The large, hospital-based, case-control study by Zang and Wynder (1) provides evidence for greater susceptibility to tobacco carcinogens among women. In contrast, as the authors noted, the early cohort studies of lung cancer (2,3) were not consistent with the hypothesis of greater susceptibility to tobacco carcinogens among women. We are writing to provide further evidence from a small cohort study supporting the hypothesis that cigarette smoking is a stronger predictor of lung cancer among women than among men. Our findings are based on a 23-year follow-up of the Alameda County Study, a prospective, population-based study conducted in Alameda County, California, 1965-1988 (4). Our findings were originally presented in 1987 to the Society for Epidemiologic Research (5).

In our earlier work (5), cited in subsequent publications (6,7), we reported that pack-years was a stronger predictor of lung cancer mortality in women than in men in the Alameda County Study. The study population consisted of whites, blacks, and Asians, who were 30 years or older in 1965 and were current or never smokers. These 1815 men and 2478 women were followed for mortality during the period from 1965 through 1988. During that period, 64 deaths from lung cancer were identified in the cohort through in-state and out-of-state tracing and linkage to vital statistics records. The sex ratio for lung cancer mortality depended on age at entry, reflecting the rapidly rising rates of lung cancer mortality among women during the 1980s. The sex ratio showed a statistically significant inverted U-shape with age. There was no sex difference in lung cancer mortality for birth cohorts under 50 years of age at entry in 1965, but there was a large male excess for birth cohorts aged 60-69 years. Multiple logistic regression was used to model this age-by-sex interaction and to estimate the association between pack-years and lung cancer mortality. We found a significant pack-years-by-sex interaction (P < 0.01) despite the small number of cases available. The odds ratio for 40 pack-years (versus non-smokers) among women was 6.9 (95% confidence interval = 3.3-14.4). It was 2.1 (95% confidence interval = 1.2-3.5) among men. This finding persisted when the Cox proportional hazards model was used for analysis and occurred despite evidence that inhalation and packs per day were lower among women.

The discrepancy between these findings and those in earlier cohort studies may be due to the inclusion of women with higher smoking exposures in our cohort. We agree with Zang and Wynder (1) that lower exposures among female smokers probably masked larger relative risks for women in the early cohort studies of lung cancer. Larger smoking associations among women were reported for case-control studies with cases collected in the 1980s and beyond [e.g., Zang and Wynder (1), Brownson et al. (7), Risch et al. (6)]. This later period reflects rising lung cancer incidence and mortality in birth cohorts with higher female smoking exposures. The history of this evidence reminds us that epidemiologic associations depend on the timing of observation. Uncovering a larger relative risk for women has important public policy implications and may advance our understanding of the cause of lung cancer.

BARBARA A. COHN
DEBORAH L. WINGARD
PIER A M. CIRILLO
RICHARD D. COHEN
PEGGY REYNOLDS
GEORGE A. KAPLAN

References


Notes

Affiliations of authors: B. A. Cohn, P. M. Cirillo (Center for Research on Women's and Children's Health), R. D. Cohen (Human Population Laboratory), California Public Health Foundation, Berkeley; D. L. Wingard, Department of Family and Preventive Medicine, University of California, San Diego; P. Reynolds (Environmental Epidemiology and Geographic Information Section), G. A. Kaplan (Human Population Laboratory), California Department of Health Services, Berkeley

Correspondence to: Barbara A. Cohn, Ph.D., Center for Research on Women's and Children's Health, California Public Health Foundation, 1683 Shattuck Ave., Suite B, Berkeley, CA 94709-1611.

Study protocol including informed consent procedures were approved by the State of California Health and Welfare Agency Committee for the Protection of Human Subjects. Supported by Public Health Service grants RO1AGO5687 and R29AG08387 from the National Institute on Aging, National Institutes of Health, Department of Health and Human Services.

Response

The results of the cohort study by Cohn et al. (1) provide further evidence that both amount and duration of exposure are crucial variables in estimating cancer risk (2). In accordance with our findings (2,3) and results of several other investigations (4-6), Cohn et al., using pack-years of smoking as the exposure measure, observed a higher relative risk for lung cancer in females. In other studies (7-9), however, this sex difference may have been masked as a result of a failure to adjust for differences in either duration of smoking or tar yield.