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## Evaluating the evidence for the relationship between passive smoking and lung cancer

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Dear sir,

“No Clear Link Between Passive Smoking and Lung Cancer”—this was the title of a news article published in the December, 2013 issue of the *Journal of the National Cancer Institute (JNCI)*.<sup>1</sup> It was reported in the article that investigators from Stanford and other institutions examined data from the Women’s Health Initiative Observational Study (WHI-OS) and observed no association between passive smoking and lung cancer in an unpublished analysis. The only level of exposure with some indication of increased risk for lung cancer was living with a smoker for at least 30 years, with a hazard ratio of 1.61 and a confidence interval (CI) including the null. However, the analysis clearly lacked statistical power to detect an association even if one existed. Of the approximately 40,000 women who had never smoked, only about 10% reported no exposure to secondhand smoke and only 152 women developed lung cancer during follow-up. Therefore, as Dr. Heather Wakelee pointed out, “It’s hard to say anything conclusive with such small numbers.”<sup>1</sup>

Limited sample size is a common problem among studies on the association between passive smoking and lung cancer, because it is difficult to identify nonsmoking lung cancer patients. Therefore, it is useful to increase statistical power by combining data from multiple sources. A recent study by researchers of the International Lung Cancer Consortium using pooled data on more than 2,500 never-smoking cases showed a clear association between passive smoking and lung cancer, with an adjusted odds ratio (OR) of 1.31 (95% CI: 1.17–1.47).<sup>2</sup> Although some may question the validity of case–control studies due to recall bias, meta-analyses of case–control studies on the risk of lung cancer among nonsmokers exposed to secondhand smoke from their spouses produced results very similar to those of cohort studies, with summary risk ratios of 1.20 (95% CI: 1.11–1.29) and 1.29 (95% CI: 1.125–1.49), respectively.<sup>3</sup> Furthermore, in our unpublished analysis of 458 lung cancer cases and

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1,065 controls of never-smoking Chinese women pooled from two studies,<sup>4,5</sup> the OR for the association between passive smoking at home for at least 30 years and lung cancer was 1.74 (95% CI: 1.32–2.29) after adjusting for age, income, education, and study site. The point estimate from our analysis is comparable to that of the analysis reported in the JNCI article,<sup>1</sup> but with greater statistical power.

Dr. Gerard Silvestri was quoted in the article as saying, “With regard to passive smoke, it’s only the heaviest exposure that produces the risk.” However, in our unpublished study, women exposed at home for 1–29 years and those exposed at a low intensity also experienced an increased risk of lung cancer, with adjusted ORs of 1.45 (95% CI: 1.08–1.95) and 1.39 (95% CI: 1.03–1.88), respectively. The adjusted OR obtained when treating years of passive smoking at home as a continuous variable was 1.012 (95% CI: 1.005–1.018) with a *p*-value of 0.0003. In addition, some gene-environment studies suggest individuals differ in their susceptibility to secondhand-smoke-related lung cancer.<sup>6–8</sup> Therefore, even low-level exposures may increase the risk in individuals with genetic susceptibility. Given the vast volume of literature demonstrating the effects of passive smoking, the public health message regarding this topic should be that there is a clear link between passive smoking and lung cancer and there is no safe level of exposure.

Yours sincerely,

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