
**Time Since Stopping Smoking
and the Risk of Oral and
Pharyngeal Cancers**

In the largest study to date of oral and pharyngeal cancers that contained 1114 case subjects and 1268 control subjects from four areas of the United States,

Table 1. Distribution of data from 638 oral cancer case subjects, 642 pharyngeal cancer case subjects, and 4179 control subjects, according to smoking status* and time since smoking cessation, and corresponding odds ratios (ORs)† and 95% confidence intervals (CIs) for data from Italy and Switzerland (1984 through 1997)

	Oral	Pharyngeal	Control subjects	OR (95% CI)		
	No. (%)	No. (%)	No. (%)	Oral	Pharyngeal	Total
Never smokers	70 (11.0)	32 (5.0)	1556 (37.2)	1‡	1‡	1‡
Current smokers	441 (69.1)	459 (71.5)	1456 (34.8)	6.18 (4.62–8.26)	13.45 (9.13–19.81)	8.36 (6.57–10.64)
Ex-smokers, time since smoking cessation, y						
1–2	28 (4.4)	31 (4.8)	127 (3.0)	4.64 (2.77–7.76)	9.88 (5.59–17.47)	6.22 (4.14–9.34)
3–5	38 (6.0)	28 (4.4)	195 (4.7)	3.93 (2.49–6.21)	6.27 (3.58–10.98)	4.53 (3.11–6.59)
6–9	31 (4.8)	27 (4.2)	183 (4.5)	2.89 (1.78–4.67)	4.78 (2.72–8.40)	3.45 (2.34–5.08)
10–14	12 (1.9)	26 (4.0)	238 (5.7)	0.82 (0.42–1.60)	3.23 (1.83–5.71)	1.62 (1.05–2.50)
≥15	18 (2.8)	39 (6.1)	424 (10.1)	0.71 (0.41–1.24)	2.87 (1.73–4.75)	1.42 (0.98–2.05)

*Smoking status: never smoker = subject who had never smoked at least one cigarette per day for at least 1 year; current smoker = smoker of greater than or equal to 1 cigarette per day; and ex-smoker = subject who had not smoked for more than 1 year.

†Derived from unconditional multiple logistic regression models, including terms for age, sex, study center, education, and alcohol drinking.

‡Reference category.

cessation of smoking was associated with a sharply and markedly reduced risk (1). The odds ratio (OR) for all current smokers combined was 3.4 for males and 4.7 for females. For ex-smokers (i.e., subjects who had not smoked for at least 1 year), the OR was 1.1 for males and 1.8 for females 1–9 years after smoking cessation, 1.1 for males and 0.8 for females 10–19 years after cessation, and 0.7 for males and 0.4 for females 20 years or longer after cessation.

Such a drop in risk in a relatively short time suggested that smoking mainly affects the later stages of oral and pharyngeal carcinogenesis (1) and, if confirmed, would have relevant public health implications. However, the U.S. veterans cohort study (2) showed elevated risks of oral (relative risk = 1.5) and pharyngeal (relative risk = 2.6) cancers in all former smokers combined.

To clarify the issue, we decided to assess the pattern of risk of oral and pharyngeal cancers after a person stops smoking by analyzing the combined results of two case-control studies, the first conducted in Italy (3) and the second conducted in Italy and Switzerland (4). Briefly, from 1984 through 1997, data were collected by trained interviewers on 1280 case subjects, younger than 75 years old, who had incident, histologically confirmed oral and pharyngeal cancers (638 patients with oral cancer and 642 patients with pharyngeal cancer, 1085 males and 195 females) and who were admitted to a network of hospitals in the greater Milan area and Pordenone (northern Italy), Rome and Latina (central Italy), and the Swiss

Canton of Vaud. Control subjects were 4179 patients (3068 males and 1111 females) admitted to the same network of hospitals for acute, nonneoplastic conditions that were unrelated to alcohol or tobacco consumption.

Table 1 gives the distribution for the groups of patients with oral and pharyngeal cancers and the comparison group, according to smoking status and time since cessation. The overall multivariate OR, after allowance for study center, age, sex, education, and alcohol drinking, was 8.4 for current smokers. Among ex-smokers, the ORs were 6.2 for those who had stopped smoking for less than 2 years, 4.5 for those who had stopped for 3–5 years, 3.5 for those who had stopped for 6–9 years, 1.6 for those who had stopped for 10–14 years, and 1.4 for those who had stopped for 15 or more years. For oral cancer, the OR was 2.9 for those who had stopped smoking for 6–9 years, but was no longer above unity after 10 or more years. For pharyngeal cancer, which in Italy and Switzerland represents a higher proportion of cases than in North America (1,2), the OR was 3.2 for those who had stopped smoking for 10–14 years and 2.9 for those who had stopped for 15 years or longer.

For ex-smokers, the relative risk of lung cancer declines with time since stopping smoking, to reach asymptotically the relative risk of never smokers (i.e., subjects who had never smoked at least one cigarette per day for at least 1 year) 10 or more years after stopping (5–7). The pattern of risk for oral and pharyngeal cancers observed in this

study suggests the existence of similarities in the process of carcinogenesis for these major tobacco-related neoplasms. The decrease in risk, however, may be steeper for oral cancer.

CARLO LA VECCHIA
SILVIA FRANCESCHI
CRISTINA BOSETTI
FABIO LEVI
RENATO TALAMINI
EVA NEGRI

REFERENCES

- (1) Blot WJ, McLaughlin JK, Winn DM, Austin DF, Greenberg RS, Preston-Martin S, et al. Smoking and drinking in relation to oral and pharyngeal cancer. *Cancer Res* 1988;48:3282–7.
- (2) McLaughlin JK, Hrubec Z, Blot WJ, Fraumeni JF Jr. Smoking and cancer mortality among U.S. veterans: a 26-year follow-up. *Int J Cancer* 1995;60:190–3.
- (3) Franceschi S, Talamini R, Barra S, Baron AE, Negri E, Bidoli E, et al. Smoking and drinking in relation to cancers of the oral cavity, pharynx, larynx, and esophagus in northern Italy. *Cancer Res* 1990;50:6502–7.
- (4) Talamini R, La Vecchia C, Levi F, Conti E, Favero A, Franceschi S. Cancer of the oral cavity and pharynx in nonsmokers who drink alcohol and in nondrinkers who smoke tobacco. *J Natl Cancer Inst* 1998;90:1901–3.
- (5) Doll R. The age distribution of cancer: implications for models of carcinogenesis. *J R Stat Soc A* 1971;134:133–55.
- (6) Public Health Service, U.S. Department of Health and Human Services (DHHS). The health benefits of smoking cessation. A report of the Surgeon General, U.S. Centers for Disease Control, Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health 1990 Report No. DHHS Publ No. (CDC)90–8416.
- (7) Halpern MT, Gillespie BW, Warner KE. Patterns of absolute risk of lung cancer mortality

in former smokers. J Natl Cancer Inst 1993; 85:457-64.

NOTES

Affiliations of authors: C. La Vecchia, Istituto di Ricerche Farmacologiche "Mario Negri," and Istituto di Statistica Medica e Biometria, Università degli Studi, Milan, Italy; S. Franceschi, R. Talamini, Servizio di Epidemiologia, Centro di Riferimento Oncologico, Aviano (PN), Italy; C. Bosetti, E. Negri, Istituto di Ricerche Farmacologiche "Mario Negri," Milan, Italy; F. Levi, Registre Vaudois des Tumeurs, Institut universitaire de médecine sociale et préventive, Lausanne, Switzerland.

Correspondence to: Carlo La Vecchia, M.D., Istituto di Ricerche Farmacologiche "Mario Negri," Via Eritrea 62, 20157 Milan, Italy.
