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SHORT REPORT

Lung Cancer Risk Is Proportional to Cigarette Tar Yield: Evidence from a Prospective Study

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The age-adjusted risk for lung cancer among over 120,000 male current cigarette smokers in the American Cancer Society's 1959–1972 prospective study was analyzed according to tar yield and quantity smoked per day. At each quantity level, the risk increased with increasing tar yield, and at each tar level, the risk increased with numbers of cigarettes smoked daily. The risks in smokers of cigarettes with the lowest yields, however, far exceeded those of former smokers and nonsmokers. The excess lung cancer risk for current smokers was directly proportional to the estimated total milligrams of tar consumed daily: SMR = 100 + 1.731 × milligrams tar per day. Tar yields today are much lower than they were at the time of this study and presage an eventual reduction (but not elimination) of lung cancer risk for those who continue to smoke cigarettes, especially among lifetime smokers of low-tar cigarettes.

INTRODUCTION

The carcinogenic potential of cigarette smoke is now believed to reside mainly in the particulate matter or tar (1). Numerous studies over the years have demonstrated that the risk for lung and other cancers among cigarette smokers, relative to nonsmokers, varies with the tar yield (2). This relationship has been consistently observed, despite varied representations of tar yield, which have ranged from classifying cigarettes as filter or nonfilter (3), to fairly elaborate schemes based on machine-rated yields and other smoker characteristics (4).

There have been very few attempts to present classical dose–response curves in relation to tar yields (5) that would allow a visual quantification of relative risk. Opportunities for measuring such curves in Western populations are fading, as the distribution of cigarette yields becomes compressed at the low end of the spectrum. We present here a new analysis of data originally collected by the American Cancer Society in its prospective study conducted from 1959 to 1972. Hammond *et al.* (6) had previously shown that lung cancer risk was greater in both men and women who smoked "high tar/nicotine" cigarettes in this population, but in order to emphasize this point, data were adjusted for quantity smoked, and the dose–response relationship by tar yield within categories of amount smoked was not shown. In the following analysis, we demonstrate that tar yield operates independently of daily quantity smoked and that lung cancer risk increases roughly in proportion to the machine-derived dosage of tar consumed daily.

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METHODS AND MATERIALS

The data are from Cancer Prevention Study I (CPS-1),[2] details of which have been presented previously (7–10). Between October 1, 1959, and March 31, 1960, volunteer workers of the American Cancer Society enrolled over 1,000,000 men and women in a prospective mortality study. The volunteers successfully traced 98.4% of the subjects through September 30, 1971. This article is based upon information recorded in the initial baseline questionnaire, and follow-up is confined to experience during the time period July 1, 1960 to June 30, 1966. The analysis is restricted to white males with no self-reported history of cancer, heart disease, or stroke, and who answered "No" to the question "Are you sick at the present time." These exclusions serve to eliminate very ill persons from the study, so that follow-up pertains largely to an initially healthy population. To reduce confounding by socioeconomic status, which is associated with both choice of cigarette brand and with mortality, analysis was further restricted to men who had completed at least some high school.

Mortality data were confined to the first 6 years of the study so as to minimize the effect upon death rates of well-documented reductions in cigarette smoking habits in this population (11). In addition, during the first 6 years of follow-up additional information was sought from doctors and hospitals whenever cancer was mentioned on death certificates, so that mortality information is based upon best evidence of cause of death.

Information on the tar content of the smoke from various brands of cigarettes was obtained from several sources (6), including analyses released by Foster D. Snell, Inc., and published in the Reader's Digest in 1959 and 1961. Each subject was classified according to the tar content (H, high; M, medium; L, low) of the cigarette brand he usually smoked at the time of the initial questionnaire. Under this categorization, high T/N cigarettes contained 25.7 to 35.7 mg of tar, medium T/N cigarettes contained 17.7 to 25.6 mg, and low T/N had yields up to 17.6 mg.

Current smokers of cigarettes at time of enrollment were classified jointly according to their tar level and the number of cigarettes smoked per day, recorded categorically as 1–19, 20, 21–39, or 40 or more cigarettes per day, making $4 \times 3 = 12$ categories in all. Former smokers of cigarettes were placed in a separate category. Men who had never smoked regularly (nonsmokers) were also included for comparison. The largest single category of smokers consumed 20 medium tar cigarettes per day; this group was therefore considered the reference category.

All analyses were stratified by 5-year age groups; since subjects were enrolled at about the same time, this also amounts to stratification by birth cohort. Furthermore, the age at which subjects began to smoke cigarettes showed similar distributions in all age groups, with the majority in a fairly narrow band around 15–19 years (8). Duration of smoking habit in this population is thus closely correlated with age, so that adjustment for age tends to result in adjustment for duration as well. Therefore, no further adjustment for duration of smoking habit

[2] Abbreviations used: CPS-1, Cancer Prevention Study I; CPS-2, Cancer Prevention Study II; T/N, tar/nicotine yield; SMR, standardized mortality ratio.

was made. It is also nearly certain that the 20-year latency period for tobacco-induced lung cancer had already elapsed for practically all smokers in this study by the time of enrollment.

Age-, tar-, and quantity-specific lung cancer death rates were computed by dividing the number of lung cancer deaths by the person-years of exposure in each stratum. Expected numbers of deaths in each tar-quantity stratum were obtained by multiplying the number of person-years in that stratum by the corresponding lung cancer death rate in the 20 cigarette per day/medium T/N reference group and summing over age strata. The standardized mortality ratio within each tar-quantity group was formed by first dividing 100 times observed deaths by the expected number of deaths within that group, then dividing the result by 0.095, which is the ratio of observed to expected deaths in nonsmokers, whose SMR thereby becomes 100. This expedient, which is merely a shift of scale, does not affect relative comparisons and allows SMRs to be expressed relative to the more "natural" nonsmoker reference group.

RESULTS

There were 969 deaths from lung cancer during the 6 years of follow-up, in a population of 222,830 men who met the above restrictions (Table 1). Of these men, 120,583 (54.1%) were current smokers, 40,827 (18.3%) had not smoked cigarettes for at least 1 year, and 61,420 (27.6%) had never smoked. Among current smokers, at each T/N level, the SMR increased with quantity (Table 2), while at each value of daily quantity smoked, the SMR for the high T/N cigarette smokers exceeded that for the medium group, which in turn exceeded the low group SMRs (except at the lowest quantity, where the medium T/N SMR slightly exceeded the high T/N SMR). Lifetime nonsmokers had lung cancer death rates well below any group of current smokers, irrespective of cigarette yield. Ex-smokers' rates were intermediate between those of current smokers and nonsmokers.

The final column of Table 2 shows observed and expected lung cancer deaths summed across the quantity columns. The SMRs in that column can be considered adjusted for both age and quantity smoked. These SMRs, which are shown in Fig. 1 along with their 95% confidence intervals, progress from 841 among low

TABLE 1
SUBJECTS, PERSON-YEARS, AND LUNG CANCER DEATHS ACCORDING TO SMOKING HABITS

	No. subjects	Person-years	No. lung cancer deaths
Never smoked regularly	61,420	351,070	51
Ex-smokers	40,827	232,661	94
Current smokers	120,583	678,992	824
Cigarette yield			
Low T/N	17,556	99,487	93
Medium T/N	56,718	319,630	380
High T/N	46,309	259,875	351
Total	222,830	1,262,723	969

Note. Low, up to 17.6 mg tar; Medium, 17.7 to 25.6 mg tar; High, 25.7 to 35.7 mg tar.

TABLE 2

EXPECTED[a] AND OBSERVED DEATHS AND STANDARDIZED MORTALITY RATIO[b] FOR LUNG CANCER ACCORDING TO CIGARETTE YIELD AND NUMBER OF CIGARETTES SMOKED PER DAY

			Number of cigarettes smoked per day				Any number
			1–19	20	21–39	40+	
Never smoked regularly	Observed	51					
	Expected[a]	536.5					
	SMR[b]	100					
Ex-smoker	Observed	94					
	Expected[a]	361.5					
	SMR[b]	274					
Current smokers							
Low T/N[c]	Observed		20	32	25	16	93
	Expected[a]		40.2	36.7	24.2	15.3	116.4
	SMR[b]		524	917	1086	1100	841
Medium T/N[c]	Observed		87	131	95	66	379
	Expected[a]		119.1	131.0	70.7	38.1	358.9
	SMR[b]		768	1053	1414	1824	1112
High T/N[c]	Observed		62	140	88	60	350
	Expected[a]		1.0	115.0	59.4	32.7	298.1
	SMR[b]		717	1281	1560	1930	1236
Any T/N	Observed		169	303	208	142	822
	Expected[a]		250.3	282.7	154.3	86.1	773.4
	SMR[b]		711	1128	1419	1736	1119

Note. Abbreviations: SMR, standardized mortality ratio; T/N, tar/nicotine yield.

[a] Expected numbers of deaths are based on age-specific lung cancer rates for smokers of 20 Medium T/N cigarettes per day.

[b] SMR = 100 × (Observed/Expected) ÷ 0.095 in order to make the SMR for nonsmokers 100.

[c] Low, up to 17.6 mg tar; Medium, 17.7 to 25.6 mg tar; High, 25.7 to 35.7 mg tar.

T/N smokers to 1,112 for medium and up to 1,236 for the high group. The SMR for high T/N smokers was significantly higher than that of the low group ($P < 0.05$).

Within each of these T/N groupings regression lines were fitted to the expression SMR = 100 + B × number cigarettes per day. Due to coding of categorical cigarette quantities (1–19, 21–39, 40+), exact abscissas were not known for this population. To represent the "average" number of cigarettes per day at each of these levels, we used as abscissas the actual average values within those categories for male current smokers from Cancer Prevention Study 2 (CPS-2) (12), in which the exact number of cigarettes smoked per day is known. These average values are 1–19 cigarettes, 9.28; 21–39 cigarettes, 29.17; and 40+ cigarettes, 44.23. To the extent by which the CPS-1 population (surveyed in 1959) and CPS-2 (surveyed in 1982) differ in these averages, the curves will be in error.

The slopes of the regression lines with their 95% confidence intervals are presented in Table 3. Regressions were weighted by the number of lung cancer deaths at each point. The slope of the high T/N curve significantly exceeded that of the medium T/N curve, which in turn significantly exceeded that of the low T/N curve.

In a separate view of the same data, a daily "tar dosage" was computed for each individual smoker by multiplying his assigned number of cigarettes smoked per day (9.28, 20.00, 29.17, or 44.23) by estimated tar levels of 16.5 mg for low T/N smokers, 21.0 mg for medium T/N smokers, and 31.0 mg for high T/N smokers. These values are weighted averages of tar yields within each of the three T/N

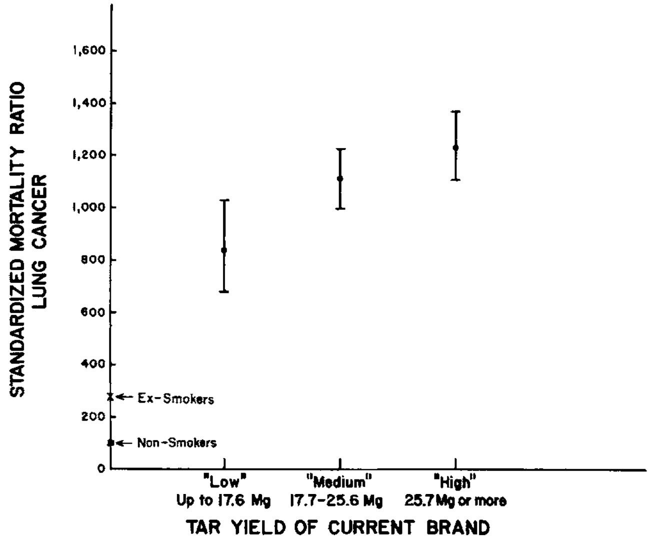

FIG. 1. Standardized mortality ratio for lung cancer among male current smokers according to tar yield of current brand, adjusted for age and number of cigarettes smoked daily, shown with 95% confidence intervals.

categories, based upon machine-derived yields measured in the late 1950s and brand distributions of study subjects. The SMRs are plotted against these putative dosages in Fig. 2 and appear to lie on a straight line, except for the highest dosage point. These data were fitted to a dose–response curve: SMR = 100 + 1.731 × milligrams tar per day (standard error of the slope = 0.012).

DISCUSSION

The literature on cancer risk in relation to cigarette yield has been reviewed recently (2). In numerous case–control and prospective studies performed in the United States and Europe, the relative risk for lung cancer has consistently been found to be lower among both men and women who smoke lower-yield cigarettes. This basic finding held irrespective of the many different ways in which "dosage" was expressed, whether in qualitative filter vs nonfilter analyses, such as those of Wynder and Stellman (3) and Benhamou *et al.* (13), or quantitatively, using ex-

TABLE 3
REGRESSION COEFFICIENTS, B, AND 95% CONFIDENCE INTERVALS FOR THE EQUATION SMR = 100 + B × (NO. CIGARETTES PER DAY)

Cigarette yield	B^a	95% Confidence interval
Low T/N	30.2	(28.7, 31.8)
Medium T/N	43.4	(42.8, 44.0)
High T/N	48.4	(47.6, 49.2)

Note. Low, up to 17.6 mg tar; Medium, 17.7 to 25.6 mg tar; High, 25.7 to 35.7 mg tar.
[a] Each data point is weighted by the number of lung cancer deaths at that T/N quantity level.

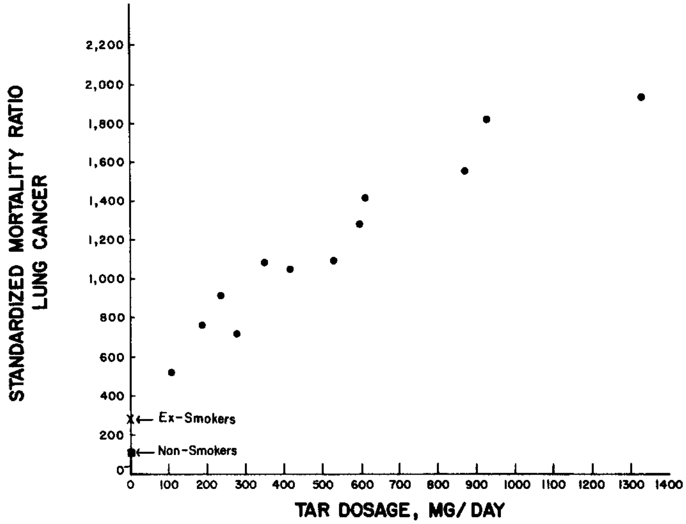

FIG. 2. Standardized mortality ratio for lung cancer among male current smokers according to the daily tar consumption (estimated as machine-rated yield of usual brand times average No. of cigarettes smoked daily).

plicit tar yields or ranges, as in the study by Vutuc and Kunze (4). A similar conclusion was reached by an international workshop on low tar-yield cigarettes (14). Risks for other cancers besides the lung, notably larynx (3), esophagus (15), and bladder (16), have also been found to be lower among smokers of filter cigarettes than among smokers of nonfilters.

The data presented here are consistent with prior reports (2) implicating tar as the main carcinogenic agent in cigarette smoke and furthermore suggest a linear dose–response relationship. The quantitative model presented, while idealized through reference to machine-measured yields and use of an age-adjusted endpoint, seems a plausible approximation for a dose–response and also suggests a way of quantifying potential risk reduction. Under this model, a slope of 1.731 per milligram tar per day translates to a relative risk of 7.9 for a smoker of one pack of cigarettes with a 20-mg (machine-measured) yield daily, compared with 4.4 for a smoker of one pack of cigarettes with a 10-mg yield. This is, of course, the maximum risk reduction that could be expected by a person halving his yield, since it does not explicitly account for latency; one who switches from a higher to a lower yield cigarette can at best expect a gradual, not instantaneous, risk reduction.

The tar yields to which this cohort has been exposed are extremely high by the standards of today's American marketplace, and one hopes they will never again be this high. Between 1950 and 1980, the sales-weighted average tar yield delivered by U.S. cigarettes declined from 37 mg to about 15 mg (17, 18). There are very few smokers in the United States today who consume cigarettes approaching even the median yield of CPS-1. In the successor to the study described here, CPS-2, which was begun in 1982 (12), the mean tar yield for current smokers among men was 13.8 mg and among women was 11.8 mg; 71.6% of men and 81.8% of women were currently smoking cigarettes with less than 16.2 mg tar.

The effect which this overall decline in machine-measured tar yields will have on lung cancer rates is of great interest, but is quite difficult to evaluate. In the United States, where lung cancer incidence rates for both men and women had been rising for several decades, the rate of increase for men has diminished in recent years, and the actual incidence rates have in fact declined among men ages 35–44 and 45–54 years since about 1980 (19). Some proportion of the decrease is undoubtedly due to cessation of smoking by selected segments of the population (20), but this is unlikely to have had much influence on rates in the younger groups. Overall rates among men have already begun to fall in the United Kingdom (21), and Peto has argued that an approximate halving of lung cancer death rates among British men in "early middle age" (ages 30–54 years) between 1963 and 1983 may be closely linked to a similar decrease in tar deliveries there (22).

Another problem affecting prediction of long-term effects of lower-tar cigarettes on lung cancer rates is the phenomenon of "compensation," or behavioral adjustment by smokers of lower-yield cigarettes in favor of greater puff frequency, deeper inhalation, and consumption of greater numbers of cigarettes (18). To the extent that smokers of lower-tar cigarettes increase their physiologic dosage of carcinogenic components, apparent differences in risk between low- and high-tar cigarette smokers will tend to diminish. Fortunately, compensation-related errors are much less likely to affect smoking studies in populations such as CPS-1, where the range of tar yields is extremely wide, than those in modern-day populations whose exposures cover a much narrower range. Furthermore, many of today's long-term smokers still have had significant exposures during their lifetimes to the high-tar cigarettes described here. Analysis of lung cancer mortality in CPS-2 is expected to document whether rates will decrease in such smokers (12), but studies of lung cancer rates in life-time smokers of cigarettes having yields below 10 mg cannot yet be made, since these cigarette brands have only been smoked by large numbers of people for less than 10 years.

Regrettably, the tobacco industry has seen fit to market high-tar brands in less developed countries (1). Consequently, the dose–response curves demonstrated in this study may still be relevant in other parts of the world and may be of special interest to agencies engaged in programs of cancer control in those countries.

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