A Prospective Study of the Attributable Risk of Cancer Due to Cigarette Smoking

ABSTRACT

Background. The goals of this study were to measure the impact of cigarette smoking on cancer incidence and to determine the attributable risk of cancer due to smoking.

Methods. A cigarette smoking history was obtained from 8006 Japanese-American men examined from 1965 through 1968. After 22 years, 1389 incident cases of cancer were identified. There were 212 men with lung cancer; 202 with oral, esophageal, laryngeal, pancreatic, renal, ureteral, or bladder (oral–bladder) cancer; and 975 with cancer at other sites.

Results. Current smokers at time of examination had a higher incidence than nonsmokers for each of the three cancer site categories. Eighty-five percent of lung cancer cases diagnosed among current and never smokers can be attributed to cigarette smoking. The attributable risks were 46%, 16%, and 29%, respectively, for oral–bladder cancers, other cancers, and all cancers combined. In turn, the corresponding attributable risks were 60%, 26%, 13%, and 21% in comparing current smokers with past smokers.

Conclusions. Current smokers can greatly reduce their risk of cancer, especially lung cancer, if they quit smoking. (*Am J Public Health.* 1992;82:37–40)

Po-Huang Chyou, PhD, Abraham M. Y. Nomura, MD, and Grant N. Stemmermann, MD

Introduction

Cancer is the second leading cause of death in the United States. It was estimated, for 1991, that more than 1 million new cancer cases and 514 000 cancer deaths would occur in the country.[1] The surgeon general of the US Public Health Service has reported that cigarette smoking is a major cause of cancer mortality in the US population.[2]

Eight large prospective studies in five countries have provided much of the information on the association between tobacco and cancer.[3–10] These mortality studies have consistently reported that cigarette smoking increases the risk of cancer deaths, especially lung cancer. They also have found that cigarette smoking leads to oral, laryngeal, and esophageal cancer and is associated with cancer of the pancreas, urinary bladder, and kidney.[2]

None of these prospective studies reported results on the incidence of cancer and the attributable risk associated with cigarette smoking. Because some subjects afflicted with cancer do not succumb to their disease, it is also important to study the impact of smoking on cancer incidence. We had the opportunity to determine the association of cancer incidence with cigarette smoking in a large cohort of 8006 men and to compute the attributable risk due to cigarette smoking. The attributable risk provides an estimate of the extent to which the excess cancer risk might be reduced if cigarette smoking were discontinued or not initiated in a study population.

Methods

American men of Japanese ancestry, born in the years 1900 through 1919 and living on the Hawaiian island of Oahu, were identified by the Honolulu Heart Program in 1965.[11] Of the 11 148 identified men, 8006 (71.8%) were interviewed and examined between 1965 and 1968, 180 (1.6%) died before they could be examined, and 2962 (26.6%) did not participate in the program. Of the 8006 men examined, the following were excluded from this analysis: 81 men with prevalent cases of cancer, 164 men with a diagnosis of cancer not confirmed by histology, and 1 subject in whom the smoking status was unknown. A total of 7760 men remained.

During the interview, information on cigarette smoking was obtained. Current smokers recorded the usual number of cigarettes smoked per day and the number of years they had smoked. Past smokers recorded the age they started smoking, the maximum number of cigarettes smoked per day, the number of years smoked, and the age they stopped smoking.

Since examination, newly diagnosed cases of cancer have been identified through continuous surveillance of all general hospitals on Oahu. From time of examination to May 1990, the study identified 1389 incident cancer cases (*International Classification of Diseases,* 8th version, codes 140–209) with tissue confirmation of their diagnosis. There were 212 men with lung cancer (code 162.1); 104 with renal, ureteral, or bladder cancer (codes 189 and 188); 35 with pan-

The authors are with the Japan-Hawaii Cancer Study, Kuakini Medical Center, Honolulu.

Requests for reprints should be sent to Po-Huang Chyou, PhD, Japan-Hawaii Cancer Study, Kuakini Medical Center, 347 North Kuakini Street, Honolulu, HI 96817.

This paper was submitted to the journal January 29, 1991, and accepted with revisions July 10, 1991.

TABLE 1—Percentage of Smokers and Nonsmokers by Age Groups

Age at Exam	Smoking Status at Time of Interview: Never No.	Never %	Past No.	Past %	Current No.	Current %	Total
45–49	476	26.1	475	26.0	876	47.9	1827
50–54	825	30.3	667	24.5	1229	45.2	2721
55–59	497	32.3	423	27.5	617	40.2	1537
60–64	423	33.4	341	26.9	504	39.7	1268
65+	123	30.2	125	30.7	159	39.1	407
Total	2344	30.2	2031	26.2	3385	43.6	7760

creatic cancer (code 157); 25 with esophageal cancer (code 150); 24 with laryngeal cancer (code 161); 14 with oral-cavity cancer (codes 140–146); and 975 with cancer at other sites.

On the basis of a separate 19-year follow-up survey of the study subjects since their examination, we found that only 1.3% of the men could not be located on Oahu. However, these men were kept in the study because some of them could still be hospitalized on Oahu later even if they had left the island, and others could still be on Oahu even though their whereabouts were unknown.

The lung cancer cases were analyzed separately, while other cancers that have been related to cigarette smoking were combined because of their smaller numbers. These included cancer of the oral cavity, larynx, esophagus, pancreas, kidney, ureter, and bladder. They were designated as oral–bladder cancers for ease of presentation.

Site-specific and total cancer incidence rates for never, past, and current smokers were adjusted for age at examination via the direct method of standardization, with the entire cohort serving as the reference population. The reference population is the same as the one used to provide age standardization. The relative risks (RR) and 95% confidence intervals for the above cancers associated with cigarette smoking were derived from Cox's proportional hazards regression models[12] while adjusting for age at exam. Separate likelihood ratio tests were performed to evaluate the linear trend associations between cancer risks for each site and current smoking in pack-years (treated as a continuous variable).

To determine the percentage of cancer risk attributable to smoking among current and never smokers, we calculated the population attributable risk (AR) using Bruzzi's method[13] with adjustment for age. The estimated AR is similar to the incidence–density fraction of Greenland and Robins.[14] Similar analysis was done for current smokers compared with past smokers.

Results

Table 1 shows the percentage of current, past, and never smokers by 5-year age groups. The percentage of current smokers decreased with age.

The age-adjusted incidence rates and relative risks for specific cancers and all cancers by smoking status are presented in Table 2. The rates for past smokers were consistently higher than those of nonsmokers. However, the highest rates were found among current smokers. The increase in relative risk among current smokers was statistically significant ($P < .05$) for each comparison with nonsmokers.

Table 3 gives the age-adjusted relative risk of cancer by site for current smokers according to their pack-years of cigarette smoking. There was a significantly positive trend for each site by increasing amount of cigarette use. The relative risk of lung cancer was 23.3 for those who had smoked more than 45 pack-years.

The age-adjusted attributable risks of cancer for current smokers at time of interview compared with nonsmokers and past smokers are presented in Table 4. With adjustment for age, 85% of the total number of lung cancer cases among current and never smokers can be attributed to cigarette smoking. The attributable risks were 46%, 16%, and 29%, respectively, for oral–bladder cancers, other cancers, and all cancers combined. In turn, 60% of the total number of lung cancers among current and past smokers can be attributed to the persistence in smoking. The attributable risks were, correspondingly, 26% for oral–bladder cancers, 13% for other cancers, and 21% for all cancers.

Discussion

All Cancers

The incidence data in this study showed that current and past smokers at time of interview had a significantly greater risk for all cancers than their nonsmoking counterparts. The observed relative risks were 1.9 for current smokers and 1.2 for past smokers. These results were similar to those of cancer mortality studies that found that the overall cancer mortality risks ranged from 1.7 to 2.6 for current cigarette smokers and from 1.4 to 1.5 for past smokers.[5,15,16]

A principal observation in this study is that 29% of total cancer risk among current and never smokers can be attributed to cigarette smoking. It was also observed that total cancer risk among smokers could be reduced by 21% if current smokers became past smokers, as shown in Table 4. These data are encouraging and suggest that the cessation of cigarette smoking can reduce the risk of cancer. The 1982 surgeon general's report noted that smoking contributed to 43% of all US male cancer deaths.[2] However, the report neither separated the effect among current and past smokers nor adjusted for age. If current and past smokers are combined in our study, 26% of all incident cancer cases can be attributed to cigarette smoking.

Lung Cancer

Lung cancer is the site with the highest relative risk due to cigarette smoking. Current smokers at time of interview had a relative risk of 12, while a threefold increase in risk for lung cancer was also observed for past smokers. In addition, a strong dose–response trend was observed with increasing number of pack-years among current smokers.

Our findings are similar to those of the 16-year follow-up study of US veterans.[5] It reported that the mortality ratios for lung cancer were 11.3 for current smokers and 4.0 for past smokers. Seven other prospective studies[3,4,6–10] and three case–control studies[17–19] showed a consistently positive pattern between cigarette smoking and lung cancer, with a relative risk up to 14.2 in the Canadian Veterans Study.[6]

Our study observed that 85% of lung cancer incidence among current and never smokers could have been avoided if current smokers had never smoked cigarettes. If current smokers had ceased smoking, 60% of the lung cancer risk that occurred within the population of current

TABLE 2—Age-adjusted Incidence Rates per 1000 Men, and Relative Risks (RR) for Specific Cancer Sites, by Smoking Status at Time of Interview

		Smoking Status										
		Never			Past				Current			
Cancer Site	No.	No.	Rate	RR	No.	Rate	RR	95% CI	No.	Rate	RR	95% CI
Lung	212	12	5.9	1.0	31	18.0	3.2	1.6, 6.2	169	62.5	12.0	6.7, 21.6
Oral–Bladder[a]	202	37	17.6	1.0	49	27.8	1.6	1.1, 2.5	116	42.9	2.7	1.8, 3.9
Other	975	270	116.1	1.0	243	124.0	1.1	0.9, 1.3	462	154.1	1.5	1.3, 1.7
All	1389	319	133.8	1.0	323	157.8	1.2	1.0, 1.4	747	225.6	1.9	1.7, 2.2
Noncases	6371	2025			1708				2638			

Note. CI = confidence interval.
[a]Cancer of the oral cavity, larynx, esophagus, pancreas, kidney, ureter, or bladder.

TABLE 3—Age-adjusted Relative Risks (RR) for Specific Cancers and All Cancers, by Current Smoking in Pack-Years at Time of Interview

			Current Smoking (pack-years)									
	Never smoked		<31			31–45			46+			P-value for
Cancer Site	No.	RR	No.	RR	95% CI	No.	RR	95% CI	No.	RR	95% CI	trend
Lung	12	1.0	33	6.3	3.3, 12.3	44	9.0	4.8, 17.1	92	23.3	12.8, 42.6	<.0001
Oral–Bladder[a]	37	1.0	37	2.3	1.4, 3.6	42	2.8	1.8, 4.3	36	3.0	1.9, 4.8	<.0001
Other	270	1.0	138	1.2	1.0, 1.5	182	1.6	1.4, 2.0	136	1.6	1.3, 2.0	<.0001
All	319	1.0	208	1.5	1.3, 1.8	268	2.0	1.7, 2.3	264	2.4	2.1, 2.9	<.0001
Noncases	2025		996			880			738			

Note. Current smokers whose smoking history in pack-years were unknown were excluded. CI = confidence interval.
[a]Cancer of the oral cavity, larynx, esophagus, pancreas, kidney, ureter, or bladder.

and past smokers could have been avoided. For smokers in a case–control study in Louisiana, 90% of the lung cancer risk was attributable to active cigarette smoking.[19] The 1982 surgeon general's report estimated that 91% of lung cancer deaths were attributable to the effects of smoking.[2]

Oral–Bladder Cancers

The risk of oral–bladder cancers among current smokers at time of interview was significantly elevated in this study. An accentuation in risk was observed with increasing number of pack-years of cigarette smoking among current smokers.

Wynder et al. have noted that smoking-related cancers in men include cancer of the mouth, larynx, esophagus, pancreas, and bladder, in addition to the lung.[20] In four earlier studies,[3,15,21,22] the mortality risks for the combination of oral, pharyngeal, laryngeal, and esophageal cancer ranged from 2.2 to 7.0 for smokers compared with nonsmokers. Other studies have reported results separately for cancer of the pancreas,[5,22–26] bladder,[5,22,26–28] and kidney.[5,22,29] The risks for these cancers ranged from 1.4 to 5.4 for current smokers, 1.2 to 1.6 for past smokers, and 1.4 to 2.7 for smokers as a group, compared with nonsmokers.

TABLE 4—Age-adjusted Attributable Risks for Specific Cancers and All Cancers for Current Smokers at Time of Interview Compared with Never Smokers and Past Smokers

Cancer Site	Current Smokers vs Never Smokers (%)	Current Smokers vs Past Smokers (%)
Lung	85	60
Oral–bladder[a]	46	26
Other	16	13
All	29	21

[a]Cancer of the oral cavity, larynx, esophagus, pancreas, kidney, ureter, or bladder.

The 1982 surgeon general's report noted that the percentages of death among US males possibly due to smoking were 75% for mouth, pharyngeal, laryngeal, or esophageal cancer; 56% for bladder cancer; and 40% for pancreatic cancer. Our findings showed that 46% of the incidence due to oral–bladder cancers among current and never smokers could be avoided if current smokers had never smoked. Alternatively, if they give up smoking, their excess risk for these cancers could be reduced by 26%.

Other Cancers

Current smokers had a modest risk (RR = 1.5) for other cancers in the study. A positive trend in risk with increasing pack-years of smoking among current smokers was also noted, but the dose–response trend was not linear. If there is a true increase in risk of other cancers due to cigarette smoking, it is not as substan-

tial as that for lung and oral–bladder cancers. The data suggest that up to 16% of the incidence of other cancers among current and never smokers could be avoided if current smokers had never smoked.

Limitations of the Study

The assumption was made in this study that a person's smoking status at time of interview would remain the same throughout the follow-up period. Other studies,[3,5] however, have indicated that some men who reported themselves as current cigarette smokers at the beginning of the study had stopped smoking during the course of the study. Consequently, the group of current smokers included an appreciable proportion of ex-cigarette smokers. If such misclassifications/biases existed in our study, the reported risks of cancer for current smokers would probably be underestimated, suggesting that the actual benefits of smoking cessation could be greater than those shown. It is very unlikely that nonsmoking subjects, who were 45 through 68 years of age at time of interview, started smoking during the course of the study.

Conclusion

The present study provides cancer incidence data consistent with past cancer mortality data of the harmful effects of cigarette smoking. Evidence is especially overwhelming on the association between current cigarette smoking and the risk of lung cancer. An effective way of reducing the risk of cancer associated with cigarette smoking is to quit smoking, as shown by the data on attributable risk. Development of smoking-cessation programs that would enable current smokers to permanently quit their cigarette habit within the shortest time period should be strongly supported. □

Acknowledgments

This research was supported by Grant R01 CA 33644 from the National Cancer Institute, National Institutes of Health.

References

1. Boring CC, Squires TS, Tong T. Cancer statistics, 1991. CA. 1991;41:19–36.
2. US Department of Health and Human Services. *The Health Consequences of Smoking. Cancer: A Report of the Surgeon General.* Rockville, Md: US Department of Health and Human Services; 1982.
3. Doll R, Peto R. Mortality in relation to smoking: 20 years' observations on male British doctors. *Br Med J.* 1976;2:1525–1536.
4. Hammond EC, Horn D. Smoking and death rates—report on forty-four months of follow-up of 187,783 men. II. Death rates by cause. *JAMA.* 1958;166:1294–1308.
5. Rogot E, Murray JL. Smoking and causes of death among U.S. veterans: 16 years of observation. *Public Health Rep.* 1980;95:213–222.
6. Best EWR, Josie GH, Walker CB. A Canadian study of mortality in relation to smoking habits: a preliminary report. *Canadian J Public Health.* 1961;52:99–106.
7. Weir JM, Dunn JE Jr. Smoking and mortality: a prospective study. *Cancer.* 1970;25:105–112.
8. Hammond EC. Smoking in relation to the death rates of one million men and women. In: Haenszel W, ed. *Epidemiological Approaches to the Study of Cancer and Other Chronic Diseases.* Natl Cancer Inst Monogr No. 19. Rockville, Md: US Department of Health, Education, and Welfare; 1966:127–204.
9. Hirayama T. Smoking in relation to the death rates of 265,118 men and women in Japan. A report on 5 years of follow-up. Presented at the American Cancer Society's 14th Science Writers' Seminar; March 24–29; Clearwater Beach, Fla.
10. Cederlof R, Friberg L, Hrubec Z, Lorich U. *The Relationship of Smoking and Some Social Covariables to Mortality and Cancer Morbidity. A Ten Year Follow-up in a Probability Sample of 55,000 Swedish Subjects Age 18 to 69. Part I and II.* Stockholm, Sweden: Karolinska Institute; Department of Environmental Hygiene; 1975.
11. Worth R, Kagan A. Ascertainment of men of Japanese ancestry in Hawaii through World War II Selective Service registration. *J Chronic Dis.* 1970;23:389–397.
12. Cox DR. Regression models and life tables (with discussion). *J Royal Stat Soc, Series B.* 1972;34:187–220.
13. Bruzzi P, Green SB, Byar DP, Brinton LA, Schairer C. Estimating the population attributable risk for multiple risk factors using case-control data. *Am J Epidemiol.* 1985;122:904–914.
14. Greenland S, Robins JM. Conceptual problems in the definition and interpretation of attributable fractions. *Am J Epidemiol.* 1988;128:1185–1197.
15. Dorn HF. Tobacco consumption and mortality from cancer and other diseases. *Public Health Rep.* 1959;74:581–593.
16. Friedman GD, Dales LG, Ury HK. Mortality in middle-aged smokers and nonsmokers. *N Engl J Med.* 1979;300:213–217.
17. Damber LA, Larsson L-G. Smoking and lung cancer with special regard to type of smoking and type of cancer. A case-control study in north Sweden. *Br J Cancer.* 1986;53:673–681.
18. Stayner LT, Wegman DH. Smoking, occupation, and histopathology of lung cancer: a case-control study with the use of the Third National Cancer Survey. *JNCI.* 1983;70:421–426.
19. Fontham ETH, Correa P, Chen VW, Craig JF, Pickle LW, Falk R. Tobacco and cancer. *J Louisiana State Med Soc.* 1988;140(4):29–30, 35–40.
20. Wynder EL, Hoffman D. Tobacco. In: Schottenfeld D, Fraumeni JF, eds. *Cancer Epidemiology and Prevention.* Philadelphia: WB Saunders Company; 1982:277–292.
21. Hammond EC, Seidman H. Smoking and cancer in the United States. *Prev Med.* 1980;9:169–173.
22. Doll R, Peto R. The causes of cancer. Oxford Medical Publications. *JNCI.* 1981;66:1191–1308.
23. Hirayama T. Epidemiology of pancreatic cancer in Japan. *Int J Pancreatology.* 1988;3:S203–S204.
24. Mills PK, Beeson WL, Abbey DE, Fraser GE, Phillips RL. Dietary habits and past medical history as related to fatal pancreas cancer risk among Adventists. *Cancer.* 1988;61:2578–2585.
25. MacMahon B, Yen S, Trichopoulos D, Warren K, Nardi G. Coffee and cancer of the pancreas. *N Engl J Med.* 1981;304:630–633.
26. Whittemore AS, Paffenbarger RS Jr, Anderson K, Lee JE. Early precursors of site-specific cancers in college men and women. *JNCI.* 1985;74:43–51.
27. Cole P, Monson RR, Haning H, Friedell GH. Smoking and cancer of the lower urinary tract. *N Engl J Med.* 1971;284:129–134.
28. Brownson RC, Chang JC, Davis JR. Occupation, smoking, and alcohol in the epidemiology of bladder cancer. *Am J Public Health.* 1987;77:1298–1300.
29. Wynder EL, Mabuchi K, Whitmore WF Jr. Epidemiology of adenocarcinoma of the kidney. *JNCI.* 1974;53:1619–1634.