Published in final edited form as:

JAMA Intern Med. 2017 June 01; 177(6): 892. doi:10.1001/jamainternmed.2017.1086.

When to Adjust for Potentially Confounding Variables: In Reply

Maki Inoue-Choi, PhD, MS and Neal D. Freedman, PhD, MPH

Division of Cancer Epidemiology & Genetics, National Cancer Institute, Rockville, Maryland

We thank Dr Lehner for his interest in our article.¹ As described previously, in both articles cited by Dr Lehner^{2,3} and elsewhere, cigarette smoking has a complex relationship with body weight, body mass index (BMI), body fat distribution, and their metabolic consequences.⁴ For example, smokers tend to have a lower BMI than nonsmokers. Quitting smoking has also been linked to weight gain in a number of different studies.⁵ Furthermore, having a high BMI may reflect quite different physiologic states among smokers and nonsmokers.⁴

As argued in our article,¹ we judge that regression models without BMI are preferred for the aims of our analysis. At the request of Dr Lehner, we compared models with and without BMI and found that it would not change our conclusions. After additional adjustment for BMI, the results are largely the same, although of slightly stronger magnitude. For example, the hazard ratio (HR) for all-cause mortality among lifelong smokers of less than 1 cigarettes per day (CPD) changed from 1.64 (95% CI, 1.07–2.51) to 1.96 (95% CI, 1.26–3.04) after adjustment for BMI. Similarly, the HR among lifelong smokers of 1 to 10CPD changed from 1.87 (95% CI, 1.64–2.13) to 1.91 (95% CI, 1.66–2.20) after adjustment. The HRs among lifelong moderate to heavy smokers stayed virtually the same after adjusting for BMI. The HR among lifelong smokers of 11 to 20 CPD was 2.91 (95% CI, 2.68–3.16) before adjustment and 2.89 (95% CI, 2.65–3.16) after adjustment, and the HR among lifelong smokers of 21 to 30CPD was 3.73 (95% CI, 3.23–4.31) before adjustment and 3.07 (95% CI, 2.64–3.57) after adjustment.

As such, the conclusions of our article are unchanged by additional adjustment for BMI. Individuals who smoke fewer than 1 or 1 to 10 CPD over their lifetime had higher mortality risks than never-smokers. Furthermore, all smokers should be targeted for smoking cessation, regardless of how few cigarettes they smoke per day.

References

1. Inoue-Choi M, Liao LM, Reyes-Guzman C, Hartge P, Caporaso N, Freedman ND. Association of long-term, low-intensity smoking with all-cause and cause-specific mortality in the National Institutes of Health-AARP Diet and Health Study. JAMA Intern Med. 2017; 177(1):87–95. [PubMed: 27918784]
2. Dare S, Mackay DF, Pell JP. Relationship between smoking and obesity: a cross-sectional study of 499,504 middle-aged adults in the UK general population. PLoS One. 2015; 10(4):e0123579. [PubMed: 25886648]

Conflict of Interest Disclosures: None reported.

3. Plurphanswat N, Rodu B. The association of smoking and demographic characteristics on body mass index and obesity among adults in the U.S., 1999–2012. *BMC Obes.* 2014; 1:18. [PubMed: 26217505]
4. Song M, Giovannucci E. Estimating the influence of obesity on cancer risk: stratification by smoking is critical. *J Clin Oncol.* 2016; 34(27):3237–3239. [PubMed: 27458311]
5. Aubin HJ, Farley A, Lycett D, Lahmek P, Aveyard P. Weight gain in smokers after quitting cigarettes: meta-analysis. *BMJ.* 2012; 345:e4439. [PubMed: 22782848]