THE AUTHORS REPLY

Pouwels and Hak (1) raise several important and thoughtful concerns about our analysis (2), which we will discuss further in this letter. First, the authors raise concerns that our analysis using patients taking antihypertensive medications as the referent group may create biases toward the null. We chose to do this analysis to address 1 specific type of bias: access to medical care. We agree that this analysis does not entirely prevent confounding by indication. We also agree with the authors’ point that if the antihypertensive medications used by our referent group were antiinflammatory, and if reducing inflammation was the mechanism by which statins were preventing lower urinary tract symptoms (LUTS), our results might be biased toward the null. It should be noted that use of antihypertensive medications is included in our multivariable-adjusted models, and the association between use of these medications and LUTS is in the direction of increased risk (for diuretics, hazard ratio = 1.11, 95% confidence interval: 1.02, 1.20; for nondiuretics, hazard ratio = 1.23, 95% confidence interval: 1.15, 1.31), not protection, as would have to be the case to create the bias toward the null suggested by the authors. In addition, we think that it is striking that, despite having conducted analyses using 2 different referent groups (nonusers of statins and users of antihypertensive medications) and having conducted several different sensitivity analyses, the findings never changed with respect to statin use and risk of LUTS. It seems likely that if any of these biases were strongly affecting the results of our analysis, that the association would not have been robust to all of our different analytical strategies.

The authors also raise an interesting point regarding the inclusion of both new and prevalent users in the “statin use” group. This issue has been raised as 1 explanation for the differences when comparing findings from randomized trials and observational studies (3). Because very few men (only 6%) in our study population were using statins at baseline, our exposed group does consist of mostly incident users. Further, our time-dependent duration analysis included a category of less than 5 years, which thus compared newer users with men not taking a statin drug, and this analysis produced similar results to those reported for all other analyses in the paper. A method for avoiding the prevalent-user bias by analyzing observational studies as though they were randomized experiments has been developed by Hernán et al. (4). In response to the authors’ concerns, we applied this method to our data and found that our point estimate was unchanged compared with the analysis presented in the paper (moderate or worse LUTS: incident statin use vs. nonuse, hazard ratio = 1.11, 95% confidence interval: 1.00, 1.23). This is likely due to the aforementioned characteristics of our study population, which minimized the amount of prevalent use in our population. We agree with the authors that this is an important bias that must be considered when examining medication use in observational studies, and we hope that future studies will use these methods.

We thank the authors for their interest in our work and for their thoughtful comments. One of the main points we had hoped to make with our paper was that these types of analyses are methodologically complex, so we appreciate the opportunity to engage in a dialogue on these points in the scientific literature.

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REFERENCES


Alison M. Mondul1, Edward Giovannucci2,3,4, and Elizabeth A. Platz5,6,7

1 Nutritional Epidemiology Branch, Division of Cancer Epidemiology and Genetics, Department of Health and Human Services, National Cancer Institute, National Institutes of Health, Bethesda, MD
2 Department of Epidemiology, Harvard School of Public Health, Boston, MA
3 Department of Nutrition, Harvard School of Public Health, Boston, MA
4 Channing Laboratory, Harvard Medical School and Brigham and Women's Hospital, Boston, MA
5 Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
6 The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Johns Hopkins University School of Medicine, Baltimore, MD
7 The Brady Urological Research Institute, Johns Hopkins University School of Medicine, Baltimore, MD

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