CORRESPONDENCE

Re: Multicenter Case–Control Study of Exposure to Environmental Tobacco Smoke and Lung Cancer in Europe

Boffetta et al. (1) claim smoking misclassification only has a minimal effect, of 1.01–1.02, on the lung cancer risk associated with spousal smoking, which they estimate from their multicenter study as 1.16. The bias is probably much larger and could explain most of the excess risk.

In 1996, we (2) estimated the effect that misclassification bias had on spousal risk estimates from five U.S. studies of environmental tobacco smoke (ETS) and lung cancer, by use of a version of the complex Wells–Stewart procedure used by the U.S. Environmental Protection Agency (EPA) (3) that had been modified to avoid some mathematical errors. Assuming, as had EPA, that 1.07% of regular, 17.7% of occasional, and 10.8% of former smokers report they are never smokers and that the observed excess risks for misclassified occasional and former smokers are, respectively, 20% and 9% of those for regular smokers, the bias we estimated for all five studies was similar to that using an alternative procedure, which simply assumed the equivalent of 1.75% of ever smokers with average lung cancer risk denied smoking. We also reviewed evidence on misclassification rates in U.S. and Western European populations (4) and found that these rates were higher than EPA had assumed. We argued that, for bias estimation, an equivalent rate (ER) of 2.5% was better than one of 1.75%, but we noted that large between-study variation in misclassification rates suggested that the ER might plausibly lie in the range 1%–4%. Finally, we noted that correcting for bias using a 2.5% ER explains virtually all the lung cancer risk associated with spousal ETS exposure from 13 U.S. studies, reducing the meta-analysis estimate from 1.13 to 1.01.

Boffetta et al. (1) assume an actual misclassification rate of 2% and that misclassified smokers have a relative risk of 2.0. Because the relative risk for average ever smoking is about 8–10 and the bias is approximately proportional to the excess risk, their assumptions imply an ER about 0.2%–0.3%, much lower than our estimated 2.5%. They suggest that we ignored the much-lower-than-average risk in misclassified smokers, but clearly we have not. They err in using misclassification rates that are far too low. This seems due, in part, to confusing misclassification rates expressed as a proportion of nonsmokers with those expressed as a proportion of smokers, in part to not combining all the sources of misclassified ever smokers and in part to not considering all available evidence on misclassification rates.

We also note that misclassification rates of regular smoking are much higher in Asian than in U.S. or Western European women (5), perhaps explaining why spousal risks are elevated in Asian women despite their lower reported smoking frequency (2.5).

Misclassification may bias estimates for workplace exposure. We have limited, unpublished data showing that concordance between smoking and working with a smoker is similar to that between smoking and spousal smoking. Although more data are needed, this suggests that the biases for workplace and spousal smoking may be similar.

PETER N. LEE
BARBARA A. FOREY

REFERENCES


NOTES

P. N. Lee and B. A. Forey have served as consultants to various tobacco companies and tobacco trade organizations. They received no payment from tobacco companies, their trade associations, or their legal representatives for the preparation and/or submission of this correspondence, and the draft correspondence was not reviewed or approved by such organizations or individuals.


RESPONSE

We disagree with Lee and Forey’s assumption that misclassification of smokers as never smokers is of the same magnitude in various types of studies of smoking misclassification and in all epidemiologic studies of environmental tobacco smoke and lung cancer. Lee and Forey apply to our study values for the prevalence of smoking misclassification derived from surveys that compared urinary cotinine levels with self-reports of nonsmoking status (1). Although the U.S. Environmental Protection Agency used these figures in their adjustment for possible misclassification bias, they also noted that misclassification in case–control studies is likely be smaller than in population surveys. In addition, it has been shown that misclassified smokers are, in general, hardly average smokers but tend to be long-term former smokers and very light smokers (2,3). One would predict a low risk of lung cancer for such subjects: The only available direct estimate of lung cancer risk in misclassified smokers, among men in a Swedish cohort study (2), is consistent with this hypothesis (relative risk = 1.9; 95% confidence interval = 0.4–9.1).

In our study (4), we used a detailed two-stage screening approach (screening questionnaire covering regular smoking and main interview covering regular or any occasional smoking) to identify and exclude not only current smokers but also long-term former smokers and light smokers. The low misclassification rates that were reported in our validation study (5) on a subset of study subjects represent possible misclassification according to reports from next-of-kin after exclusion of these groups of smokers. If misclassification rates for active smoking are truly low, a concordance between smoking and working with a smoker also becomes less relevant. We therefore consider it possible that misclassification of
smokers in our study might have played a small role, without however altering our conclusions.

PAOLO BOFFETTA
FREDRIK NYBERG
RODOLFO SARACCI
(ON BEHALF OF THE IARC STUDY GROUP)

REFERENCES


NOTES

Affiliations of authors: P. Boffetta, International Agency for Research on Cancer (IARC), Lyon, France; F. Nyberg, IARC, Lyon, and Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden; R. Saracci, IARC, Lyon, and National Research Council, Pisa, Italy.

Correspondence to: Paolo Boffetta, M.D., M.P.H., International Agency for Research on Cancer, 150 cours Albert Thomas, 69372 Lyon cedex 08, France (e-mail: boffetta@iarc.fr).