC ratings. By convention, cigarette smoke has been partitioned into a gas phase (containing those volatile chemicals that pass through the pores of standard Cambridge filter paper) and a particulate phase (containing those chemicals that are trapped on the filter paper). The particulate phase has been found to contain four nonvolatile tobacco-specific nitrosamines (TSNA) (N’-nitrosonornicotine [NNN], 4-(N-methyl-N-nitrosamino)-1-(3-pyridyl)-1-butanone [NNK], N’-nitrosoanatabine [NAT], and N’-nitrosoanabasine [NAB]).⁸⁻⁹ The nitrosamines NNN and NNK, in particular, have been found to be potent animal carcinogens.⁹⁻¹⁰ In the process of curing the tobacco leaves or in the burning of tobacco during cigarette smoking, the nitrates in tobacco give rise to nitrogen oxides that, in turn, combine with alkaloids (including nicotine and nicotine derivatives) to form nitrosamines.¹¹⁻¹³ Although current means for diluting cigarette smoke, such as aerated filter tips, may reduce the yields of tar and other smoke chemicals, the TSNA deliveries of cigarettes may be influenced by specific methods of tobacco curing or manufacturers’ blending practices, especially the inclusion of nitrogen-rich burley tobacco.¹⁴ In fact, during 1978–1993, as the nitrate content of many US tobacco blends rose, the NNK content of a leading filter cigarette was found to have increased by about 50%, even though the FTC tar

delivery remained stable.^{15,16} A separate study in 1991 of 170 European cigarettes found little correlation between tar and TSNA delivery.¹⁷

This study analyzes the relationship between the tar ratings of 26 brands of US cigarettes as measured by the conventional machine-based FTC method, and the corresponding smoking-machine yields of the four TSNAs.¹ The TSNA yields were measured under smoking-machine parameters that more accurately reflected actual human smoking of “low tar” cigarettes than did the FTC parameters.² Both the FTC tar and the TSNA measurements were derived from the 1999 Massachusetts Benchmark Study, an analysis of 26 marketed brands that was voluntarily submitted by four US cigarette manufacturers in response to a proposed regulation, promulgated by the Massachusetts Department of Public Health (MDPH), to test all marketed brands.^{7,18,19}

METHODS

Data

Table 1 shows the basic characteristics of the 26 marketed brands tested in the Massachusetts Benchmark Study, including type of filter tip (if any), mean tar yield (in mg/cigarette), and the latest available data on the market shares of each brand (measured as the percentage share of US domestic shipments in 1997).^{18,19} The tar measurements (in mg/cigarette), which were based on the original machine-smoking parameters specified by the FTC (35 ml puff volume; 2 s puff duration; 60 s puff interval; no blocking of filter perforations), represented the average of 80 measurements in four manufacturers’ laboratories.¹ (No laboratory-specific effect was observed.) In addition to the characteristics in Table 1, data for each brand was analyzed on: mean nicotine (mg/cig) and CO yields (mg/cig) by the FTC method; the tobacco weight (mg/cig); cigarette length (mm) and circumference (mm); tip dilution (i.e., the percentage of the puff volume that arose from air entering through ventilation holes in the filter tip); and paper permeability (CORESTA units). Data for a non-marketed reference cigarette (1R4F, not shown in Table 1) that has been routinely used as a control in comparative cigarette studies was also analyzed.^{18,19} The data in Table 1, as well as the additional data on nicotine and CO yields, cigarette characteristics, and the results for 1R4F were likewise derived from the Benchmark Study.^{18,19}

Table 2 shows the mean yields of each of the four TSNAs, as measured by the Brown & Williamson Laboratory according to analytical methods specified by the Massachusetts Department of Public Health

Table 1. Characteristics of the 26 brands tested in the Massachusetts Benchmark Study

Brand number	Manufacturer	Filter type ^a	FTC tar (mg/cig)	Market share (percent)
1	C	Conc. paper	1.03	0.05
2	B	CA/plastic	4.27	0.14
3	C	CA	4.48	0.05
4	C	CA	10.29	8.95
5	A	CA	11.21	0.35
6	C	CA	15.40	8.26
7	B	CA	19.23	0.86
8	D	CA	0.92	0.06
9	C	CA	5.42	0.32
10	A	CA	4.79	0.07
11	C	CA	11.03	3.34
12	B	CA	13.47	0.14
13	D	CA	13.67	1.48
14	D	NF	23.68	0.64
15	A	CA	0.75	0.31
16	D	CA	4.52	0.82
17	C	Rec. charc.	12.13	0.25
18	D	CA	13.03	0.16
19	A	CA	16.55	1.24
20	C	NF	26.45	0.12
21	A	CA	0.83	0.28
22	A	CA	5.20	0.21
23	C	CA	12.36	0.25
24	D	CA	10.57	0.11
25	C	CA	15.41	3.40
26	B	CA	17.49	1.70

DATA SOURCE: Reference 18.

^aNF = non-filter; CA = cellulose acetate; CA/plastic = cellulose acetate/plastic; Conc. paper = concentric paper; Rec. charc. = recessed charcoal.

(MDPH), which were in turn taken from the official methods established by Health Canada and promulgated by British Columbia.²⁰ In contrast to the FTC tar measurements, the TSNA yields were determined under MDPH-specified smoking parameters (45 ml puff volume; 2 s puff duration; 30 s puff interval; 50% blocking of filter perforations). Each TSNA measurement in Table 2 represents the mean yield from five different cigarettes of the same brand. The standard errors of the means ranged from 0.7% to 2.5% of the estimated mean values for NNN; 0.9% to 3.0% for NNK; 0.5% to 2.8% for NAT; and 1.0 to 4.2% for NAB (not shown in Table 2).

Statistical methods

I employed analysis of covariance (ANCOVA)²¹ in which the dependent variables were the mean yields of the four species of TSNA, as given in Table 2. The inde-

pendent variables were the mean FTC tar as well as separate zero-one indicator variables for three of the four manufacturers, as given in Table 1. (Manufacturer "A" was the reference category.) I used the market shares in Table 1 as sampling weights to ensure that the most heavily purchased brands had the greatest influence on the statistical estimates.

For each species of TSNA, I first computed the adjusted R^2 statistic (i.e., the proportion of the variance of the dependent variable that is explained by the regression model), specifying only the FTC tar as the independent variable. Next, I computed the same R^2 statistic specifying both the FTC tar and indicators for each manufacturer as independent variables. I relied upon the F statistic to test whether the inclusion of the manufacturer-specific indicators contributed significantly to the explanatory power of the model. Finally, I computed t-statistics to assess whether

Table 2. Mean yields of four tobacco-specific nitrosamines of the 26 brands tested in the Massachusetts Benchmark Study

Brand number	NNN (ng/cig)	NNK (ng/cig)	NAT (ng/cig)	NAB (ng/cig)
1	99.9	55.2	108.2	14.2
2	166.8	92.5	161.2	23.3
3	173.4	104.7	155.1	17.4
4	220.9	148.6	201.1	21.8
5	159.9	127.7	170.2	25.4
6	302.0	184.0	287.0	33.4
7	243.1	198.4	229.9	24.4
8	102.2	53.5	95.2	19.5
9	242.1	145.9	210.2	28.8
10	149.6	101.6	152.2	24.9
11	261.7	158.6	221.9	32.6
12	264.1	184.2	233.8	40.6
13	270.3	193.4	180.8	36.1
14	303.4	220.7	279.3	45.3
15	110.3	56.1	102.6	15.8
16	136.4	94.3	115.2	17.6
17	314.5	197.0	298.6	45.2
18	190.2	151.0	181.2	28.5
19	176.0	146.0	191.3	26.0
20	317.3	199.9	289.8	43.8
21	106.5	55.5	112.3	17.7
22	131.8	100.8	126.7	21.9
23	259.8	165.4	259.4	37.6
24	170.5	135.4	160.7	26.3
25	289.8	180.2	271.5	32.4
26	207.9	176.1	203.0	34.0

DATA SOURCE: Reference 18.

NNN = N'-nitrosonornicotine; NNK = 4-(N-methyl-N-nitrosamino)-1-(3-pyridyl)-1-butanone; NAT = N'-nitrosoanatabine; NAB = N'-nitrosoanabasine (NAB).

the TSNA yields of cigarettes sold by manufacturers B, C, or D differed significantly from those of manufacturer A.

By way of sensitivity analysis, I repeated the foregoing ANCOVA analysis, specifying other covariates (filter type, tobacco density, tip dilution, paper permeability, and nicotine and CO yield as measured by the FTC method) as independent variables. I also added a 27th observation that corresponded to the data on the 1R4F reference cigarette. Finally, I repeated my regression estimates without market shares as weights.

RESULTS

Table 3 shows the main results of the analysis of covariance. The FTC tar was significantly correlated with the yields of all four TSNA's ($p < 0.01$). However, the

FTC tar was by itself a relatively poor predictor of TSNA yield. The R^2 statistics for the model in which FTC tar was the sole independent variable were less than 0.5 for three of the TSNA's and only 0.76 for NNK. Inclusion of manufacturer-specific independent variables significantly improved the explanatory power of the ANCOVA model for NNN, NNK, and NAT ($p < 0.001$), but not for NAB. In the case of the first three TSNA's, the inclusion of the manufacturer classification increased the R^2 statistic to approximately 0.8.

As Table 3 shows, the yield of three tobacco-specific nitrosamines (NNN, NNK, and NAT) from manufacturer C's brands was significantly greater ($p < 0.01$) than the yields of manufacturer A (the reference category). Moreover, manufacturer D's brands had significantly greater yields than those of manufacturer A in the cases of NNN ($p < 0.05$) and NNK ($p < 0.01$),

Table 3. ANCOVA estimates for four tobacco-specific nitrosamines^a

	Dependent variable ^b			
	NNN	NNK	NAT	NAB
Regression coefficients				
Intercept	59.6*	51.3**	62.5**	10.6*
FTC tar	8.7**	6.1**	9.2**	1.2**
Mfr B ^c	10.0	23.0*	-10.7	-0.1
Mfr C ^c	93.0**	37.1**	62.8**	3.3
Mfr D ^c	60.2*	36.9**	-1.0	6.3
R ² statistics				
FTC tar only	0.38	0.76	0.46	0.49
FTC tar + Mfr	0.78	0.88	0.81	0.49
p-value of				
Mfr Classific. ^d	<0.0001	0.0006	<0.0001	0.42

^aEstimates based on the 26 brands listed in Tables 1 and 2 with the market shares (Table 1) as regression weights.

^bNNN = N'-nitrosanornicotine; NNK = 4-(N-methyl-N-nitrosamino)-1-(3-pyridyl)-1-butanone; NAT = N'-nitrosoanatabine; NAB = N'-nitrosoanabasine (NAB).

^cEstimates are differences relative to the omitted reference category, which is Manufacturer A.

^dp-value based on F-test of the contribution of the manufacturer-specific classification to the variance of the dependent variable (NNN, NNK, NAT, or NAB).

* = Coefficient significantly different from zero at $p < 0.05$.

** = Coefficient significantly different from zero at $p < 0.01$.

while manufacturer B's brands had a higher yield of NNK ($p < 0.05$).

Figures 1 and 2 plot the nitrosamine yield and FTC tar for NNN and NNK, respectively, the two TSNA's with the strongest evidence of animal carcinogenicity.^{9,10} The relative size of each plotted data point (symbolized by a diamond for manufacturer A; a square for manufacturer B; a circle for manufacturer C; and a triangle for manufacturer D) corresponds to the relative market share of each brand. The straight lines (labeled A through D) show the fitted relationships for each manufacturer, based on the ANCOVA regression. In both figures, there is a positive relationship between FTC tar and TSNA yield, but with a relatively large scatter of the data points. For example, brand 6 (with a market share over 8%) had an FTC tar delivery of 15.4 mg/cig and an NNN yield of 302.0 ng/cig (standard error, 5.2 ng/cig). By contrast, brand 19 (with a market share over 1.2%) had a somewhat higher FTC tar delivery of 16.6 mg/cig, but a significantly lower NNN yield of only 176 ng/cig (standard error, 1.8 ng/cig).

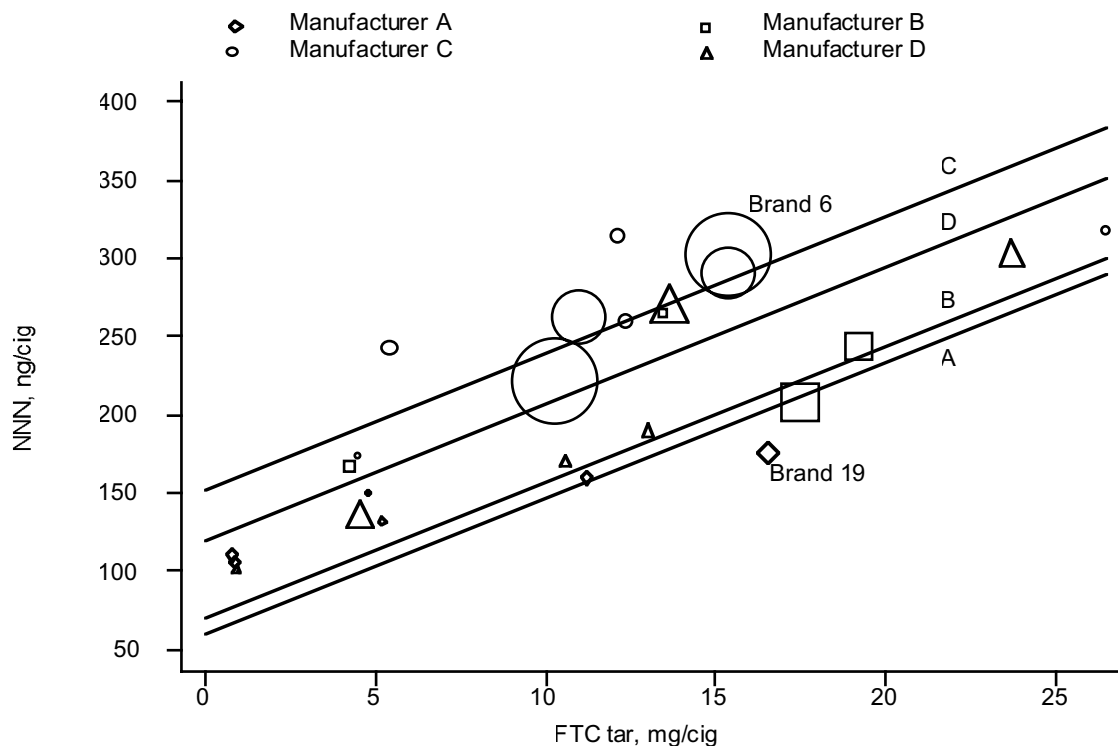
Figures 1 and 2 also illustrate the manufacturer-specific effects delineated in Table 3. Thus, in Figure 1, the data points for brands of manufacturers C and D lie significantly above those of manufacturer A. In Figure 2, the data points for brands of manufacturers B, C, and D all lie significantly above those corresponding to manufacturer A.

Sensitivity analyses did not significantly alter my findings. By itself, FTC tar remained a relatively weak predictor of TSNA yields when I estimated unweighted regressions or when I included the 1R4F reference cigarette as a 27th observation. Inclusion of manufacturer as an independent variable significantly improved the classification even when other covariates (such as filter type, paper permeability, tip dilution, tobacco density, or the squared value of mean FTC tar) were included. Regression models with interaction effects suggested that for NNN and NAT, the slope of the tar/nitrosamine relationship was larger for brands of manufacturers C and D. By itself, FTC nicotine or FTC carbon monoxide was no better a predictor of TSNA yield than was FTC tar, as measured by R². When either FTC nicotine or FTC carbon monoxide was used as an independent variable instead of FTC tar, the manufacturer was still a significant predictor of TSNA yield (results not shown).

The findings concerning the increased TSNA yields of some manufacturers' brands can be converted into tar equivalents as follows: As noted in Table 2 and depicted in Figure 1, the ANCOVA analysis showed that manufacturer C's brands had an NNN yield that was estimated to be 93.0 ng/cig (with 95% confidence interval [CI], 51–131) more than the brands of manufacturer A. Because Table 3 shows that each mg of tar increased the NNN yield by 8.7 ng (with 95% CI, 6.1–11.3), one can compute that manufacturer C's cigarettes had an additional NNN yield that was the equivalent of a 10.7 mg difference in tar (that is, the ratio $93.0 \div 8.7 = 10.7$, with 95% CI, 5.8–15.6). By the same calculation, C's brands had an additional yield of NNK that was the equivalent of a 6.1 mg difference in tar (95% CI, 3.5–8.7) and an additional yield of NAT that was the equivalent of a 6.8 mg difference in tar (95% CI, 4.2–9.4).

CONCLUSIONS

In the 1999 Massachusetts Benchmark Study, the yields of four tobacco-specific nitrosamines (NNN, NNK, NAT, and NAB) were measured by one participating manufacturer for 26 marketed US brands under machine-puffing parameters specified by the Massachusetts Department of Public Health. Based upon my analysis of

Figure 1. NNN yields versus FTC tar for 26 US brands

The relative size of each data point represents the brand's US domestic market share. The lines represent the best-fit linear relationships for each manufacturer, as derived from the ANCOVA regression.

the Benchmark data, I find that FTC-published tar level alone was a relatively weak predictor of cigarette TSNA yield. Moreover, the identity of the cigarette manufacturer was a significant predictor of a brand's delivery of three of the four species of tobacco-specific nitrosamine studied (NNN, NNK, and NAT).

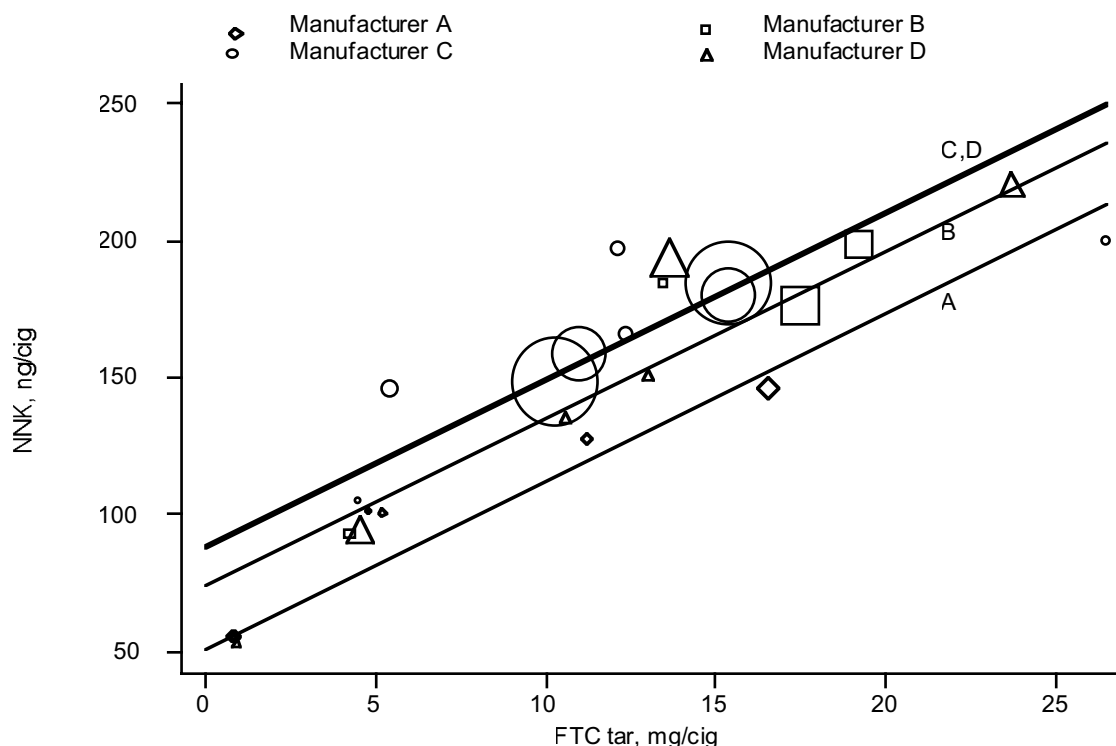
Errors in the measurement of the dependent variable will tend to reduce the R^2 statistic in a linear regression model. Hence, it is conceivable that laboratory errors in the measurement of smoke of TSNA reduced the explanatory power of FTC tar alone. However, there is no evidence that systematic errors in the measurement of TSNA (which were all performed in the same company's laboratory according to standard methods) could have also resulted in the finding of significant company-specific effects.²⁰ Nor is there any evidence that the MDPH-specified smoking parameters (45 ml puff volume; 2 s puff duration; 30 s puff interval; 50% blocking of filter perforations) could be responsible for the observed company-specific effects.

I studied how FTC tar predicted the delivery of TSNA from standardized machine smoking, rather than from actual human smoking. Human smoking

patterns are highly variable.² Smokers compensate for lower FTC tar and nicotine yields by blocking ventilation holes, increasing the puff volume and duration, and smoking more cigarettes.²² Still, there is no evidence that FTC tar would be any better a predictor of an individual smoker's intake of TSNA, nor is it obvious why company-specific blending or curing practices would not similarly affect an individual smoker's TSNA dosage.

I used market shares as regression weights so that the results in Table 3 would more accurately correspond to a random sample of all cigarettes currently sold in the marketplace. In an unweighted analysis, a rarely purchased outlier brand with very high FTC tar and TSNA yields could in principle produce a statistical correlation between FTC tar and TSNA that would have little relevance to consumers. Nonetheless, in the current study, both weighted and unweighted regressions gave the same results.

The burley variety of tobacco in blended US cigarettes is known to be rich in nitrogen. Different types of curing methods are also thought to affect nitrogen chemistry in flue-cured varieties.¹⁰⁻¹⁴ Accordingly, these

Figure 2. NNK yields versus FTC tar for 26 US brands

The relative size of each data point represents the brand's US domestic market share. The lines represent the best-fit linear relationships for each manufacturer, as derived from the ANCOVA regression.

results support the proposition that a manufacturer's blending and processing of tobacco may significantly influence a cigarette's yield of carcinogenic nitrosamines. However, the same conclusions may not apply to the yields of other noxious constituents of cigarette smoke, whose relation to FTC tar, nicotine, and CO need further systematic study.

Modifications of the FTC reporting systems have been under consideration for some time. Large scale labeling of cigarettes similar to the FDA mandated labeling of packaged food has been proposed.²³ The Massachusetts Department of Public Health continues to evaluate its proposed cigarette constituent testing regulations.⁷ The Government of British Columbia has begun measurement and reporting of a wide range of cigarette constituents including TSNAs, but no analysis of the Canadian data has been reported thus far.⁴⁻⁵

The present findings contradict the hypothesis that the FTC tar level of a cigarette brand is, by itself, an adequate indicator of the yields of all other harmful smoke constituents. These findings reinforce proposals to mandate the disclosure of additional cigarette constituents beyond tar, nicotine, and carbon monox-

ide. Such disclosure will not only enhance the comparative information available to consumers, but it may also stimulate manufacturers to compete to develop technologies to reduce TSNA yields.²³

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