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Attributable risk of lung cancer in lifetime nonsmokers and long-term ex-smokers (Missouri, United States)

Michael C. R Alavanja, Ross C. Brownson, Jacques Benichou, Christine Swanson, and John D. Boice, Jr.

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A population-based case-control study of incident lung cancer among women in Missouri (United States) who were lifetime nonsmokers and long-term ex-smokers was conducted between 1986 and 1992. The study included 618 lung cancer cases and 1,402 population-based, age matched controls. Information on lung-cancer risk factors was obtained by interviewing cases, next-of-kin of cases (36 percent and 64 percent of the cases, respectively) and controls. Year-long radon measurements also were sought in every dwelling occupied for the previous five to 30 years. Population attributable risks (PAR) for specific risk factors were computed for all subjects, for lifetime nonsmokers, for long-term ex-smokers, by histologic cell type *(i.e.*, adenocarcinoma *cf* nonadenocarcinoma) and for direct interviews with case (for living cases) and for next-of-kin interviews (for dead cases or cases too ill to complete an interview). The mean age at lung cancer diagnosis was 71 years, and nearly 50 percent of the lung cancers were histologically confirmed adenocarcinomas. Almost 40 percent of all lung cancers among lifetime nonsmokers and almost 50 percent of lung cancers among all subjects could be explained by the risk factors under study. Dietary intake of saturated fat and nonmalignant lung disease were the two leading identified risk factors for lung cancer among the lifetime nonsmokers, followed by environmental tobacco smoke, and occupational exposures to known carcinogens. A small nonsignificant risk was found for study subjects exposed to median domestic radon concentration of 4 pCi/l (25-year time-weight average). Since only a small fraction of the population is exposed at this level, it is estimated that the PAR for domestic radon was less than two percent in Missouri. The risk for saturated fat intake was similar for lifetime nonsmokers, ex-smokers, adenocarcinoma cases, and nonadenocarcinoma cases; however, the increased risk was much more pronounced for next-of-kin interviews (PAR = 31 percent) than for interviews with the study subjects (PAR = nine percent). A similar pattern of PAR was identified among ex-smokers but, in this group, the lingering effect of a history of smoking was also very important. Along with saturated fat intake (PAR = 20 percent), the combined effect of previous active and passive smoking even after 15 years of cessation of active smoking was responsible for more lung cancer than any other risk factor under study (PAR = 59 percent). *Cancer Causes and Control* 1995, **6,** 209-216

Key words: Females, lung cancer, radon, saturated fat, tobacco smoking, United States.

Drs Alavanja, Benichou, Swanson, and Boice are with the Epidemiology and Biostatistics Program, National Cancer Institute, Bethesda, MD, USA. Dr Brownson is with the Department of Community Health, Saint Louis University School of Public Health, St Louis, MO, USA. Address correspondence to Dr Alavanja, Epidemiology and Biostatistics Program, National Cancer Institute, EPN/543, 6130 Executive Blvd, Bethesda, MD 20892, USA.

Introduction

Cigarette smoking is the major cause of lung cancer, accounting for more than 80 percent of the 145,000 lung cancer deaths that occur each year in the United States. Lung cancer in nonsmokers, however, is also important and may account for more deaths than any other cancer except colon and breast in women and colon and prostate in men.[1] Between 1 June 1986 and 1 April 1991, 19 percent of all lung cancer in Missouri (US) women occurred among lifetime nonsmokers and long-term ex-smokers.[2] Despite its large public health impact, the etiology of lung cancer among nonsmokers is poorly defined.

We previously determined the risk of various factors for lung cancer in a large, population-based, case-control study of lifetime nonsmokers and ex-smokers who had ceased smoking for at least 15 years.[2-7] Here we present population attributable risk (PAR) estimates to characterize, to the extent possible, the proportion of lung cancer that might be caused by each of the identified risk factors.

Materials and methods

Study subjects

The study design and methods have been described previously.[2-7] Briefly, White nonsmoking women aged 30-84 years, who were residents of Missouri between 1 June 1986 and 1 June 1991, were eligible for inclusion. Lifetime nonsmokers consisted of those women who had not smoked more than 100 cigarettes or used any other tobacco products for more than six months in their lifetime. Ex-smokers were defined as women who ceased using all tobacco products 15 or more years prior to interview. Of the 3,475 women with lung cancer reported to the Missouri Cancer Registry, 650 were eligible for this study, of whom 618 (95 percent) agreed to participate. In addition to the registry-reported diagnoses of lung cancer, tissue slides were reviewed for

Table 1. Relative risk and population attributable risk for nonsmoking Missouri women (618 cases, 1,402 controls)

Risk factor	Odds ratio (CI)	Proportion of controls with risk factor	All subjects	Population attributable risk (95% confidence interval [CI])					
				Smoking status		Histologic type		Interview status	
				Lifetime nonsmokers/ all controls	Former smokers/ all controls	Adenocarcinoma/ all controls	Non-adenocarcinoma/ all controls	Direct with study subject/ all controls	Next-of-kin/ all controls
Saturated fat	1.7[a] (1.2-2.4)	48.5	22.2[a] (10.5-34.1)[e]	23.8[a] (10.0-37.7)	20.3[a] (−1.5-42.1)[b]	19.4[a] (2.9-35.9)	21.4[a] (4.0-38.8)	9.0[a] (−10.6-28.6)	30.6[a] (17.4-43.8)
History of active smoking (ex-smokers *cf* lifetime nonsmokers)	2.3[b] (1.7-2.9)	17.5	17.4[b] (11.6-23.3)	NA	55.6[b] (43.7-67.5)	13.3[b] (5.5-21.2)	22.5[b] (12.8-32.2)	18.3[b] (9.4-27.1)	17.1[b] (9.8-24.4)
Nonmalignant lung disease (ever *cf* never)	1.3[c] (1.0-1.7)	35.2	9.9[c] (1.3-18.5)	10.7[c] (1.1-20.4)	5.0[c] (−14.9-25.0)	11.2[c] (−0.2-22.7)	11.3[c] (−2.7,25.2)	16.0[c] (3.4-28.6)	4.2[c] (−6.6-15.0)
ETS[g] from spouse (≥40 pack years *cf* < 40)	1.3[d] (1.0-1.8)	19.3	6.1[d] (−0.2-12.5)	7.6[d] (0.3-14.8)	1.7[d] (−11.9-15.2)	1.5[d] (−6.6-9.7)	7.2[d] (−2.7-17.2)	2.3[d] (−6.4-11.0)	8.7[d] (0.7-16.7)
Occupation (ever *cf* never)	2.0[d] (1.3-3.2)	4.9	5.1[d] (1.7-8.4)	5.5[d] (1.6-9.5)	4.1[d] (2.4-10.6)	5.1[d] (0.6-9.7)	4.1[d] (−1.1-9.4)	5.9[d] (0.8-10.9)	4.5[d] (0.4-8.6)
Family history (ever *cf* never)	1.4[d] (1.0-2.1)	10.2	4.2[d] (0.1-8.2)	0.4[d] (−4.4-5.3)	14.0[d] (6.6-21.4)	3.4[d] (−1.9-8.6)	9.0[d] (2.0-16.0)	3.7[d] (−2.1-9.5)	5.2[d] (0.1-10.3)
Domestic radon (25 years' exposure 4pCi/l)	1.2[d] (0.8-2.0)	6.4	1.4[d] (−2.0-4.8)	1.9[d] (−2.0-5.8)	−0.9[d] (−8.3-6.6)	4.3[d] (−0.7-9.2)	0.9[d] (−4.4-6.1)	3.9[d] (−1.5-9.3)	−0.4[d] (−4.3-3.5)
Smoking exposure (active or passive, 2 variables) (ever *cf* never)	1.8[b] (1.4-2.3)	33.1	22.2[b] (14.0-30.5)	NA	59.0[b] (47.5-70.4)	13.9[b] (2.5-25.3)	26.3[b] (13.3-39.4)	16.7[b] (4.6-28.9)	26.0[b] (15.6-36.3)
Nonsmoking exposure (one or more of 5 variables) (ever *cf* never)	1.6[e] (1.1-2.2)	73.6	28.9[e] (11.8-45.9)	31.2[e] (11.7-50.7)	23.1[e] (−14.1-60.3)	28.3[e] (5.0-51.5)	35.9[e] (10.9-60.9)	35.3[e] (12.1-58.5)	23.8[e] (1.6-46.0)
All exposure (one or more of 7 variables)	2.2[f] (1.5-3.2)	80.5	48.1[f] (31.0-65.1)	36.1[f] (15.4-56.7)	70.4[f] (59.1-81.7)	50.2[f] (26.9-73.5)	53.7[f] (28.7-78.8)	56.4[f] (33.7-79.0)	41.1[f] (17.7-64.5)

[a] Adjusted for age at self-administered questionnaire (SAQ), history of active smoking, daily caloric intake, and previous lung disease.
[b] Adjusted for age at interview, daily caloric intake, previous lung disease, and daily saturated-fat intake.
[c] Adjusted for age at interview, history of active smoking, daily caloric intake, and daily saturated-fat intake.
[d] Adjusted for age at interview, history of active smoking, daily caloric intake, previous lung disease, and daily saturated fat intake.
[e] Adjusted for age at interview, history of active smoking, and daily caloric intake.
[f] Adjusted for age at interview and daily caloric interview.
[g] ETS = environmental tobacco smoke.
NA = not applicable.

and the prevalence of exposure affect PARs, they are both tabulated (Table 1).

For smoking history, nonmalignant lung disease, occupation (use of asbestos or pesticides, or working in the dry cleaning industry), and a family history of lung cancer, both the OR and PAR were computed based on the comparison of ever *cf* never exposed. For variables such as ETS, saturated fat intake, and domestic radon, where exposure is ubiquitous, judgments had to be made to define exposure cut-points along the exposure continuum that might be achieved as preventive measures in Missouri. For ETS, the exposed group comprised women with 40 or more pack-years of smoking from a spouse, while the unexposed group comprised women with less than 40 pack-years of exposure. For saturated fat intake, which showed a significant monotonic dose-response effect,[5] we compared the upper half of the exposure continuum with the lower half, assuming that a dietary modification of this extent might be possible. Finally, for domestic radon exposure, we estimated PAR by defining the exposed group as those subjects with a time-weighted-average (25 years) of domestic radon exposure of 4pCi/l or greater (the current Environmental Protection Agency's action level). Cut-points for each of these exposures, except radon, were associated with a significant excess relative risk (RR) of lung cancer in our earlier study and are modifications that seem achievable if the etiologic link proves real.[5,7] If we used more 'restrictive' baseline levels the PARs would be greater.[12,13]

Since interview status *(i.e.,* next-of-kin *cf* direct interview with study subject) was related to both case-control status and some exposure variables, it could act as a potential confounding factor in the analysis. To address this possibility, the PAR analysis was stratified also by interview status in Table 1.

Results

Most women in our series developed lung cancer after the age of 70 years, were married, and had completed high school (Table 2). There were few differences between the 618 cases and 1,402 controls in any of the demographic characteristics evaluated. However, the proportion of former smokers (women who had quit smoking more than 15 years previously; median period of cessation =26 years for the combined study population), was about twice as high among lung cancer cases (30 percent) as among controls (17 percent).

Pathologic material from 468 cases was available for review. Adenocarcinoma was the most frequent lung cancer cell type (62 percent), followed by squamous cell carcinoma (six percent), bronchoalveolar adenocarcinoma (four percent), small cell carcinoma (three percent), and all other cell types combined (25 percent) (Table 3).

When all study subjects were included in the analysis, women in the upper half of the saturated-fat-consumption

Table 2. Sociodemographic characteristics of nonsmoking women with lung cancer and controls at the time of cancer diagnosis, Missouri, 1986-91

Characteristic	Cases (n = 618)		Controls (n = 1,402)	
	No.	%	No.	%
Age at interview (yrs)				
<55	46	7	103	7
55-64	85	14	233	17
65-74	193	31	457	32
75+	294	48	609	43
Education (yrs)				
<12	240	39	536	38
12	228	37	477	34
>12	121	20	355	25
Unknown	29	5	34	2
Marital status				
Married	292	47	752	54
Widowed	269	44	537	38
Separated	3	<1	6	<1
Divorced	28	5	59	4
Never married	26	4	47	3
Unknown			1	<1
Current Missouri driver's license (<65 years old)				
Yes	118	90	335	>99
No	13	10	1	<1
Health Care Finance Registration (>65 years old)				
Yes	487	100	1,066	100
No	0	0	0	0
Smoking history				
Never	432	70	1,168	83
Former (>15 years nonsmoker)	186	30	234	17
Next-of-kin interviews (n = 402; 64%)				
Spouse, resident with study subject	105	17	0	
Next-of-kin other than spouse, resident with study subject	25	4	0	
Daughter or son, nonresident with study subject	173	28	0	
Sister or brother, nonresident with study subject	43	7	0	
Other relative, nonresident with study subject	56	9	0	

Table 3. Lung cancer cell types in Missouri women, by smoking status: 1986-91

Histologic type	Former smokers No.	Lifetime nonsmokers No.	Total cases	
			No.	% histopathologically confirmed (n = 468)
Adenocarcinoma	73	219	292	62
Squamous cell carcinoma	17	10	27	6
Small cell carcinoma	9	3	12	3
Bronchoalveolar	2	17	19	4
Other cell types[a]	39	79	118	25
No pathologic confirmation[b]	46	104	150	—
Total	186	432	618	100

[a] Including those not otherwise specified and unknown cell types.
[b] Histologic material not available for these cases.

continuum were at a 70 percent excess RR of lung cancer compared with women in the lower half. This translates into a PAR of 22 percent. Similar results were obtained with lifetime nonsmokers, former smokers, adenocarcinoma cases and nonadenocarcinoma, cases (Table 1). When the analyses were stratified by interview type, more varied risk estimates are obtained. The RR of lung cancer increases significantly with increased saturated-fat consumption, both when cases with next-of-kin interviews and cases interviewed directly are considered. However, the increase is much more pronounced for next-of-kin interviews than for direct interviews. The ORs associated with deciles of saturated fat exposure among study subjects with next-of-kin exposures are 1.2, 2.1, 2.6, 2.8, 4.3, 4.5, 6.4, 10.7, 13.3, (linear trend $P < 0.001$); while for study subjects who were interviewed directly, the corresponding ORs, are 1.1, 1.1, 0.8, 1.3, 0.9, 1.3, 2.2, 2.6, 3.2, (linear trend P = 0.034). When the upper half of the fat-consumption continuum is compared with the lower half, these RR estimates translate to a PAR of 31 percent for next-of-kin interviews but only nine percent for interviews with the study subject. Since these estimates vary substantially, both estimates are presented in our discussion and conclusions. Further reducing the saturated fat consumption below the 20th percentile would reduce the risk of lung cancer even more. The PAR for saturated fat for the combined group of living and dead cases would be 48 percent if we could reduce fat consumption to the level of the 20th percentile (Next-of-kin estimate alone, PAR = 61 percent and direct interview with study subject estimate = 23 percent). Fruit and/or vegetable consumption, which has been found to have a beneficial effect of reduced lung cancer incidence in some smoking and nonsmoking populations,[14] did not have a measurable impact on lung cancer risk in this study.

Even after 15 years of smoking cessation, former smokers had over twice the lung cancer risk (OR = 2.3) of lifelong nonsmokers. This lingering risk accounts for approximately 56 percent of all lung cancers among former smokers and 17 percent of the lung cancers among all study subjects combined (Table 1). If all ex-smokers (including those who quit smoking one to 15 years earlier) were included in this study, the percent of risk attributed to a history of smoking would increase substantially. Prior active smoking was associated with 22 percent of the nonadenocarcinoma compared with 13 percent of adenocarcinoma. These results did not vary by interview type for cases.

A history of nonmalignant lung disease such as pneumonia, asthma and tuberculosis was associated with a significant excess RR of lung cancer of 30 percent overall, which translates into a PAR of approximately 10 percent (Table 1). The PAR was higher when the analysis was limited to interviews with the study subject only (16 percent) compared with next-of-kin interviews (four percent). Nonmalignant lung disease occurred in over one-third of the women in our control group. Small but nonsignificant difference in risk was experienced between long term ex-smokers (five percent) and lifetime nonsmokers (11 percent). The PAR for adeno carcinoma (11 percent) and nonadenocarcinoma cell types (11 percent) was the same.

Exposure to ETS (40 or more pack-years) from a smoking spouse was experienced by one-fifth of all women in our study. The 30 percent excess RR among these women was responsible for approximately six percent of all lung cancers in this population (Table 1). This number rose to eight percent in lifetime non-smokers. Other sources of ETS might increase the PAR even further, but the current study was unable to assess the effect of ETS in most public places. A small additional increment of risk might be expected if a more

comprehensive assessment of ETS related risk could be made. Seven percent of all nonadenocarcinoma cases could be attributed to spousal sources of ETS while only about one percent of the adenocarcinoma cases could be attributed to ETS. Interviews with next-of-kin yielded a PAR of approximately nine percent, but only two percent when living cases were interviewed. The combined effect of previous active smoking and ETS was responsible for 22 percent of lung cancer in this population, and the figure rose to 26 percent for nonadenocarcinoma cell types.

Working with asbestos or pesticides, or in drycleaning facilities, was associated with a moderate excess risk of lung cancer (OR = 2.0). However, since exposure to these substances or workplace environments was uncommon in Missouri (approximately five percent of the female population), it was responsible for only about five percent of all lung cancer among women in this population. Both adenocarcinoma and nonadenocarcinoma cases were affected equally by these occupational factors, as were individuals who had direct and next-of-kin interviews and lifetime nonsmokers and long-term ex-smokers.

A family history of lung cancer among first degree relatives resulted in a small increased risk of lung cancer (RR = 1.4). Approximately 10 percent of the controls in our study population had such a history resulting in a PAR of four percent. It should be noted, however, that the risk was not distributed uniformly, rather, most of the risk was associated with former smokers (PAR =14 percent) and no significant excess risk was observed among lifetime nonsmokers (PAR = 0.4 percent). A family history of lung cancer was associated with a PAR of nine percent in nonadenocarcinoma cases and three percent in adenocarcinoma cases. The PAR did not vary by interview type.

Only six percent of the women in Missouri had a history of radon exposure at or exceeding 4pCi/l that spanned a 25-year period. The mean radon level found in homes was 1.6pCi/l. This pattern of radon exposure is somewhat higher than that observed in the US as a whole.[15] In Missouri, the mean radon level found in homes was 1.6pCi/l. For those living in dwellings with a 4PCi/l exposure or over, the excess RR was 20 percent, resulting in an (nonsignificantly elevated) attributable risk of 1.4 percent in nonsmoking Missouri women. In our study, directly interviewing cases resulted in slightly elevated, estimated risk of lung cancer associated with domestic radon exposure (RR = 1.6) resulting in a PAR of four percent, while there was no elevated risk when considering cases with next-of-kin interviews. The reason for this discrepancy is unclear. Radon seemed to affect lifetime nonsmokers but not ex-smokers. Four percent of adenocarcinoma cases were associated with radon exposure but no excess risk was found among nonadenocarcinoma cases.

Discussion

Overall, 48 percent of all lung cancers among current nonsmokers could be attributed to a history of smoking, saturated fat intake, nonmalignant lung disease, ETS, occupational exposures (especially to asbestos, pesticides or dry cleaning environment), a family history of lung cancer, and possibly domestic radon. In Missouri, domestic radon exposure in excess of the EPA action level was associated with a small but nonsignificant risk of lung cancer. For lifetime nonsmokers, 31 percent of all lung cancer could be attributed to the five nonsmoking risk factors.

The amount of evidence from other studies supporting the association between these factors and lung cancer varies greatly and, thus, cautious interpretation is warranted. The strongest etiologic links identified involved a history of active smoking,[16] and occupational exposures to carcinogens such as asbestos.[17] Etiologic links also have been demonstrated for ETS,[18,19] while causal relationships are suspected for a family history of lung cancer.[20] Evidence from other studies supporting the etiologic association of saturated fat intake[21,22] and domestic radon exposure *(i.e.*, >= 4pCi/l),[23-26] on the other hand, is not yet adequate and is in need of additional investigation.

Strengths and weaknesses

The major strengths of our investigation include the evaluation of incident cases of lung cancer in a population-based setting, the relatively large number of nonsmoking women available for study and the comprehensive effort to ascertain domestic radon measurements in homes occupied by the study subjects during a 30-year period prior to enrollment in the study. Finally, we conducted a pathology review of cases, which enhances our histologic-specific findings. The potential weaknesses of this study include the use of self-reported data on previous lung disease, family history of lung cancer, ETS, diet, and a history of active smoking. Moreover, we had no information on exposure to ambient air pollution, which has been associated with lung cancer in certain industrial urban centers. Since we could not eliminate these potential weaknesses from the current study, a second interview conducted in a sample of cases and controls was conducted which suggested that the reporting of nonmalignant lung disease and smoking was highly reproducible.[27] Although air pollution may be an independent risk factor for lung cancer,[28] it is not likely to confound seriously the results reported in this paper. Finally, a caution must be added about

extrapolations of these results beyond the state of Missouri. PARs are only relevant to the particular population being studied and to other populations that may share the same mix of exposure and susceptibility factors.

Conclusion

Cessation of cigarette smoking remains the most constructive action to reduce the occurrence of many serious chronic diseases, including lung cancer. In this population, approximately 17 percent of lung cancer could be attributable with some confidence to their prior cigarette smoking. Smoke inhaled involuntarily by a lifelong nonsmoking spouse also could account for about eight percent of lung cancers. Other exposures among nonsmoking women appear less important, such as occupation and domestic radon. Occupational attributable risks are low because women of this generation were unlikely to work in hazardous jobs with toxic exposures. This will likely change in the future as more employment opportunities have opened for women for most occupations. While radon exposures in underground (exposed) miners are clearly carcinogenic and linked to PARs as high as 73 percent among nonsmoking miners,[23] the picture is less clear for domestic radon,[24,28] and it is estimated that the PAR is likely less than two percent. This percentage is much lower than that estimated by extrapolation of risks from underground miners, for whom the attributable risk for radon-related lung cancer among nonsmokers would be about 12 percent based on a multiplicative model and over 30 percent based on a submultiplicative model between radon and smoking.[29]

Consumption of high levels of saturated fat and a history of prior lung diseases, especially pneumonia, were major contributors to PAR in this series. The etiologic link between saturated fat and lung cancer has been examined in only a few other studies so that a cautious interpretation of the high PAR seems warranted. Nonetheless, it seems prudent to assume that dietary factors could contribute to lung cancer risk, as they do other chronic diseases such as coronary heart disease. Thus, a person should strive to reduce saturated fat and, based on other studies,[14] increase consumption of fruit and vegetables in their diets.

References

1. Schneiderman MA, Davis DL, Wagener DK. Lung cancer that is not attributable to smoking (Letter). *JAMA* 1989; **261:** 2635-6.
2. Alavanja MCR, Brownson RC, Boice JD Jr, Hock E. preexisting lung disease and lung cancer among nonsmoking women. *Am J Epidemiol* 1992; **136:** 623-32.
3. Brownson RC, Alavanja MCR, Hock E, Loy TS. Passive smoking and lung cancer in nonsmoking women. *Am J Public Health* 1992; **82:** 1525-30.
4. Brownson RC, Alavanja MCR, Chang JC. Occupational risk factors for lung cancer among nonsmoking women: a case-control study in Missouri (United States). *Cancer Causes Control* 1993; **4:** 449-54.
5. Alavanja MCR, Brown CC, Swanson C, Brownson RC. Saturated fat intake and lung cancer risk among nonsmoking women in Missouri. *JNCI* 1993; **85:** 1906-16.
6. Brownson RC, Alavanja MCR, Berger E, Chang JC. Family history of cancer risk of lung cancer among nonsmoking women in Missouri. *Epidemiology* (Submitted).
7. Alavanja MCR, Brownson RC, Lubin JH, Brown C, Berger E, Boice JD Jr. Residential radon exposure and lung cancer among nonsmoking women. *JNCI* 1994; **86:** 1829-37.
8. Brownson RC, Loy TS, Ingram E, *et al.* Histologic types of lung cancer among nonsmoking women: pathologic review and survival patterns. *Cancer* 1995; **75:** 29-33.
9. Martin G, Alavanja MCR, Zahm SH. Department of Health and Human Services epidemiology research 1989 data users conference proceedings. Baltimore, MD (USA): Health Care Finance Administration, 1989; HCFA Pub. No.03293: 181-6.
10. 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:** 904-14.
11. Benichou J, Gail MH. Variance calculations and confidence intervals for estimates of the attributable risk based on logistic models. *Biometrics* 1990; **46:** 991-1003.
12. Hsieh C-c, Walter SD. The effect of nondifferential exposure misclassification on estimates of the attributable and prevented fraction. *Stat Methods* 1988; **7:** 1073-85.
13. Wacholder S, Benichou J, Heineman EF, Hartge P, Hoover RN. Attributable risk: advantages of a broad definition of exposure. *Am J Epidemiol* 1994 **l40:** 1-7.
14. Steinmetz KA, Potter JD. Vegetables, fruit and cancer. I. Epidemiology. *Cancer Causes Control* 1991; **2:** 325-57.
15. Marcinowski F, Lucas RM, Yeager WM. National and regional distribution of airborne radon concentrations in US homes. *Health Physics Society* 1994; **66:** 699-706.
16. US Department of Health and Human Services. *Reducing the Health Consequence of Smoking: 25 Years of Progress. A Report of the Surgeon General.* Hyattsville, MD (USA): DHHS, 1989; DHHS Pub. No. (CDC) 89-8411.
17. World Health Organization. *Overall Evaluation of Carcinogenicity: An Updating of IARC Monographs. Volume 1 to 42, Supplement 7.* Lyon, France: International Agency for Research on Cancer, 1987.
18. US Environmental Protection Agency *Respiratory Health Effects of Passive Smoking: Lung Cancer and Otber Disorders.* Washington, DC: EPA 1992.
19. Fontham ETH, Correa P, Wu-Williams A, *et al.* Lung cancer in nonsmoking women: a multi-center case-control study. *Cancer Epidemiol Biomarkers Prev* 1991; **1:** 35-43.
20. Ernster VL. The epidemiology of lung cancer in women. *Ann Epidemiol* 1994; **4:** 102-10.
21. Byers TE, Graham S, Haughey BP, Marshall JR, Swanson

MK. Diet and lung cancer risk: findings from the Western Diet Study. *Am J Epidemiol* l967; **125:** 351-63.
22. Jain M, Burch JD, Howe GR, Risch HA, Miller AB. Dietary factors and the risk of lung cancer: results from a case-control study, Toronto, 1981-1958. *Int J Cancer* 1990; **45:** 287-93.
23. National Research Council. *Health Risks of Radon and Other Internally Deposited Alpha-emitters. BEIR IV*. Washington, DC: National Academy Press, 1988.
24. Pershagen G, Akerblom G, Axelson O, *et al.* Residential radon exposure and lung cancer in Sweden. *N Engl J Med* 1994; **330:** 159-64.
25. Blot WJ, Xu ZY, Boice JD Jr, *et al.* Indoor radon and lung cancer in China, *JNCI* 1990, **82:** 1025-30.
26. Lubin JH. Invited commentary: Lung cancer and exposure to residential radon. *Am J Epidemiol* 1994; **140:** 323-32
27. Brownson RC, Alavanja MCR, Hock E. Reliability of passive smoke exposure histories in a case-control study of lung cancer. *Int J Epidemiol* 1993; **22:** 804-48.
28. Dockery DW, Pope A, Xu X-P, *et al.* An association between air pollution and mortality in six U.S. cities. *N Engl J Med* 1993; **329:** 1753-9.
29. Lubin JH, Boice JD Jr., Hornung RW, *et al. Radon and Lung Cancer Risk: A Joint Analysis of 11 Underground Studies.* Rockville, MD: National Institutes of Health, 1994; NIH Pub. No. 94-3644.