TWO AUTHORS REPLY

We thank Murphy et al. (1) for their interest in our recent pooled analysis of data from 18 prospective cohort studies in the Asia Cohort Consortium (2). Our goal was the identification of associations between body mass index, smoking, and alcohol use and prostate cancer mortality in populations without widespread prostate cancer screening. Murphy et al. emphasized a limitation of our study, one that we ourselves described in our article—the fact that this pooled cohort study utilized baseline data for analysis. Clearly, more and better data are always preferable, but harmonizing tobacco-exposure variables and other variables across many studies required us to focus on baseline exposure in order to maintain a sufficient sample size. Murphy et al. implied that this may be why we did not observe the same consistent and strong direct connection between tobacco and prostate cancer as other investigators have seen between tobacco and lung cancer for decades.

First, Murphy et al. are incorrect in stating that we relied on an ever/never variable for tobacco use (1); we also reported on pack-years of smoking and evaluated trends in the association between pack-years and prostate cancer mortality. As we described in Table 1 (2), tobacco use was highly prevalent in our older and male study populations, and we noted that most studies of tobacco and prostate cancer to date have found little association, whereas the findings of some others are heterogeneous and include opposing associations. Consistent with the overall literature, we found no patterns or significant associations, though we also acknowledge the possibility of susceptible subgroups.

Murphy et al. also expressed concern about residual confounding with the body mass index coding scheme (1). However, we attempted several coding schemes for body mass index, including the World Health Organization criteria, Asia-specific criteria, quartiles of the distribution, a continuous variable, and alternative measurement approaches and time periods; all schemes showed similar results. Similarly, there have been many null studies of alcohol and prostate cancer outcomes. Indeed, any role of alcohol in prostate cancer may be limited to specific susceptible subgroups. We refer readers to our recent publication—cited in our manuscript—for evidence that alcohol may interact with hormone-based therapies that have potential for prostate cancer prevention (3).

Finally, we agree with Murphy et al. that the interpretation of prostate cancer incidence differs from that of prostate cancer mortality. An analysis of incidence provides etiological clues. However, in the United States, such analyses may be confounded by the strong association between utilization of prostate cancer screening and its efficacy. The existing literature has failed to provide a clear modifiable risk-factor profile for prostate cancer, perhaps because studies were not designed to control confounding by selective prostate cancer screening. Mortality analyses may also provide etiological clues, as well as determine the impact of a risk factor on a fatal outcome, in the context of available treatment options. Until recently, men diagnosed with advanced prostate cancer would receive only palliative care; thus, treatment is less of an issue among men diagnosed with advanced prostate cancer, such as is seen in many Asian populations, where screening is not widely utilized and most men are diagnosed clinically.

We must also recognize that the situation within any study population may be uniquely complex. Investigators should plan to obtain a full prostate cancer screening and clinical detection history to ensure that detection bias is removed and to enable identification of modifiable prostate cancer risk and prognosis factors.

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REFERENCES


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