

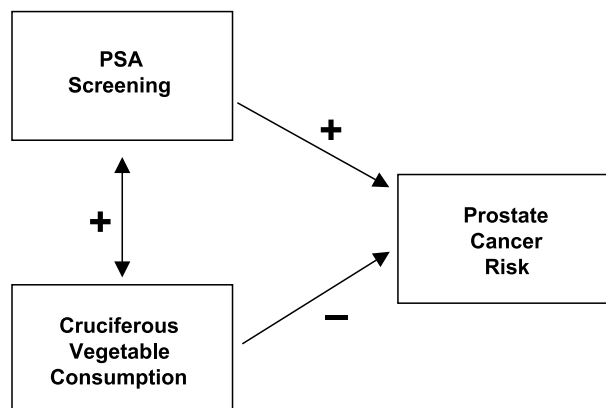
## Letters to the Editor

### Cruciferous Vegetables and Prostate Cancer Risk: Confounding by PSA Screening

**To the Editors:** The recent publication by Giovannucci et al. (1) describing associations of cruciferous vegetable consumption with prostate cancer risk is an important contribution to existing literature on diet and cancer. Although cruciferous vegetables were not associated with risk in the primary analyses that included all men in the Health Professionals Follow-up Study, results of analyses among the subgroup of men who reported receiving at least one prostate-specific antigen (PSA) screening test were strikingly different. In these secondary subgroup analyses, there were statistically significant linear decreases in relative risk associated with increasing consumption of cruciferous vegetables. The authors interpret this result as evidence that cruciferous vegetables affect only early stages of prostate carcinogenesis because most cancers detected by PSA screening are organ confined. There is, however, a somewhat more parsimonious interpretation of these results, which has broad implications for current studies of risk factors for prostate cancer.

PSA screening is a strong risk factor for prostate cancer. In a population-based case-control study completed in western Washington State, the age-adjusted odds ratios (95% confidence interval) for prostate cancer were 4.0 (3.1-5.3), 5.5 (3.7-7.3), and 7.1 (4.8-10.5), comparing no PSA test to 1 to 2, 3 to 4, and 5+ PSA tests in the previous 5 years (2). Thus, studies in populations not uniformly screened with PSA are subject to detection bias. In addition, if frequency of PSA testing is positively associated with an hypothesized behavioral risk factor, PSA screening may act as a special type of confounding variable termed a distorter variable (3), which could mask a true association between behavior and prostate cancer risk (Fig. 1). Indeed, in studies examining healthful dietary behavior and prostate cancer, this is most likely the case. In a population-based survey of Washington State residents, men eating four or more servings of vegetables per day were almost three times more likely to have reported a PSA test in the previous 2 years than men eating fewer than two servings per day (4). Results from the case-control study mentioned above were consistent with this finding, as statistical control for number of PSA tests increased the magnitude of the association between cruciferous vegetable consumption and prostate cancer risk (5). Based on these arguments, we believe that epidemiologic studies of prostate cancer risk need to be controlled for PSA screening, preferably for numbers of recent PSA tests.

In our experience, confounding variables that can mask true associations are rare in epidemiology. However, such confounding may be the norm in studies of environmental and behavioral risks for prostate cancer.



**Figure 1.** PSA screening as a distorter variable.

Our interpretation of the report by Giovannucci et al. (1) is that the analyses including only men receiving PSA screening should be the primary result, which provides evidence from a large and extraordinarily well-conducted cohort study supporting an association of cruciferous vegetables with reduced prostate cancer risk.

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**AACR** American Association  
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